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CLINICAL EXPERIENCE

WILEY

Post-intubation laryngeal disorders in COVID-19 patients: Our experience on 43 patients

1 | INTRODUCTION

Approximately 20% of patients with coronavirus disease 2019 (COVID-19) had severe acute respiratory distress requiring mechanical ventilation.[1] The proportion of survivors after severe or critical COVID-19 ranges from 20% to 62% regarding studies.[1] Survivors may keep neurological and systemic postdischarge complications, for example, breathlessness, psychological distress, cognitive impairments, voice and swallowing disorders at post-intensive care unit (ICU) discharge.[1] The aim of this study was to investigate post-intubation laryngeal complications in severe COVID-19 patients.

2 | METHODS

2.1 | Ethical considerations

The Hospital IRB reviewed and approved the study (ref.AP-HP202201). A waiver of informed consent of study participants was granted because participant data were protected and anonymized.

2.2 | Setting

From September 2020 to April 2021, patients presenting to our laryngology unit with voice or swallowing disorders post-severe-to-critical COVID-19 infection and intubation histories were consecutively included. The study was conducted according to the reporting guidelines for prospective studies (CONSORT Statements). The following epidemiological and clinical data were collected: demographics; age; gender; comorbidities; dates/features of documented COVID-19 infection, hospital stay; intubation and tracheostomy; voice, swallowing, and airway complaints; medical and surgical required treatment and follow-up.

The laryngological examination was performed by two senior blinded laryngologists with a videolaryngostroboscopy (XION GmbH) at posteriori considering the following laryngeal disorders: laryngopharyngeal reflux (LPR), laryngeal diffuse edema, posterior commissure hypertrophy, laryngeal necrosis, granuloma, posterior glottic stenosis, subglottic stenosis, and posterior glottic diastasis.[3] According to the laryngeal disorders, the following medical treatments included antibiotics, corticosteroids, proton pump inhibitors (PPIs), and alginate. Patients with no improvement of lesion with medical treatment benefited from surgical treatments, that is, CO_2 laser posterior transverse cordotomy, placement of Montgomery-type laryngeal calibration tube, laser flange (scare), or vocal fold fat injection.

Statistical analyses were performed with the Statistical Package for the Social Sciences for Windows (SPSS version 24.0; IBM Corp). The following tests were used to compare outcomes between patients with a history of <2-week tracheostomy versus those with a > 2-week tracheostomy: Chi-square and Mann–Whitney U Test. The relationship between patient epidemiological and clinical features was investigated with Spearman analysis and multivariate analysis. A level of significance of $p < 0.05$ was used.

3 | RESULTS

Forty-three patients completed the evaluations. Patients consulted in our laryngology division (Foch Hospital, Paris, France) on average 51.6 ± 30.2 days after their hospitalisation in UCI (range: 2–5 months). The epidemiological and clinical features of patients are described in Table 1. Twenty-two patients were intubated less than 2 weeks (Group 1), while 21 were intubated more than 2 weeks (group 2), respectively. Patient groups were comparable regarding demographic and clinical outcomes. The average intubation duration was 9.9 ± 3.7 days in group 1, while patients in group 2 were intubated during 26.3 ± 6.8 days. In our medical centre, the position of patients in the ICU bed was changed daily (stomach/back). There were 3 and 5 tracheostomies in groups 1 and 2 with a mean duration decannulation of 34.9 ± 22.0 days. One patient was not decannulated at the time of the consultation.

Dysphonia (100%), dyspnea (44.1%) dysphagia (20.9%), and neck pain (9.3%) were the most prevalent symptoms (Table 1). The videolaryngostroboscopy examination reported posterior commissure hypertrophy, posterior glottis stenosis, laryngeal diffuse edema, and granuloma as the most prevalent laryngeal abnormalities in patients (Table 2, Figure 1). Two laryngeal examinations were considered as normal. The proportions of posterior commissure hypertrophy and laryngeal edema were significantly higher in group 1 compared with group 2 ($p < 0.001$), while posterior glottic stenosis was more prevalent in group 2 compared with group 1 ($p < 0.001$). The posterior commissure hypertrophy occurred concurrently to another abnormality in 16 cases, for example, diffuse laryngeal edema ($N = 8$), granuloma ($N = 5$), bilateral vocal fold insufficiency ($N = 2$), and posterior glottic stenosis ($N = 2$). According to the

classification of Bogdasarian,[2] the posterior glottic stenoses of group 1 were type 3 and 4, while the posterior glottic stenoses of group 2 were type 2, 3, and 4 in 1, 6, and 5 cases, respectively. Patients with a history of tracheostomy developed posterior glottic stenosis ($N = 4$), and laryngeal edema ($N = 4$) associated with granuloma in two cases.

The surgical therapeutic approaches are reported in Table 2. Laryngeal necroses and posterior glottic stenoses were treated with corticosteroids and antibiotics, which led to effective results in seven cases. Patients with posterior commissure hypertrophy, laryngeal diffuse edema, and granuloma received antireflux diet, PPIs, and alginate after confirmation of the LPR diagnosis through 24-h hypopharyngeal-oesophageal multichannel intraluminal impedance-pH monitoring. The following surgical approaches were performed in 16 patients: granuloma laser excision ($N = 4$), Montgomery-type calibration tube placement ($N = 4$), dilatation ($N = 3$), laser posterior transverse cordotomy ($N = 2$), laser flange resection ($N = 1$), and vocal fold fat medialization ($N = 1$). One patient benefited from concurrent posterior transverse cordotomy and laser excision of granuloma. Patients benefited from speech therapy prior to and after treatment. The number of intubation days was significantly higher in patients with posterior glottic stenosis (26.1 ± 9.4) compared with those presenting posterior commissure hypertrophy (11.5 ± 2.9) or granuloma (15.1 ± 5.8; $p < 0.001$).

Key Points

- At the start of the pandemic, many COVID-19 patients were intubated more than 14 days in intensive care units.
- A long intubation period (> 14 days) was associated with tardive laryngeal lesions.
- COVID-19 patients who were intubated >14 days mainly reported posterior glottic stenosis, posterior commissure hypertrophy or laryngeal diffuse edema, and granuloma 51.6 days after the hospital discharge.
- A long period of intubation was associated with a high risk of posterior glottic stenosis.
- Prolonged intubation used in severe COVID-19 patients during the pandemic is associated with significant laryngeal disorders.

4 | DISCUSSION

The relationship between COVID-19 and laryngeal disorders was initially supported in an epidemiological study in which 26% of COVID-19 patients reported dysphonia.[4] The COVID-19 was an opportunity to collect more cases with long-term intubation, and related surgical therapeutic data.

TABLE 1 Epidemiological and clinical features of patients.

	Group 1: <2 w Intubation ($N = 22$)	Group 1: >2 w Intubation ($N = 21$)	*p*-value
Mean age (yo)	**60.2 ± 11.6**	**57.9 ± 11.2**	**NS**
Gender			
Male	16 (72.7)	17 (81.0)	NS
Female	6 (27.3)	4 (19.0)	
Comorbidities			
Hypertension	14 (63.6)	16 (76.2)	NS
Type 2 diabetes mellitus	11 (50.0)	9 (42.9)	NS
Dyslipidemia	6 (27.3)	6 (28.6)	NS
Obesity	4 (18.2)	6 (28.6)	NS
Heart failure	1 (4.5)	6 (28.6)	-
Obstructive sleep apnea	1 (4.5)	3 (14.3)	-
Chronic tobacco	8 (36.4)	10 (47.6)	NS
Tobacco (pack-year)	19.3 ± 3.5	15.7 ± 3.5	NS
Intensive care unit features			
Intubation duration (days)	9.9 ± 3.7	26.3 ± 6.8	<0.001
Tracheostomy (*N*, %)	3 (13.6)	5 (23.8)	NS
Laryngology unit symptoms			
Dysphonia	22 (100)	21 (100)	NS
Dyspnea	5 (22.7)	14 (66.6)	NS
Dysphagia	3 (13.6)	6 (28.5)	NS
Neck pain	1 (4.5)	3 (14.2)	NS

Abbreviations: NS, non-significant, w, week.

TABLE 2 Laryngeal disorder findings and treatments.

Outcomes	Group 1: <2 w Intubation ($N = 22$)	Group 1: >2 w Intubation ($N = 21$)	Total
Laryngeal disorders (*N* of findings)	$N = 32$	$N = 26$	$N = 58$
Posterior commissure hypertrophy	15 (15.4)	4 (15.4)	19 (32.8)
Isolated posterior commissure hypertrophy	2 (13.3)	0 (0)	-
Concurrently to another abnormality	13 (86.7)	4 (100)	-
Posterior glottic stenosis	2 (6.3)	12 (46.2)	14 (24.1)
Unilateral ankylosis	1 (50)	5 (41.7)	-
Bilateral ankylosis	1 (50)	7 (58.3)	-
Laryngeal diffuse edema	9 (28.1)	1 (3.8)	10 (17.2)
Granuloma	5 (15.6)	3 (11.5)	8 (13.8)
Laryngeal necrosis	0 (0)	2 (7.7)	2 (3.4)
Normal	1 (3.1)	1 (3.8)	2 (3.4)
Subglottic stenosis	0 (0)	1 (3.8)	1 (1.7)
Posterior glottic flange	1 (3.1)	1 (3.8)	2 (3.4)
Vocal fold atrophy	1 (3.1)	1 (3.8)	2 (3.4)
Treatments (*N* of procedures)	$N = 5$	$N = 12$	$N = 17$
Granuloma laser excision	4 (80.0)	1 (8.3)	5 (29.4)
Montgomery-type calibration	1 (20.0)	3 (25.0)	4 (23.5)
Posterior glottic stenosis	1 (100)	3 (100)	-
Laser posterior transverse cordotomy	0 (0)	3 (25.0)	3 (17.6)
Posterior glottic stenosis	-	3 (100)	-
Dilatation	0 (0)	3 (25.0)	3 (17.6)
Laryngeal necrosis and fibrosis	-	1 (33.3)	-
Severe laryngeal edema and dyspnea	-	1 (33.3)	-
Subglottic stenosis	-	1 (33.3)	-
Laser flange resection	0 (0)	1 (8.3)	1 (5.9)
Vocal fold fat injection		1 (8.3)	1 (5.9)
Vocal fold atrophy		1 (100)	-

Abbreviation: w, week.

In the present study, we observed a high prevalence of laryngeal injuries in patients with a history of severe-to-critical COVID-19 and >2-week intubation. Depending on the intubation duration, the most common findings included posterior commissure hypertrophy and laryngeal edema, posterior glottic stenosis, and granuloma. Some recent studies reported similar laryngeal injuries in patients with a post-COVID-19 history of intubation.[5,6] Naunheim et al. observed vocal fold immobility (40%), posterior glottic stenosis (15%), subglottic stenosis (10%), laryngeal edema (10%), LPR (10%) and posterior glottic diastasis (10%) in a cohort of 20 adults with a history of post-COVID-19 intubation.[5] Neevel et al. reported a substantial prevalence of vocal fold motion impairment (50%), early glottic injury (39%), subglottic/tracheal stenosis (22%), and posterior glottic stenosis (17%) in 24 patients who required endotracheal intubation for a severe COVID-19.[6] Rouhani et al. showed that 19% of COVID-19 patients with a history of tracheostomy in ICU had vocal fold immobility and subglottic stenosis at 2-month postdischarge.[7] More recently, Felix et al. observed laryngotracheal lesions in 40% of patients with a history of post-COVID-19 intubation, including posterior glottic or subglottic stenosis (17%), granuloma (16%) and hypermia of glottis (6%).[8] In the study of Felix et al., 60% of patients had a normal laryngeal examination.[8]

Whatever the intubation indication, the laryngeal injuries observed in this study are known to arise after endotracheal intubation.

The two most prevalent lesions in our study were posterior glottic stenosis and posterior commissure hypertrophy/laryngeal edema. The duration of intubation was a predictor of the development of posterior glottic stenosis. This observation supports the findings of Hillel et al. who reported that duration of intubation, ischemia, and diabetes mellitus were significant risk factors for the development of posterior

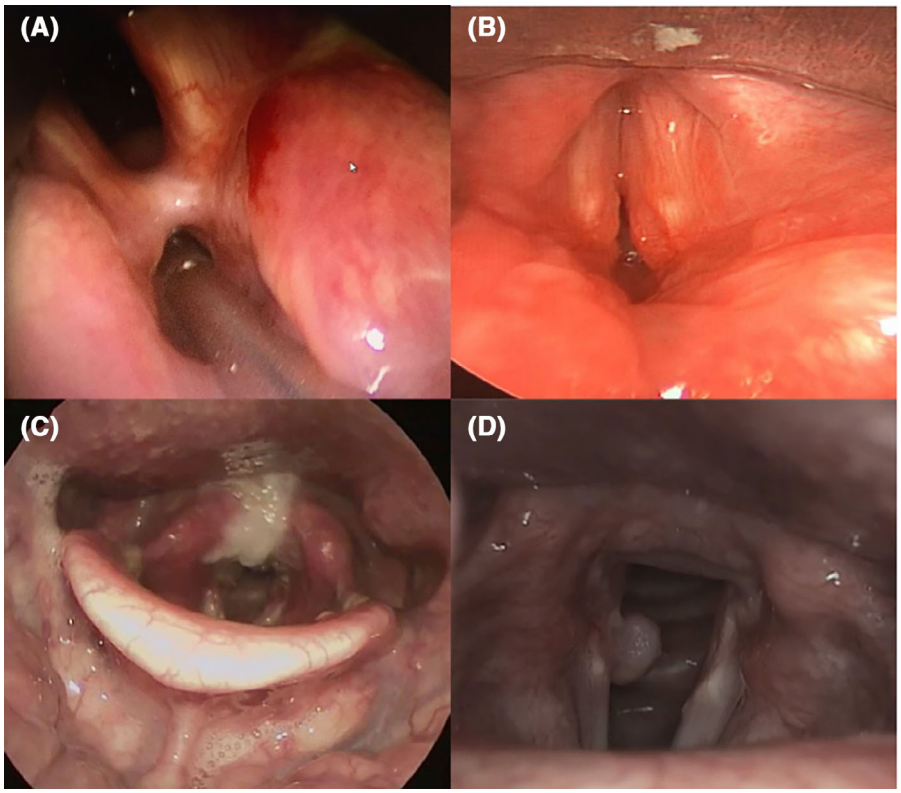

FIGURE 1 Laryngeal abnormalities associated with post-COVID-19 intubation. Laryngeal findings associated with a post-COVID-19 history of intubation included posterior synechia (A), posterior glottic stenosis (B), laryngeal necrosis (C), or granuloma (D).

glottic stenosis.[9] However, note that prior to the pandemic, it was unusual to keep intubation for >2 weeks. The relationship between the duration of intubation and the development of posterior laryngeal lesions was supported in a recent meta-analysis.[10] An additional potential factor that may increase the laryngeal inflammation is reflux. COVID-19 patients commonly require moderate to high positive end-expiratory pressure, which may increase the stomach pressure and the backflow of gastric content into the laryngopharyngeal cavity. The deposited pepsin into the laryngeal tissue may, therefore, decrease the defence mechanisms of laryngeal mucosa, increasing the risk of injuries and lesions. The posterior commissure hypertrophy and laryngeal diffuse edema are furthermore two more prevalent findings associated with LPR.

Tracheotomy is commonly considered as a relevant factor in the reduction of the occurrence of laryngeal lesions.[10] In our study, the patients who benefited from tracheostomy reported similar proportions of laryngeal injuries than those who had no tracheostomy, which is attributed to the delay between the intubation and the tracheostomy decision (>14 days). Indeed, in our hospital, this delay was due to the greater risk of contaminating health professionals during an early procedure.

The small sample size and the lack of a control group evaluating the prevalence of post-intubation laryngeal injuries in patients without COVID-19 history are the most important limitations. However, it was difficult to have a control group because it was unusual to keep intubation more than 2 weeks in ICU patients before the pandemic. Moreover, we did not assess some important ICU outcomes, including the tube size or the lung pressure of mechanical ventilation device, which may have a significant impact on the development of laryngeal injuries.

5 | CONCLUSION

Prolonged intubation used in severe COVID-19 patients is associated with significant laryngeal disorders including laryngeal edema, posterior glottic stenosis, granuloma, laryngeal necrosis, or vocal fold insufficiency. Patients with a history of >2-week intubation have a higher risk of posterior glottic stenosis, which may be managed medically or surgically. Future studies are needed to determine whether COVID-19 infection is associated with a higher risk of laryngeal injuries than other intubation causes.

KEYWORDS

complications, coronavirus, COVID-19, intubation, laryngeal, larynx, otolaryngology, SARS-CoV-2, stenosis, voice

AUTHOR CONTRIBUTIONS

Jerome R. Lechien: design, acquisition of data, data analysis & interpretation, drafting, final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. **Stéphane Hans**: design, acquisition of data, data analysis & interpretation, revising the manuscript for important intellectual content; final approval of the version to be published,

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Data are available on request.

ETHICS STATEMENT

The Hospital IRB reviewed and approved the study (ref.APHP202201). A waiver of informed consent of study participants was granted because participant data were protected and anonymized.

INFORMED CONSENT

None.

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REFERENCES

1. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475–81. https://doi.org/10.1016/S2213-2600(20)30079-5
2. Bogdasarian RS, Olson NR. Posterior glottic laryngeal stenosis. Otolaryngol Head Neck Surg. 1980;88:765–72.
3. McCaffrey TV. Classification of laryngotracheal stenosis. Laryngoscope. 1992;102:1335–40.
4. Lechien JR, Chiesa-Estomba CM, Cabaraux P, Mat Q, Huet K, Harmegnies B, et al. Features of mild-to-moderate COVID-19 patients with dysphonia. J Voice. 2020;S0892-1997(20):30183–1. https://doi.org/10.1016/j.jvoice.2020.05.012
5. Naunheim MR, Zhou AS, Puka E, Franco RA Jr, Carroll TL, Teng SE, et al. Laryngeal complications of COVID-19. Laryngoscope Investig Otolaryngol. 2020;5(6):1117–24. https://doi.org/10.1002/lio2.484
6. Neevel AJ, Smith JD, Morrison RJ, Hogikyan ND, Kupfer RA, Stein AP. Postacute COVID-19 laryngeal injury and dysfunction. OTO Open. 2021;5(3):2473974X211041040. https://doi.org/10.1177/2473974X211041040
7. Rouhani MJ, Clunie G, Thong G, Lovell L, Roe J, Ashcroft M, et al. A prospective study of voice, swallow, and airway outcomes following tracheostomy for COVID-19. Laryngoscope. 2021;131(6):E1918–25. https://doi.org/10.1002/lary.29346
8. Félix L, Tavares TL, Almeida VPB, Tiago RSL. Incidence of laryngotracheal lesions after orotracheal intubation in coronavirus disease patients. Laryngoscope. 2021;132:1075–81. https://doi.org/10.1002/lary.29862

9. Hillel AT, Karatayli-Ozgursoy S, Samad I, Best SR, Pandian V, Giraldez L, et al. Predictors of posterior glottic stenosis: a multi-institutional case-control study. Ann Otol Rhinol Laryngol. 2016; 125(3):257–63. https://doi.org/10.1177/0003489415608867
10. Brodsky MB, Levy MJ, Jedlanek E, Pandian V, Blackford B, Price C, et al. Laryngeal injury and upper airway symptoms after oral endotracheal intubation with mechanical ventilation during critical care: a systematic review. Crit Care Med. 2018;46:201–7.

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