

Dysphagia in Patients With Severe Coronavirus Disease 2019—Potential Neurologic Etiologies

IMPORTANCE: Dysphagia is a common complication of critical illness, and many known risk factors are also present in critically ill coronavirus disease 2019 victims.

OBJECTIVES: To investigate dysphagia in patients with severe coronavirus disease 2019.

DESIGN, SETTING, AND PARTICIPANTS: In this case series, we report results of dedicated evaluation of swallowing function in six consecutive, tracheotomized coronavirus disease 2019 patients after they had survived acute respiratory distress syndrome and were weaned from the respirator.

MAIN OUTCOMES AND MEASURES: Dysphagia was assessed with flexible endoscopic evaluation of swallowing.

RESULTS: Three patients suffered from severe dysphagia and airway compromise precluding decannulation, whereas in the other, three swallowing was less critically impaired, and the tracheal cannula could be removed. Four patients presented with additional laryngeal dysfunctions not typically seen in acute respiratory distress syndrome survivors.

CONCLUSION AND RELEVANCE: Dysphagia with impaired airway protection is a key feature in coronavirus disease 2019 acute respiratory distress syndrome survivors. Apart from critical illness polyneuropathy, coronavirus disease 2019–related involvement of the peripheral and central nervous system may contribute to swallowing impairment and laryngeal dysfunction.

KEY WORDS: acute respiratory distress syndrome; coronavirus disease 2019; dysphagia; flexible endoscopic evaluation of swallowing; tracheostomy

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) spread worldwide with more than 17 million cases and close to 700,000 deaths to date (1). Although in the majority of patients, COVID-19 takes a mild course with no or flu-like symptoms only, around 5–10% of patients require ICU treatment with a high proportion in need of prolonged mechanical ventilation (MV) due to acute respiratory distress syndrome (ARDS) and of vasopressor treatment for sepsis and septic shock (2).

Dysphagia is a common complication of critical illness and ICU treatment (3, 4) and is related in particular to overall disease severity, length of MV, the presence of neurologic disorders, and emergency hospitalization (5). Since all these factors are also highly prevalent in critically ill COVID-19 victims, different authors have already speculated that dysphagia may be among the key

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DOI: 10.1097/CCE.0000000000000332

complications in this patient cohort (6, 7), whereas specific observations have rarely been published so far.

Therefore, in this case series, we report results of dedicated evaluation of swallowing function in six consecutive COVID-19 patients after they had survived ARDS.

PATIENTS AND METHODS

Patients

All COVID-19 patients were treated in the medical ICU of the university hospital Münster, Germany, required a period of MV and received a dilatational tracheostomy during the course of the disease. Following our in-house guidelines, patients were referred by the medical team for a flexible endoscopic evaluation of swallowing (FEES) when they had been weaned from the respirator, and based on clinical bedside evaluation, decannulation was considered unsafe. FEES was carried out by a neurologist (R.D.) and a speech and language pathologist (L.-M.H.) and followed a previously established protocol (see below). Demographics and clinical characteristics, such as severity of ARDS (classified according to [8]), length of MV, number and type of complications, days on antibiotics, findings of neurologic examination, etc, were extracted from the medical records. Written informed consent was obtained from all patients for their data being included in this case series, and the nature of the study was approved by the local ethics committee (2016-391-f-S).

FEES

Patients were examined in a sitting position with the cannula's cuff deflated and after careful subglottic suctioning. FEES was done according to the Standardized Endoscopic Swallowing Evaluation for Tracheostomy Decannulation in Critically Ill Neurologic Patients protocol which is described in detail elsewhere (9, 10). In brief, after an assessment of laryngeal and pharyngeal structures and motor functions, the patient's management of secretions, spontaneous swallow frequency, and laryngeal sensitivity were assessed in a stepwise manner. The presence of any of the following meant that a patient was not ready for decannulation: 1) massive pooling of saliva in the laryngeal vestibule, 2) limited spontaneous swallows (< 1/min), and/or 3) no sensation elicited by endoscope contact with the

arytenoids. In case the patient was assessed to be ready for decannulation, semisolid and liquid boluses were tested thereafter. Any further follow-up examination basically followed the FEES standard protocol proposed by Langmore et al (11) and focused on swallowing safety and swallowing efficacy.

RESULTS

For this case series, six male COVID-19 survivors between 43 and 63 years old were recruited. Three patients were free of any relevant preexisting health conditions, two patients had mild-to-moderate comorbidities, and one patient presented with severe prior disorders, including morbid obesity. As summarized in **Table 1**, all patients suffered from COVID-19-related moderate-to-severe ARDS, required MV of 12–46 days and received a dilatational tracheostomy within the first 10 days after intubation. Four of the six patients were temporarily ventilated in prone position, and two patients needed treatment with extracorporeal membrane oxygenation. Pulmonary complications occurred frequently in our patients, in particular a bacterial superinfection of the lungs in all and a fungal superinfection in one patient. In addition, a variety of extrapulmonary complications were diagnosed including septic shock, pulmonary embolism, deep vein thrombosis, stroke, and cardiac conditions. With regard to treatment, all patients were given antibiotics, one received antimycotics, five needed transient renal replacement therapy, two short-term, and three long-term (> 1 wk) vasopressor treatment.

Neurologic examination revealed clinical signs of critical illness polyneuropathy (CIP) in five patients, encephalopathy was diagnosed in three patients, and one patient had a right-sided tongue palsy.

Based on FEES, decannulation was possible in three patients, whereas in the other three, the tracheal tube could not be removed at that time. In the latter group, all patients showed severe laryngeal hypesthesia, impaired management of pharyngeal secretions with constant aspiration, and a reduced swallowing frequency. In two of these patients, the swallow was weak evidenced by a missing white-out phenomenon. Key finding of FEES in the other three patients was a reduced laryngeal sensation. In addition, when testing food items, further pathologic findings were detected, that is, predeglutitive silent aspiration of liquids due to

TABLE 1.
Clinical Characteristics of the Patients and Results of FEES

Clinical Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (yr)/sex	60/male	45/male	63/male	60/male	56/male	50/male
Comorbidities	None	None	Hypertension, coronary heart disease, former smoker	Hypothyroidism	Morbid obesity, congestive heart failure, hypertension, atrial fibrillation, former smoker	None
Length of MV (d)	23 ^a	20 ^a	33	32	46	12
Acute respiratory distress syndrome (classification based on [8])	Moderate-severe	Moderate-severe	Severe	Severe	Moderate	Severe
MV in prone position (d)	0	5	6	4	0	4
Septic shock	Yes	No	Yes	Yes	No	No
Vasopressor use (d)	8	1	9	10	1	0
Renal replacement therapy (d)	3	8	12	20	5	0
Tracheostomy (days after start of intubation)	9	7	5	9	9	6
Extracorporeal membrane oxygenation (d)	0	0	8	9	0	0
Bacterial superinfection (number of antibiotics/days of use)	Yes (5/23)	Yes (3/9)	Yes (3/22)	Yes (4/19)	Yes (1/8)	Yes (1/5)
Fungal superinfection (number of antimycotics/days of use)	No (0/0)	No (0/0)	Yes (2/18)	No (0/0)	No (0/0)	No (0/0)
Complications during ICU treatment	Pulmonary embolism	Urinary tract infection, deep vein thrombosis	Septic cardiomyopathy	Deep vein thrombosis, subcortical stroke, myocarditis, mediastinal emphysema, gastritis	Pericardial effusion	None

(Continued)

TABLE 1. (Continued).
Clinical Characteristics of the Patients

Clinical Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Neurological diagnoses	CIP	Encephalopathy, CIP, right-sided tongue palsy ^b	Encephalopathy, CIP	Encephalopathy, CIP	Encephalopathy, CIP	None
Salient FEES findings	Moderate-to-severe laryngeal hypesthesia (right > left), delayed swallowing reflex, predeglutitive silent penetration, aspiration of liquid, and bilateral vocal fold adductor pareses	Severe laryngeal hypesthesia, reduced spontaneous swallowing, massive pooling and impaired clearing of pharynx, secretions, right-sided vocal cord palsy	Severe laryngeal hypesthesia, reduced spontaneous swallowing, massive pooling and impaired clearing of pharyngeal secretions, impaired pharyngeal contraction, weak tongue-base retraction and incomplete epiglottic inversion	Moderate to severe laryngeal hypesthesia (left > right), impaired oral bolus control with premature spillage and aspiration of liquid, incomplete left-sided vocal cord palsy	Severe laryngeal hypesthesia, massive pooling and impaired clearing of pharyngeal secretions, reduced spontaneous swallowing, impaired pharyngeal contraction and incomplete epiglottic inversion	Moderate pharyngolaryngeal hypesthesia, irregular arytenoid cartilage movement
Time of decannulation (post intubation/post weaning/post FEES [d])	28/2/0	54/36/35 ^c	61/26/25 ^c	38/6/1	None (FEES done at day 24 after intubation)	13/1/0

CIP = critical illness polyneuropathy, FEES = flexible endoscopic evaluation of swallowing, MV = mechanical ventilation.

^aTwo episodes of MV.

^bMRI without abnormalities.

^cDecannulation after discharge.

a delayed swallow reflex in one patient and a severely impaired oral bolus control with premature spillage and subsequent silent aspiration on liquids in another patient.

In addition, in four patients, FEES revealed further pathologic findings not directly related to swallowing. Thus, two patients showed a unilateral vocal cord palsy (one in conjunction with ipsilateral tongue palsy), one patient presented bilateral vocal fold adductor paresis, and another patient exhibited an irregular arytenoid cartilage movement.

With regard to the clinical course, two patients were given a first trial of decannulation prior to FEES.

The first patient needed to be reintubated (and retractorized) because of massive bolus aspiration and subsequent respiratory distress 4 days later. The second patient was reintubated and recannulated due to impaired management of pharyngeal secretion and respiratory distress 3 days later.

DISCUSSION

The main finding of this case series was that dysphagia is potentially a key problem in COVID-19 ARDS survivors, delaying decannulation, and putting patients at risk of airway compromise. In a previous study,

Lima et al (12) have assessed swallowing function by clinical testing in 101 COVID-19 patients with a mean period of MV of 8.8 ± 8.1 days. In keeping with our findings, close to 20% of patients had severe dysphagia 24 hours post extubation requiring full or partial artificial feeding, and a further 53% had moderate dysphagia necessitating dietary or behavioral interventions. A second survey-based study enrolled 702 patients with mild-to-moderate COVID-19 without ICU admission and MV. Contrasting with the high numbers in COVID-19 patients post ventilation, in this cohort, more than 80% of patients were free of subjective swallowing problems, moderate dysphagia was reported by around 2%, and severe dysphagia by 0.1% of patients (13).

Overall, these numbers suggest that the severity of COVID-19 and associated medical complications, in particular ARDS, constitute an important driver of COVID-19-related dysphagia. Accordingly, dysphagia has previously been identified as typical sequela of ARDS, is correlated with the length of stay on the ICU, and persists in one third of patients beyond hospital discharge (4). As Brodsky et al (14) have shown in their study dedicated to the precise analysis of swallowing physiology in ARDS survivors, weakness of the swallowing muscles turned out to be a key component of dysphagia in these patients.

An important pathophysiologic link between ARDS and associated complications on the one hand and dysphagia on the other hand is probably the development of CIP, which in general is known to be related to the lengths of MV, sepsis, use of catecholamines, and multiple organ failure (15), all of which typically occur during the course of severe COVID-19 (16). CIP was also a frequent complication in our case series affecting four of six patients. In line with the findings of Ponfick et al (17), who used FEES to prospectively study dysphagia in 22 tracheostomized CIP patients during the course of neurorehabilitation, impaired management of pharyngeal secretion, and a reduced laryngeal sensation were the hallmarks of CIP-related swallowing dysfunction in our patients, whereas an additional paresis of the pharyngeal constrictors was seen in two patients.

However, further FEES findings witnessed in our patients that are not typically associated with CIP point to an additional, possibly more specific neuro-manifestation of COVID-19 and may have aggravated

swallowing impairment. Thus, four patients presented with additional laryngeal dysfunctions, in particular incomplete unilateral vocal fold paresis in two (in conjunction with ipsilateral tongue palsy in one), bilateral vocal fold adductor paresis in one, and irregular arytenoid cartilage movement in one patient. To date, several publications have outlined a variety of different neuromanifestations of COVID-19 affecting the peripheral nervous system (PNS) and CNS (18). Although a recent study employing MRI in 19 deceased COVID-19 victims did not find evidence of brainstem involvement (19), an autopsy study including 43 patients detected neuroinflammatory changes particularly confined to the brain stem as one of the key findings. In addition, the same study identified SARS-CoV-2 in brain tissue and cranial nerves in several patients (20). We assume that the circumscribed motor dysfunctions in our patients have been caused by neuropathies confined to the 10th and 12th cranial nerves. Cranial neuropathies, either in isolation or as feature of Miller Fisher syndrome or Guillain-Barré syndrome, have repeatedly been reported in this clinical scenario (21–23). The underlying pathophysiology may include both, direct viral invasion and autoimmune response (24). On the other hand, the irregular arytenoid cartilage movement seen in one patient of the present case series is possibly caused by a different disease mechanism. Interestingly, this feature has recently been identified as most frequent and specific laryngeal dysfunction in a cohort of patients with multiple system atrophy (25). Based on neurophysiologic and anatomical studies, dysfunctional supranuclear mechanisms and nuclear damage in the medulla oblongata have been suggested to be involved in the pathophysiology of this rare laryngeal movement disorder (26). Supporting the notion of a COVID-19-related CNS dysfunction as causative pathology of this laryngeal movement disorder, there is a steadily increasing number of publications reporting CNS involvement in COVID-19 (27) with some of them specifically featuring brainstem lesions and/or dysfunctions (28–31). As with COVID-19-related PNS lesions, CNS affection is supposed to occur due to both, direct neuroinvasion and postinfectious autoimmunity (27).

A weakness of this case series is that because of practical constraints, neurologic diagnoses were mainly

based on clinical assessment, and patients did not receive a thorough diagnostic work-up including brain imaging, cerebrospinal fluid analysis, and neurophysiologic studies.

In conclusion, our findings suggest that dysphagia with impaired airway protection is a key feature in COVID-19 ARDS survivors. Future studies need to elucidate to what extent this well-known complication of ARDS is further aggravated by a COVID-19–related involvement of the PNS and CNS.

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The authors have disclosed that they do not have any potential conflicts of interest.

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