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Comparison of swallowing alteration markers between patients with and without Covid-19 post-orotracheal intubation

Comparação dos marcadores de alteração na deglutição entre pacientes com e sem Covid-19 pós-intubação orotraqueal

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ABSTRACT

Purpose: To compare the swallowing alteration markers in patients with and without COVID-19 and to study the predictive variables of oral feeding contraindication in patients requiring prolonged orotracheal intubation. **Methods:** Retrospective case-control study, with medical record data collection of clinical and demographic variables and the clinical evaluation of swallowing. The collected variables were statistically compared between patients with COVID-19 (SG) and without COVID-19 (CG). Robust Poisson regression analysis was used to evaluate the effect of COVID-19 and other variables on oral feeding contraindication. **Results:** 351 patients were included, 269 in the SG and 82 in the CG. Patients in the SG were younger when compared to the CG (50.7 ± 12.8). The total time of orotracheal intubation was significantly longer in the SG. The patients in the SG had a higher prevalence of weak cough, dysphonia, worse degrees of dysphagia and higher occurrence of contraindication of oral feeding. In the bivariate analysis, it was found that patients with COVID-19 were 65% more likely to have oral feeding contraindication. However, when COVID-19 was adjusted with other clinical and demographic variables, it was found that these variables had a greater influence on the contraindication of the oral feeding than the COVID-19. **Conclusion:** Prolonged orotracheal intubation had a worse effect on alteration markers in swallowing and reintroduction of the oral feeding in COVID-19 patients. Age over 60 years, orotracheal intubation time greater than 5 days, reintubation, and delirium were shown to be predictive of oral feeding contraindication in intubated patients.

Keywords: COVID-19; Deglutition disorders; Intubation; Respiration, Artificial; Speech, Language and Hearing Sciences; Critical Care

RESUMO

Objetivo: comparar os marcadores de alteração na deglutição de pacientes com e sem COVID-19 e estudar as variáveis preditivas de contraindicação da alimentação por via oral em pacientes com necessidade de intubação orotraqueal prolongada. **Métodos:** estudo caso-controle, retrospectivo, com coleta de prontuário de variáveis clínicas e demográficas e da avaliação clínica da deglutição. As variáveis coletadas foram comparadas estatisticamente entre pacientes com COVID-19 (grupo estudo -GE) e sem COVID-19 (grupo-controle - GC). A análise de regressão de robusta de Poisson foi utilizada para avaliar o efeito da COVID-19 e das demais variáveis na contraindicação da alimentação por via oral. **Resultados:** foram incluídos 351 pacientes, 269 no GE e 82 no GC. Pacientes do GE apresentaram menor idade, quando comparados ao GC (50,7 ± 12,8). O tempo total de intubação orotraqueal foi significativamente maior no GE. Os pacientes do GE apresentaram maior prevalência de tosse fraca, disfonia, piores graus de disfagia e maior ocorrência de contraindicação da alimentação por via oral. Na análise bivariada, verificou-se que os pacientes com COVID-19 apresentaram 65% maior probabilidade dessa contraindicação. Entretanto, quando a COVID-19 foi ajustada com outras variáveis clínicas e demográficas, verificou-se que as estas apresentaram maior influência sobre a contraindicação de alimentação por via oral do que a COVID-19. **Conclusão**: a intubação orotraqueal prolongada teve pior efeito nos marcadores de alteração na deglutição e na reintrodução da via oral de pacientes com COVID-19. A idade maior que 60 anos, tempo de intubação orotraqueal maior que cinco dias, reintubação e *delirium* demonstraram ser preditivas de contraindicação da alimentação por via oral em pacientes intubados.

Palavras-chave: COVID-19; Transtornos de deglutição; Intubação; Respiração Artificial; Fonoaudiologia; Cuidados Críticos

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INTRODUCTION

COVID-19 (Coronavirus disease) is transmitted by the new coronavirus SARS-CoV-2, which started in Wuhan, China, in 2019, with worldwide transmission. The coronavirus has a genome composed of a single-stranded, non-segmented, positive polarity RNA (ribonucleic acid) molecule belonging to the Coronaviridae family[1]. The characterization and presentation of SARS-CoV-2 are broad, ranging from asymptomatic infection and mild upper respiratory tract infection to progressive respiratory failure, with pulmonary failure and death[1,2]. The main clinical manifestations are fever, dry cough, myalgia, fatigue, alteration in the leukocyte count, anosmia, ageusia, dyspnea, and imaging examination compatible with pneumonia[1].

In severe cases, patients with COVID-19 may develop multiple organ dysfunction and severe acute respiratory syndrome (SARS). Most patients with SARS due to COVID-19 need ventilatory support through mechanical ventilation (MV), requiring orotracheal intubation (OTI), which is indicated to maintain airway permeability and control pulmonary ventilation in patients who need ventilatory support[2].

OTI has effects on the biomechanics of swallowing in the period after extubation, being one of the causes of the development of oropharyngeal dysphagia (OPD). OPD, in turn, is characterized as a swallowing disorder or any alteration in the transit of the food bolus from the mouth to the stomach and appears as a symptom of a pre-existing underlying disease. The presentation of OPD varies according to the characteristics and severity of the underlying pathology and the main complications are aspiration pneumonia, malnutrition, dehydration, and death[3]. The occurrence of post-OTI OPD ranges from 41% to 56% and silent laryngotracheal aspiration occurs in 36% of dysphagic individuals. There is an increased risk of developing aspiration pneumonia, which results in a prolonged hospital stay, aggravating the condition patient's clinical status[4,5].

The main impacts of OTI on swallowing biomechanics are related to reduced sensitivity and mobility of structures responsible for swallowing due to muscle inactivity in the oropharyngeal region and hyolaryngeal complex and possible injuries and inflammation of the oral, pharyngeal, and laryngeal mucosa. This may occur during the OTI period, especially when maintained for a prolonged period (48 hours or more) [4,6]. Other factors that are related to OPD and that also increase the risk of laryngotracheal aspiration are the use of sedatives and neuromuscular blockers (NMB) and muscle weakness[6].

Patients with COVID-19 admitted to intensive care units (ICU) most often have severe respiratory conditions and different conditions from patients without COVID-19, such as cognitive disorders resulting from the residual effect of using high concentrations of NMB and sedatives, dyspnea due to the extensive pulmonary involvement and alterations in the central nervous system caused by the virus[5,7,8]. Such alterations result in worse outcomes and higher risks of complications, whose impacts on the rehabilitation of these patients are still being investigated[9]. Thus, this study aimed to compare the markers of alterations in swallowing and to study the predictive variables of contraindication of oral feeding in patients with and without COVID-19 after prolonged OTI (48 hours or more), submitted to speech-language evaluation.

METHODS

Study design and location

Case-control, observational, retrospective study, carried out in a public university hospital, reference for the care of patients with COVID-19, from April 2020 to May 2021. The signing of the Free and Informed Consent Form (FIC) was waived, given the retrospective nature of the research, with data collected through a review of medical records. The study was approved by the Research Ethics Committee of the Hospital de Clínicas de Porto Alegre – CEP-HCPA, under No. 4.666.251.

Data and sample collection

Data collection was carried out through the review of medical records and protocols for the clinical evaluation of swallowing. The sample consisted of patients with COVID-19 who formed the study group (SG) and without COVID-19, who formed the control group (CG). The inclusion criteria were: individuals of both genders, aged 18 years or older, who were evaluated by the speech therapy team at the ICU through a medical consultation, from April 2020 to May 2021, with and without a diagnosis of COVID-19 and submitted to OTI greater than or equal to 48 hours. Prolonged OTI greater than or equal to 48 hours was considered one of the most cited risk factors for OPD in the literature[4,10]. Patients with neurological or neurodegenerative diseases, tracheostomy, a record of esophageal alteration in medical records, previous OPD, head and neck cancer, or history of surgical procedures in these regions, blocked access to medical records, evolving to death, and transfer to another hospital were excluded. In addition, in the CG, patients who tested positive for COVID-19 during their hospital stay were excluded.

The sample calculation was performed using the PSS Health tool (Power and Sample Size for Health Researchers) online version, based on the article by Lima et al.[8], considering the difference between the proportions of the functional level of swallowing (scale (American Speech-Language-Hearing Association - ASHA 6-7 at discharge) between the study and control groups, since no other articles with similar outcome were found in the literature. The power of 80%, significance level of 5%, and proportion of ASHA 6-7 were adopted at discharge in the SG of 70.3%, and in the CG of 52%. The total sample was 318 subjects, 239 in the SG and 79 in the CG, adding 10% for possible losses and refusals, the sample size was 354 (266 in the SG and 88 in the CG).

Variables

For the analysis of clinical and demographic characteristics of patients, the following variables were collected from medical records: age; gender; presence of comorbidities; presence of delirium through the application of the CAM-ICU scale (Confusion Assessment Method for the Intensive Care Unit); determination of the severity of the patient admitted to the ICU using the SAPS-3 scale (Simplified Acute Physiology Score 3); Body Mass Index (BMI); use and duration of use of

continuous NMB and sedation/analgesia; total time of OTI, extubation failure (when there was a need for reintubation in less than 48 hours after the first extubation attempt); reintubation (when there was a need for a new intubation 48 hours after extubation); length of stay in the hospital and in the ICU prior to the speech-language pathology evaluation; variables of the clinical evaluation of swallowing, such as cough strength, throat clearing strength, dysphonia, degree of dysphagia; permitted consistencies and feeding route; number of speech therapy consultations performed.

The CAM-ICU scale is a validated diagnostic tool that allows the assessment of four characteristics of delirium: fluctuating mental status, lack of attention, disorganized thinking, and altered level of consciousness. In order to confirm the diagnosis, the presence of three of these characteristics is necessary, including, obligatorily, the first two. The SAPS-3 scale is used to determine the severity of the patient admitted to the ICU, and its application measures 20 variables that include demographic aspects, reasons for admission to the ICU, and physiological variables. To determine the BMI, different cutoff points were used for adults[11] and the elderly aged 60 years or more[12].

The variables related to the clinical evaluation of swallowing were collected from the protocol used by speech therapists in the institution's routine, based on the Preliminary Speech Therapy Assessment Protocol (PAP)[13] and Speech Therapy Risk Assessment Protocol for Dysphagia (PARD)[14]. The clinical evaluation of swallowing and the follow-up of the assessed patients were carried out by more than one professional from the institution of origin. Bearing in mind the retrospective nature of this study, calibration of the evaluators was not carried out for the application of the protocol.

The assessment of cough and throat-clearing strength was based on the evaluator's perception. Coughing was classified as strong when it was able to mobilize stasis of secretions and clear the airway, and throat clearing was classified as strong when it was enough to clear the airway when a wet voice quality was identified. The vocal assessment was carried out by auditory-perceptual analysis, based on the auditory impression that the evaluator has on the individual's vocal utterance. This was derived from the sustained utterance of the vowel "a" and spontaneous speech using the GRBASI scale, which is constituted of six parameters: G - general degree of dysphonia; R - roughness; B - breathiness; A - asthenia; S - strain and I - instability. All parameters were evaluated according to absence or presence and the degree of severity, as follows: 0 = absence; 1 = light; 2 = moderate, and 3 = severe[15]. The presence of dysphonia was considered when the presence of an alteration in at least one of the scale parameters was identified.

From the clinical evaluation of swallowing, information was collected related to the released consistencies and feeding route in the first evaluation and at discharge, oral contraindication in the first evaluation and at discharge, and degrees of dysphagia. Namely: normal swallowing (no strategy or extra time is needed, full oral feeding is recommended); functional swallowing (may be abnormal or altered, but does not result in aspiration or reduced swallowing efficiency, it is possible to maintain adequate nutrition and hydration orally, expected spontaneous compensations of mild difficulties, in at least one consistency, with absence of signs of aspiration risk); mild dysphagia (swallowing disorder present, requiring specific guidance by the speech therapist during swallowing, need for minor changes in diet, spontaneous and effective coughing and/or throat clearing, slight oral alterations with adequate compensation); mild to moderate dysphagia (existence of risk of aspiration, however reduced with the use of therapeutic maneuvers and techniques, need for sporadic supervision to carry out therapeutic precautions, signs of aspiration and restriction of consistency, weak reflex cough and strong voluntary cough); moderate dysphagia (existence of significant risk of aspiration, supplemented oral feeding by alternative route, signs of aspiration for two consistencies, weak or absent cough reflex); moderate to severe dysphagia (tolerance of only one consistency, with maximum assistance for the use of strategies, signs of aspiration requiring multiple requests for clearing, aspiration of two or more consistencies, absence of cough reflex, weak and ineffective voluntary cough); severe dysphagia (impossibility of oral feeding, choking with difficulty in recovery, presence of cyanosis or bronchospasm, silent aspiration for two or more consistencies, ineffective voluntary cough, inability to initiate swallowing)[13].

Statistical analysis

For statistical analysis, quantitative variables with normal distribution were described by mean and standard deviation and analyzed using Student's t-test, and asymmetric variables were described by the median and interquartile range and analyzed using the Mann-Whitney test. Qualitative variables were analyzed using Pearson's chi-square test and WALD's chi-square test.

Robust Poisson regression was performed as a multivariate analysis to verify the association between the variables and the contraindication of oral feeding in the first evaluation. The measure of association used was the prevalence ratio (PR), with a confidence interval (CI) of 95%. The criterion for entering the variable in the multivariate model was that it had a $p<0.20$ in the comparative analysis between the SG and CG and in the bivariate analysis of the total sample. The significance level adopted was 5% ($p<0.05$). A multicollinearity test was performed for the variables length of hospital stay before speech therapy evaluation, length of stay in the ICU before speech therapy evaluation, total time of OTI, and time of use of sedation/analgesia, considering a cutoff point of 2.0 in the factor of variance inflation factor. From the test, the variable total time of OTI was chosen to be included in the model. In addition, the variables total time of OTI and use of sedation/analgesia were separated into quintiles. Afterward, the total time of the OTI variable was dichotomized into five days to enter the final model. All analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 18.0.

RESULTS

During the period from April 2020 to May 2021, the speech therapy team evaluated 621 post-OTI patients in the ICU, 373 patients in the ICU COVID and 248 patients in the non-COVID ICU. A total of 269 patients in the SG and 82 patients in the CG were included in this study, totaling 351 patients who met the inclusion criteria.

Concerning the clinical and demographic characteristics of patients in each group and the comparison of characteristics between the SG and CG, it was observed that the male gender

was more prevalent in both groups (55% in SG and 62.2% in CG). The mean age of the SG was 50.78 ± 12.84 and that of the CG was 55.44 ± 17.42, with this age difference being statistically significant between the groups (p = 0.009). The SAPS-3 value was higher in the CG (65.45 ± 16.8 in the CG and 57 ± 14.4 in the SG). BMI was higher in SG patients (33.23 ± 8.5), when compared to CG patients (26.9 ± 6.3), with p < 0.001 (Table 1).

The total time of OTI was also longer in the SG, with a median of 10 (7-14) days (p < 0.001). Furthermore, the SG required sedoanalgesia and NMB for a longer time, when compared to the CG (p < 0.001). The length of hospital stay and stay in the ICU before the speech-language evaluation were also longer in the SG, with a median of 14 (10-20) days of hospitalization and 12 (8-17) days of stay in the ICU, while the CG had a median of 9 (6.7-14) days of hospital stay and 7.5 (5-11) days of stay in the ICU (p < 0.001) (Table 1).

Regarding the clinical evaluation of swallowing, it was found that 48.7% of the patients in the SG had a weak cough in the evaluation, compared to 35.4% of the patients in the CG (p = 0.046). Dysphonia was more prevalent in the SG, being present in 81.8% of the patients in the first evaluation and 65.9% of the patients in the CG (p = 0.004). Regarding the consistencies delivered orally in the first evaluation, 38.3% of the patients in the SG had contraindications for the oral route, compared to 23.2% of the patients in the CG (p = 0.017). The oral route of multiple consistencies was more prevalent in the CG (36.6% in the CG and 21.6% in the SG), followed by the oral route of a single consistency (30.5% in the CG and 23.8% in the SG). (p = 0.002) (Table 2).

As for the data from the bivariate analysis on the relationship of the variables of the total sample (n=351) with the contraindication of oral feeding in the first evaluation, it was observed that patients with COVID-19 presented 65% (PR 1.65 CI 1 .08; 2.52) higher probability of this contraindication in the first evaluation when compared to patients without COVID-19 (p = 0.020). In addition, OTI maintained for more than 5 days increased

Table 1. Clinical and demographic characteristics of patients with COVID-19 (study group) and without COVID-19 (control group)

	SG	CG	p-value
	n = 269	n = 82	
Gender n(%)			
Male	148 (55%)	51 (62.2%)	0.307*
Female	121 (45%)	31 (37.8%)	
Age (Mean±SD)	50.78 ± 12.84	55.44 ± 17.42	0.009**
SAPS-3 (Mean±SD)	57 ± 14.4	65.45 ± 16.8	< 0.001**
Comorbidities n(%)			
Cardiovascular disease	19 (7.10%)	35 (42.7%)	< 0.001*
Chronic respiratory disease	37 (13.8%)	26 (31.7%)	< 0.001*
Diabetes	60 (22.3%)	23 (28%)	0.356*
Hypertension	132 (49.1%)	41 (50%)	0.983*
Cancer	5 (1.9%)	10 (12.2%)	< 0.001*
Pregnancy	10 (3.7%)	1 (1.2%)	0.439*
Obesity	164 (61%)	24 (29.3%)	< 0.001*
BMI (Mean±SD)	33.23 ± 8.5	26.9 ± 6.3	< 0.001**
IOT time Md(IQ)	10 (7-14)	6 (4-9)	< 0.001***
Extubation failure n(%)			
Yes	35 (13%)	11 (13.4%)	1.000*
No	234 (87%)	71 (86.6%)	
Reintubation n(%)			
Yes	4 (1.5%)	5 (6.1%)	0.056*
No	265 (98.5%)	77 (93.9%)	
Use of NMB n(%)			
Yes	241 (89.6%)	20 (24.4%)	< 0.001*
No	28 (10.4%)	62 (75.6%)	
Use of sedoanalgesia n(%)			
Yes	269 (100%)	79 (96.3%)	0.014*
No	0 (0)	3 (3.7%)	
Time of use of NMB Md(IQ)	4 (3-8)	2 (2-3)	< 0.001***
Time of use of sedoanalgesia Md(IQ)	9 (6-14)	4 (2-6)	< 0.001***
CAM-ICU n(%)			
Positive	46 (17.1%)	8 (9.8%)	0.150*
Negative	223 (82.9%)	74 (90.2%)	
Length of stay in the ICU Md(IQ)	12 (8-17)	7.5 (5-11)	< 0.001***
Length of hospital stay Md(IQ)	14 (10-20)	9 (6.7-14)	< 0.001***

Significant values (p<0.05) *Pearson's chi-square test; **Student's t test; ***Mann-Whitney test

Subtitle: SG = study group; CG = control group; n = number of participants; % = percentage; < = less than; SD= standard deviation; Md = median; IQ = interquartile range; SAPS-3 = Simplified Acute Physiology Score III; BMI = Body mass index; OTI = orotracheal intubation; NMB = neuromuscular blocker; CAM-ICU - Confusion Assessment Method for the Intensive Care Unit; ICU = Intensive Care Unit.

Table 2. Data from the clinical evaluation of swallowing and speech therapy of patients with COVID-19 (study group) and without COVID-19 (control group)

	SG n=269	CG n=82	p-value
Cough n(%)			
Strong	138 (51.3%)	53 (64.6%)	0.046*
Weak	131 (48.7%)	29 (35.4%)	
Throat clearing n(%)			
Strong	152 (56.5%)	56 (68.3%)	0.076*
Weak	117 (43.5%)	26 (31.7%)	
Dysphonia n(%)			
Absent	49 (18.2%)	28 (34.1%)	0.004*
Present	220 (81.8%)	54 (65.9%)	
Degree of dysphagia n(%)			
Functional	27 (10%)	19 (23.2%)	<0.001*
Mild	32 (11.9%)	13 (15.9%)	
Mild to moderate	30 (11.2%)	21 (25.6%)	
Moderate	71 (26.4%)	13 (15.9%)	
Moderate do severe	80 (29.7%)	8 (9.8%)	
Severe	29 (10.8%)	8 (9.8%)	
Consistencies released in the first evaluation n(%)			
Oral route contraindication	103 (38.3%)	19 (23.2%)	0.002*
Minimal oral route	35 (13%)	4 (4.9%)	
Oral route one consistency	64 (23.8%)	25 (30.5%)	
Oral route multiple consistencies without liquid	9 (3.3%)	4 (4.9%)	
Oral route multiple consistencies with liquid	58 (21.6%)	30 (36.6%)	
Consistencies released at discharge n(%)			
Oral route contraindication	3 (1.1%)	2 (2.4%)	0.450*
Minimal oral route	0 (0)	0 (0)	
Oral route one consistency	9 (3.3%)	5 (6.1%)	
Oral route multiple consistencies without liquid	16 (5.9%)	4 (4.9%)	
Oral route multiple consistencies with liquid	241 (89.6%)	71 (86.6%)	
Feeding route in the first evaluation n(%)			
Exclusive alternative route	103 (38.3%)	19 (23.2%)	0.036*
Mixed feeding route	136 (50.6%)	53 (64.6%)	
Exclusive oral route	30 (11.2%)	10 (12.2%)	
Feeding route at discharge n(%)			
Exclusive alternative route	3 (1.1%)	2 (2.4%)	0.094*
Mixed feeding route	1 (0.4%)	2 (2.4%)	
Exclusive oral route	265 (98.5%)	78 (95.1%)	
Contraindication of oral route (NPO) in the first evaluation n(%)			
Yes	103 (38.3%)	19 (23.2%)	0.017*
No	166 (61.7%)	63 (76.8%)	
Contraindication of oral route (NPO) at discharge n(%)			
Yes	3 (1.1%)	2 (2.4%)	0.724*
No	266 (98.9%)	80 (97.6%)	
Speech therapy services Md(IQ)	6 (4-9)	6 (4-10)	0.726**

Significant values (p<0.05) *Pearson's chi-square test; **Mann-Whitney test

Subtitle: SG = study group; CG = control group; n = number of participants; % = percentage; < = less than; Md = median; IQ = interquartile range; VO = oral route; NPO = nothing by mouth

the probability of oral feeding contraindication in the first evaluation by two times, in the total sample (PR 2.72 CI 1.62; 4.58 and p < 0.001). Other demographic and clinical variables that met the criteria for inclusion in the multivariate model (p-value < 0.20) were age greater than or equal to 60 years, reintubation, use of NMB, and positive CAM-ICU (presence of delirium) (Table 3).

In the multivariate analysis, it was found that COVID-19 had no influence on the contraindication of oral feeding in the first assessment (PR 1.2 CI 0.71; 2.04 and p = 0.486). COVID-19 was adjusted for the other variables that entered the multivariate model and it was shown that age greater than or equal to 60 years (p = 0.038) and the presence of delirium (p = 0.032) increased the probability of contraindication of food by oral route in the first assessment by 40% and that the presence of reintubation increased this probability by 69% (p = 0.037). Patients intubated for more than 5 days were twice as likely to have this contraindication (p = 0.003) (Table 4).

Table 3. Bivariate analysis comparing patients with oral route contraindication (no oral route) and with oral route approved in the first clinical evaluation of swallowing

	NPO	Oral route free	PR (CI 95%)	p-value*
	n = 122	n = 229		
COVID-19 n(%)				
No	19 (23.2%)	63 (76.8%)	1	0.020
Yes	103 (38.3%)	166 (61.7%)	1.65 (1.08; 2.52)	
Gender n(%)				
Male	68 (34.2%)	131 (65.8%)	1	0.791
Female	54 (35.5%)	98 (64.5%)	1.04 (0.78;1.39)	
Age				
<60 years old	77(32.2%)	162(67.8%)	1	0.137
≥60 years old	45(40.2%)	67(59.8%)	1.25 (0.932;1.669)	
SAPS-3 (Md)				
≤56	59(33.3%)	118(66.7%)	1	0.572
>57	63(36.2%)	111(63.8%)	1.09(0.82;1.45)	
Comorbidities n(%)				
Cardiovascular disease				
No	105 (35.4%)	192 (64.6%)	1	0.590
Yes	17 (31.5%)	37 (68.5%)	0.89 (0.58; 1.36)	
Diabetes				
No	87 (32.5%)	181 (67.5%)	1	0.093
Yes	35 (42.2%)	48 (57.8%)	1.29 (0.96;1.76)	
Chronic respiratory disease				
No	102 (35.4%)	186 (64.6%)	1	0.586
Yes	20 (31.7%)	43 (68.3%)	0.89 (0.6; 1.33)	
hypertension				
No	66 (37.1%)	112 (62.9%)	1	0.356
Yes	56 (32.4%)	117 (67.6%)	0.87 (0.65;1.16)	
Cancer				
No	116 (34.5%)	220 (65.5%)	1	0.651
Yes	6 (40%)	9 (60%)	1.15 (0.61;2.19)	
Pregnancy				
No	118 (34.7%)	222 (65.3%)	1	0.908
Yes	4 (36.4%)	7 (63.6%)	1.05 (0.47; 2.32)	
Obesity				
No	51 (31.3%)	112 (68.7%)	1	0.207
Yes	71 (37.8%)	117 (62.2%)	1.20 (0.9; 1.62)	
BMI (Md)				
≤30.5	59(33.3%)	118(66.7%)	1	0.572
>30.5	63(36.2%)	111(63.8%)	1.09(0.82; 1.45)	
OTI time				
≤ 5 days	13 (15.1%)	73 (84.9%)	1	< 0.001
> 5 days	109 (41.13%)	156 (58.8%)	2.72 (1.62; 4.58)	
Extubation failure n(%)				
No	101 (33.1%)	204 (66.9%)	1	0.075
Yes	21 (45.7%)	25 (54.3%)	1.37 (0.97; 1.96)	
Reintubation n(%)				
No	117 (34.2%)	225 (65.8%)	1	0.115
Yes	5 (55.6%)	4 (44.4%)	1.62 (0.89; 2.97)	
Use of NMB n(%)				
No	20 (22.2%)	70 (77.8%)	1	0.008
Yes	102 (39.1%)	159 (60.9%)	1.76 (1.16; 2.66)	
Use of sedoanalgesia n(%)				
<11days	63(26%)	179 (74.0%)	1	< 0.001
≥11days	59(54.1%)	50 (45.9%)	2.08 (1.58; 2.73)	
CAM-ICU n(%)				
Negative	93 (31.3%)	204 (68.7%)	1	< 0.001
Positive	29 (53.7%)	25 (46.3%)	1.71 (1.27; 2.31)	
Days of hospitalization in the ICU (Md)				
≤ 11 days	43(22.9%)	145(77.1%)	1	< 0.001
> 11 days	79(48.5%)	84(51.5%)	2.12 (1.56;2.88)	
Days of hospital stay (Md)				
≤ 13 days	44(23.8%)	141(76.2%)	1	< 0.001
> 13 days	78(47%)	88(53%)	1.98(1.46;2.68)	

Significant value (p<0.05) *WALD chi square test

Subtitle: n = number of participants; % = percentage; < = less than; ≤ = less than or equal to; > = greater than; ≥ = greater than or equal to; NPO = nothing by mouth; VO = oral route; NMB = neuromuscular blocker; CAM-ICU = Confusion Assessment Method for the Intensive Care Unit; PR = prevalence ratio; CI = confidence interval; OTI = orotracheal intubation; Md = median; BMI = Body Mass Index; SAPS-3 = Simplified Acute Physiology Score III; ICU = Intensive Care Unit

Table 4. Multivariate analysis of oral contraindication (nothing by mouth) in the first clinical evaluation of swallowing

	PR (CI 95%)	p-value*
COVID-19	1.2 (0.71 ; 2.04)	0.486
Age ≥60 years old	1.36 (1.02 ; 1.82)	0.038
OTI time > 5 days	2.26 (1.32 ; 3.89)	0.003
Reintubation	1.69 (1.03 ; 2.75)	0.037
Use of NMB	1.41 (0.82 ; 2.4)	0.212
CAM-ICU positive	1.40 (1.03 ; 1.91)	0.032

Significant values (p<0.05) * Robust Poisson regression
Subtitle: > = greater than; ≥ = greater than or equal to; PR = prevalence ratio; CI = confidence interval; NMB = neuromuscular blocker; CAM-ICU = Confusion Assessment Method for the Intensive Care Unit; OTI = orotracheal intubation

DISCUSSION

In this study, the male gender was more prevalent in both groups, in agreement with other studies in post-OTI patients[4,16]. Although the studies present such a result regarding gender, this variable and its influence on the biomechanics of swallowing is still little explored. Regarding age, the group with COVID-19 was composed of younger patients [50,78]. Demographic studies carried out in Brazil and China show mean ages of 47 to 51.8 years in hospitalized patients with COVID-19[3,17]. Although the group of patients in the SG was younger, worse markers of alterations in swallowing could be observed, which can be attributed to the need for OTI for a longer time, greater need for NMB use, and longer use of sedoanalgesia.

The SAPS-3 value was higher in patients without COVID-19. One of the reasons for this finding is that these patients were older and had previous comorbidities, scoring higher in the index measured at admission[17].

As in this research, epidemiological studies show that most patients with COVID-19 hospitalized in a serious condition, in need of MV, presented obesity as one of the previous comorbidities[18,19]. According to the literature, obesity generates inflammation in the body, resulting in changes in metabolism and immunity, which can increase the inflammatory state, aggravating the clinical picture in the case of COVID-19[20].

The average time of OTI in patients with COVID-19 reported in the literature, ranges from 7 to 16 days[16,21], which is compatible with the result of the present study. In the Lima et al.[8] study, which compared the swallowing profile of patients with and without COVID-19, showed a longer time of OTI in the group of patients with COVID-19. Although patients with COVID-19 remained, on average, ten days on MV, the multivariate analysis established that five days of OTI increases twice the probability of oral feeding contraindication in intubated patients.

In the present study, it was verified that the time of use of NMB increased by 41% the probability of contraindication of oral feeding in the first evaluation of patients with a need for prolonged OTI. Furthermore, in patients with COVID-19 with a severe manifestation of the disease and long periods of OTI, the use of high concentrations of sedoanalgesia and NMB are frequently used, increasing the risk of developing delirium and acquired weakness in the ICU[21,22]. The use of sedoanalgesia and NMB can cause pharyngeal dysfunction and change coordination between breathing and swallowing, which interferes with airway protection and increases the risk of aspiration[23,24].

Prolonged OTI can change the strength of the cough, due to generalized muscle weakness and reduced inspiratory and expiratory pressures shortly after extubation[25]. An ineffective cough increases the risk of laryngotracheal aspiration and the severity of OPD since coughing is an essential mechanism for protecting the lower airways[26]. In this study, the weak cough was more prevalent in patients with COVID-19.

Another mechanism that contributes to the increased risk of laryngotracheal aspiration and changes in lower airway protection is dysphonia after extubation, which occurs due to the position of the orotracheal tube between the vocal folds for a prolonged time[4,6,27]. In this study, dysphonia was present in most patients with COVID-19 (81.8%). The higher occurrence of dysphonia in the group with COVID-19 may be related to longer OTI time and consequent laryngeal changes[28], as well as muscle weakness acquired in the ICU and possible change in airflow due to respiratory muscle weakness[25]. Another study analyzed the swallowing and voice profile of patients with post-extubation COVID-19 and the authors found dysphonia in 66% of the patients, with previous respiratory diseases being related to worse vocal quality[29].

The contraindication of oral feeding was more prevalent in the group of patients with COVID-19, in addition to the greater occurrence of dysphagia in the moderate and moderate to severe degrees, suggesting a greater risk of laryngotracheal aspiration in this group. In the case of patients in the SG who had the oral route permitted, most required adaptations and consistency restrictions, due to the presence of dysphagia. Another study also found results with greater contraindications for oral feeding and restriction of consistencies in patients with COVID-19[29].

Although the literature already describes the relationship between prolonged OTI and oropharyngeal dysphagia, it was possible to perceive, from the present study, that patients with COVID-19 had greater severity of dysphagia (moderate, moderate to severe, and severe degrees), when compared to patients without COVID-19. The severity and characteristic of oropharyngeal dysphagia in patients with COVID-19, in addition to the time of OTI, may also have been influenced by the inflammatory nature of the disease, other associated comorbidities, and the multiple invasions that cross the patient's stay in the ICU[16]. Such factors and their influence on swallowing biomechanics still need to be better explored.

The number of speech therapy consultations did not vary between the two groups, but patients with contraindications for oral feeding in the first evaluation required a greater number of speech therapy consultations during the hospital rehabilitation process, possibly because they had greater severity of dysphagia. Speech therapy for dysphagic patients is planned based on the results of the clinical evaluation of swallowing. Therapeutic planning encompasses the choice and combination of exercises and the determination of the duration and frequency of speech therapy sessions, according to the patient's needs[30].

The length of hospital stay is also a factor that influences the process of reintroducing oral feeding in critically ill patients. In the present study, it was evidenced, in the bivariate analysis, that the stay in the ICU greater than or equal to 11 days increases twice the risk of contraindication of oral feeding in the first evaluation. This may be related to the greater clinical severity of the patient, with longer OTI time and the need to use NMB and sedoanalgesia, resulting in a greater risk of laryngotracheal aspiration[16,21].

As limitations of the study, we highlight the nature and discrepancy of the sample number between the groups, which occurred due to the greater number of visits to patients with

COVID-19 during the research period. In addition, the sample of patients without COVID-19 was more heterogeneous, with a greater presence of exclusion criteria. We also highlight the age difference between the groups (SG patients younger than CG patients), which may have generated bias in the interpretation of the findings.

CONCLUSION

Patients with COVID-19 required longer orotracheal intubation and, as a likely consequence, longer use of sedoanalgesia and NMB, as well as longer hospital stays. Regarding the markers of changes in swallowing, it was evidenced that patients with COVID-19 had worse performances in the speech-language clinical evaluation, with a higher occurrence of changes in airway protection mechanisms, dysphonia, and oropharyngeal dysphagia of moderate, moderate to severe, and severe degrees, in addition to a higher occurrence of oral feeding contraindications in the first clinical evaluation of swallowing.

Regarding the contraindication of oral feeding in the first clinical evaluation of swallowing in patients requiring prolonged OTI, it was shown that patients with COVID-19 were 65% more likely to have this contraindication. However, it is necessary to take into account that, when COVID-19 was adjusted with other clinical and demographic variables, it was found that other factors, often observed in critically ill patients with COVID-19, such as age greater than 60 years, intubation time for more than five days, need for reintubation and the presence of delirium, demonstrated to increase the probability of contraindication of oral feeding in the first clinical evaluation of swallowing in the studied sample.

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