J Osaka Dent Univ 2022 (October); **56 (2)**: 209−214.

Comparative study of dysphagia occurring after acute respiratory distress syndrome in COVID-19 versus non-COVID-19 patients

***Keigo Maeda[1, 2], Masaki Kakudo[3], Junko Tanaka[3], Toshihiko Takenobu[4] and Kosuke Kashiwagi[3]**

[1]Graduate School of Dentistry (Department of Fixed Prosthodontics and Occlusion), Osaka Dental University, 8-1 Kuzuhahanazono-cho, Hirakata-shi, Osaka 573-1121, Japan, [2]Department of Oral and Maxillofacial Surgery, Kobe City Medical Center General Hospital, 2-1-1, Minatojima Minamimachi, Chuo-ku, Kobe-city, Hyogo 650-0047, Japan, [3]Department of Fixed Prosthodontics and Occlusion, Osaka Dental University, 8-1 Kuzuhahanazono-cho, Hirakata-shi, Osaka 573-1121, Japan, and [4]Second Department of Oral and Maxillofacial Surgery, Osaka Dental University Hospital, 1-5-17 Ohtemae, Chuo-ku, Osaka 540-0008, Japan
**E-mail: k.maeda@kcho.jp*

We compared the clinical characteristics and incidence of dysphagia after mechanical ventilation in patients with acute respiratory distress syndrome (ARDS) occurring with or without coronavirus disease 2019 (COVID-19). Sixty-seven patients who were diagnosed with ARDS due to COVID-19 and were managed with mechanical ventilation between January 2020 to March 2021 were included in the COVID-19 group. This group was compared with 32 patients who were diagnosed with ARDS due to diseases other than COVID-19 between January 2017 and March 2021 (the non-COVID-19 group). Clinical characteristics and dysphagia during the time after being in the intensive care unit and hospital discharge were compared for the two patient groups. The Functional Oral Intake Scale (FOIS) was used to evaluate dysphagia. FOIS levels 1 to 5 are defined as dysphagia. There were no statistically significant differences in patient characteristics between the two groups other than their Acute Physiology and Chronic Health Evaluation II scores (18.82±5.949 vs 25.97±6.977, $p < 0.001$). Multivariate analysis showed that the incidence of dysphagia at hospital discharge in patients with COVID-19-associated ARDS was statistically significantly lower than in patients with ARDS due to other causes (OR 0.238, 95% CI 0.071−0.798; $p = 0.02$). (J Osaka Dent Univ 2022; 56: 209-214)

Key words: Post-extubation dysphagia; Mechanical ventilation; COVID-19; ARDS

INTRODUCTION

Dysphagia after prolonged mechanical ventilation has been reported in approximately 14-83% of adult patients.[1] Acute respiratory distress syndrome (ARDS) is an atypical condition of critical illnesses. Patients present with a severe illness following prolonged mechanical ventilation, and intensive care unit (ICU)-acquired muscle weakness, any of which may put them at high risk for dysphagia.[1, 2] Although several risk factors for dysphagia have been noted including prolonged mechanical ventilation and ICU admission, how mechanical ventilation causes dysphagia is largely unknown because the limited data available has not been adequately assessed.[3] Coronavirus disease 2019 (COVID-19) is a viral respiratory illness caused by a novel coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2). The COVID-19 pandemic has spread throughout the world and has led to severe morbidity and mortality on a global scale. Severe cases in patients with COVID-19 may develop into ARDS, leading to the necessity for mechanical ventilation.[4]

The development of dysphagia after mechanical ventilation has been observed in patients with COVID-19-associated ARDS.[5] However, only a few studies have evaluated the incidence of dysphagia

after mechanical ventilation. Moreover, the Society of Swallowing and Dysphagia of Japan released a position statement instructing physicians to evaluate and treat post-extubation patients under some restrictions, because dysphagia management can lead to the production of droplets and aerosols as well as to contact with viral particles.[6] Thus, under these circumstances, patients with COVID-19-associated ARDS could present with different characteristics and outcomes with regard to dysphagia after mechanical ventilation as compared to patients with ARDS occurring due to causes other than COVID-19. However, no studies have directly compared the incidence of dysphagia between COVID-19-associated ARDS and non-COVID-19-associated ARDS. The objective of this study was to assess the incidence of dysphagia after mechanical ventilation in patients with COVID-19-associated ARDS and to compare the clinical characteristics and incidence of dysphagia after mechanical ventilation of patients with COVID-19-associated ARDS to those of patients with non-COVID-19-associated ARDS.

MATERIALS AND METHODS

Patient population

We conducted this study using the medical records system at our tertiary care center in order to carry out a retrospective observational cohort investigation comparing patients with severe COVID-19-associated ARDS to patients with ARDS caused by treatment of diseases other than COVID-19. Patients who were diagnosed with ARDS due to COVID-19 from January 2020 to March 2021 and who were managed with mechanical ventilation were included in a COVID-19 group. In order to conduct comparisons with the COVID-19 group, patients who were diagnosed with ARDS due to diseases such as sepsis and aspiration pneumonia other than COVID-19 between January 2017 and March 2021 were included in a non-COVID-19 group. ARDS was diagnosed by specialists in the respiratory, ICU, and emergency departments based on the American-European Consensus Conference criteria for ARDS.[7]

Patients in both groups were eligible for study enrollment if they were at least 18 years of age, were admitted to the ICU, and received mechanical ventilation with an endotracheal tube for more than 48 hours. Patients younger than 18 years, those with a history of cerebrovascular diseases, swallowing dysfunction, pneumonia, or oropharyngeal neoplasms prior to hospitalization, and those who died during hospitalization were excluded from this study.

Primary outcome

The primary outcome evaluated in this study was dysphagia after mechanical ventilation in the ICU and at the time of hospital discharge. Dysphagia after mechanical ventilation was assessed using the Functional Oral Intake Scale (FOIS) scores. The FOIS is one of the most frequently used scales for evaluating swallowing function.[8] Specifically, the FOIS is a seven-point numerical scale that is constructed as follows. 1: No intake by mouth, 2: Tube dependent intake with minimal attempts for food and fluid ingestion, 3: Tube dependent intake with consistent intake of food and fluid, 4: Total oral diet of a single consistency, 5: Total oral diet with multiple consistencies but requiring special preparation or compensation, 6: Total oral diet with multiple consistencies not requiring special preparation, but with specific food limitations, and 7: Total oral diet with no restrictions.[9] FOIS levels 1 to 5 are defined as dysphagia, whereas levels 6 to 7 are defined as a lack of dysphagia.

Swallowing evaluation

Swallowing function was assessed via a repeatable saliva swallowing test (RSST) administered by a trained nurse and a registered dietician as soon as possible and within 24 hours following extubation. In case of a failed RSST, patients were referred to the swallowing team at our hospital and were trained in swallowing functionality. A modified water swallowing test (MWST) was performed if a safe RSST was recorded. The MWST required patients to start with 3 mL of water in the resting position. A score of 1 indicates failed swallowing with or with-

out wheezing or respiratory urgency, 2 indicates swallowing with respiratory urgency, 3 indicates swallowing without respiratory changes but with choking and/or wet hoarseness. A score of 4 indicates swallowing with no abnormality, and 5 indicates two swallowings within 30 seconds with no abnormality.[10] A score of 4 or higher on the MWST is sufficient for regular food (FOIS 6, 7). A reassessment was performed a few days after the first assessment. At this time, if no major abnormalities were observed in the MWST, oral diet was continued. If increased sputum, fever, and dysphagia was observed on re-assessment, the patient was referred to the swallowing team and was trained in swallowing functionality.

Swallowing team rounds were performed on a daily basis by specialists in dysphagia, speech therapists, language therapists, nurses, and registered dietitians. The patients were trained using both direct and indirect exercises. Videofluorography or videoendoscopic evaluations were performed, and the food texture level was advanced as appropriate.

Covariates

We collected baseline demographic variables such as age, sex, body mass index (BMI), duration of mechanical ventilation, length of ICU stay, length of hospital stay, and the presence or absence of tracheostomy based on the patients' electronic medical records. Baseline Acute Physiology and Chronic Health Evaluation (APACHE) II scores were determined to assess disease severity.

Statistical analysis

The data were analyzed with SPSS version 25 (IBM, Armonk, NY, USA). In univariate comparisons, the Fisher exact test and Mann-Whitney U test were used to compare categorical and continuous variables between the COVID-19 and non-COVID-19 groups using nonparametric tests, as appropriate. Binomial logistic regression analysis was used to determine whether the incidence of dysphagia at ICU discharge and at hospital discharge respectively differed between the two groups. This regression analysis was adjusted for the duration of mechanical ventilation, the length of ICU stay, the length of hospital stay, the presence or absence of tracheostomy, and the APACHE II scores. These covariates were selected based on the existing literature and investigators' prior knowledge in this field (i.e., according to clinical experience and the findings of previous studies).[3,10] The strength of association was measured by the odds ratio (OR) and 95% confidence intervals (CI) with the level of statistical significance set at 0.05.

Ethical approval

The study protocol was approved by the Institutional Review Board of Kobe City Medical Center General Hospital (Approval no. zn 200913). This research was conducted according to the tenets of the Declaration of Helsinki and its later amendments. Due to the retrospective nature of this study, we applied an opt-out method (available through the hospital website) to obtain informed consent.

RESULTS

Sixty-seven patients in the COVID-19 group and 32 patients in the non-COVID-19 group were included in this report. The clinical characteristics of the patients in the COVID-19 group and the non-COVID-19 group are shown in Table 1. We found no statistically significant differences between the two groups in terms of age, sex, BMI, duration of mechanical ventilation, length of ICU stay, or length of hospital stay. However, the APACHE II score was statistically significantly lower in the COVID-19 group than in the non-COVID-19 group (18.82 ± 5.949 vs 25.97 ± 6.977, $p < 0.001$). The incidence of dysphagia at ICU discharge was 59.7% in the COVID-19 group and 65.6% the non-COVID-19 group. At hospital discharge, half of the patients in the non-COVID-19 group had dysphagia symptoms. However, dysphagia was present in only approximately a quarter of the patients in the COVID-19 group at the time of discharge.

The results of binomial logistic regression analyses at ICU discharge are presented in Table 2. After controlling for the duration of mechanical ventilation, the length of hospital stay, tracheostomy, and APACHE II scores, there was no statistical difference in the incidence of dysphagia at the time of

Table 1 Patient medical and demographic characteristics

Variable	COVID-19 group (n＝67)	Non-COVID-19 group (n＝32)	p-value
Age (yrs)	67.2±9.5	64.5±17.8	0.896
Male (n (%))	50 (74.6)	24 (75.0)	0.968
BMI (kg/m^2)	22.6±4.4	22.3±4.8	0.144
Duration of mechanical ventilation (days)	11.3±12.1	8.0±5.2	0.899
Length of ICU stay (days)	13.4±11.8	11.2±4.5	0.770
Length of hospital stay (days)	41.8±29.9	41.2±20.6	0.237
Tracheostomy (n (%))	14 (16.4)	10 (31.3)	0.317
APACHE II score	18.8±5.9	26.0±7.0	0.001
Dysphagia at ICU discharge (n (%))	40 (59.7)	21 (65.6)	0.352
Dysphagia at hospital discharge (n (%))	17 (25.4)	18 (56.2)	0.010

APACHE II: Acute Physiology and Chronic Health Evaluation II, BMI: Body mass index, ICU: Intensive care unit, Mean±SD

Table 2 Multivariate adjusted binominal logistic regression evaluating the incidence of dysphagia in patients with or without COVID-19 at intensive care unit (ICU) discharge

Variable	Odds ratio	95% CI	p-value
COVID-19 patients	0.683	0.216-2.159	0.516
Tracheostomy	7.519	0.762-76.92	0.084
APACHE II score	1.066	0.983-1.156	0.120
Duration of mechanical ventilation	1.247	0.466-3.338	0.661
Length of ICU stay	1.076	0.974-1.189	0.151

Table 3 Multivariate adjusted binominal logistic regression evaluating the incidence of dysphagia in patients with or without COVID-19 at the time of hospital discharge

Variable	Odds ratio	95% CI	p-value
COVID-19 patients	0.238	0.071-0.798	0.020
Tracheostomy	2.616	0.614-11.144	0.193
APACHE II score	0.925	0.853-1.004	0.063
Duration of mechanical ventilation	0.606	0.294-1.247	0.174
Length of hospital stay	0.766	0.598-0.982	0.036

ICU discharge between the two groups (OR: 0.683, 95% CI: 0.216−2.159; p＝0.516). However, as shown in Table 3, patients in the COVID-19 group were less likely to experience dysphagia at the time of hospital discharge as compared with the non-COVID-19 group (OR: 0.238, 95% CI: 0.071−0.798, p＝0.02).

DISCCUSSION

The main finding of this study was that the overall incidence of dysphagia at the time of hospital discharge was 25.4%, and that this incidence was statistically significantly lower in the COVID-19 group than in the non-COVID-19 group. However, the incidence of dysphagia at the time of ICU discharge (i.e., in contrast to the incidence at the time of hospital discharge) was not significantly different between the two groups.

In a previous report, one-third of patients with ARDS requiring mechanical ventilation had dysphagia symptoms at the time of hospital discharge.[1, 11-13] Among COVID-19 patients with ARDS who required mechanical ventilation, approximately 20-70% of patients have been reported to have dysphagia symptoms at the time of hospital discharge.[8, 9, 14] Factors such as age, the duration of mechanical ventilation, length of hospital stay, and delayed oral intake have been correlated with dysphagia occurring following COVID-19-associated ARDS.[9, 15, 16] On the other hand, the incidence of ARDS in patients with COVID-19 ranges from 3.6 to 42% according to prior reports.[17-20] These reports included both survivors and non-survivors. It has been suggested that factors such as age, sex, and BMI are associated with the development of ARDS in patients with COVID-19.[4, 19, 20] However, little is known about the incidence of dysphagia and the development of ARDS following COVID-19. Most cohort studies have suggested that many patients with dysphagia occurring after COVID-19 improve swallowing dysfunction in the hospital setting.[5, 8, 16]

For example, Bordejé Laguna *et al.*[21] reported that dysphagia associated with severe COVID-19 (i.e., after mechanical ventilation) was fully resolved six months after hospital discharge. In the present study, the incidence of dysphagia at ICU discharge was not statistically significantly different between the COVID-19 and non-COVID-19 groups. Although a quarter of the patients in the COVID-19 group had dysphagia symptoms at hospital discharge, the incidence of dysphagia was statistically significantly lower in the COVID-19 group than in the non-COVID-19 group.

In terms of patient characteristics, only the APACHE II score differed at the level of statistical significance between the two groups. Subhash *et al.*[22] previously reported that there was no statistically significant difference in the APACHE II scores between COVID-19 and non-COVID-19 patients with ARDS who required mechanical ventilation; however, few studies have compared APACHE II scores between these two groups. The average APACHE II score in patients with severe COVID-19 has been reported to range from 9 to 22 points.[9, 21, 23] However, careful consideration is needed in interpreting these findings because some of these reports included APACHE II scores among non-survivors, which may have biased the findings. Hence, the true difference in the APACHE II scores between patients with COVID-19-associated ARDS and in ARDS patients without COVID-19 is unknown. The duration of mechanical ventilation and the lengths of ICU and hospital stays were not statistically significantly different between the two groups enrolled in this study. However in a few reports, these indicators were similar or greater in patients with COVID-19-associated ARDS than in those with non-COVID-19-associated ARDS.[19, 22, 24] There are multiple potential reasons for the increased duration of ventilation, such as differences in individual practice patterns that limit occupational exposure to SARS-CoV-2.[19]

This study has several limitations. The number of patients with and without COVID-19 ARDS was small. All study participants were recruited from a single hospital. Hence, our results may not apply to other populations considering the differences in treatment protocols and medical resources between countries. The data included in this study were collected during the first, second, and third waves of the COVID-19 pandemic in Japan. The Alfa variant was the main strain detected during the study period, though the virus evolved over the duration of the study. Differences in clinical manifestations (for example, differences in age, contagion severity, and the duration of intubation) have been reported among the variants.[25] Thus, the incidence of dysphagia may not have been comparable among the study periods. Even with these limitations, we hope that this study presents a novel contribution supporting our knowledge regarding the incidence of dysphagia due to COVID-19-associated ARDS that occurs after mechanical ventilation.

Our results suggest that dysphagia after mechanical ventilation occurring after ARDS in COVID-19 patients has a better prognosis than ARDS occurring due to diseases other than COVID-19. We hope that our findings, which should be confirmed in more detailed future investigations, will be of use in future research and in establishing future medical guidelines.

Acknowledgments

We wish to express our appreciation to former Prof. Tanaka and another member of Department of Fixed Prosthodontics and Occlusion, Osaka Dental University and patients and medical staff of Kobe City Medical Center General Hospital on this study.

REFERENCES

1. Brodsky MB, Gellar JE, Dinglas VD, Colantuoni E, Mendeztellez PA, Shanholtz C, Palmer JB, Needham DM. Duration of oral endotracheal intubation is associated with dysphagia symptoms in acute lung injury patients. *J Crit Care* 2020; **29**: 574-579.
2. Macht M, Wimbish T, Clark BJ, Benson AB, Burnham EL, Williams A, Moss M. Postextubation dysphagia is persistent and associated with poor outcomes in survivors of critical illness. *Crit Care* 2011; **15**: R231.
3. Zuercher P, Schenk NV, Moret C, Berger D, Abegglen R, Schefold JC. Risk factors for dysphagia in ICU patients after invasive mechanical ventilation. *Chest* 2020; **158**: 1983-1991.
4. Suleyman G, Fadel RA, Malette KM, Hammond C, Abdulla H, Entz A, Demertzis Z, Hanna Z, Failla A, Dagher C, Chaudhry Z, Vahia A, Abreu Lanfranco O, Ramesh M, Zervos MJ, Alangaden G, Miller J, Brar I. Clinical characteris-

tics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan Detroit. *JAMA Netw Open* 2020; **3**: e2012270.
5. Miles A, McRae J, Clunie G, Gillivan-Murphy P, Inamoto Y, Kalf H, Pillay M, Pownall S, Ratcliffe P, Richard T, Robinson U, Wallace S, Brodsky MB. An international commentary on dysphagia and dysphonia during the COVID-19 pandemic. *Dysphagia* 2022; **4**: 1-26.
6. Kimura Y, Ueha R, Furukawa T, Oshima F, Fujitani J, Nakajima J, Kaneoka Y, Aoyama H, Fujimoto Y, Umezaki T. Society of swallowing and dysphagia of Japan: position statement on dysphagia management during the COVID-19 outbreak. *Auris Nasus Larynx* 2020; **47**: 715-726.
7. Bernard GR, Artigas A, Brigham KL, Carlet JM, Falke K, Hudson LD, Lamy M, Legall JR, Morris A, Spragg R. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med* 1994; **149**: 818-824.
8. Clayton NA, Walker E, Freeman-Sanderson A. Clinical profile and recovery pattern of dysphagia in the COVID-19 patient: a prospective observational cohort within NSW. *Aust Crit Care* 2022: 1-7.
9. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and cox regression. *Am J Epidemiol* 2007; **165**: 710-718.
10. Tanaka K, Watanabe K, Kashiwagi H. Association between postextubation dysphagia and physical function in survivors of critical illness: a retrospective study. *Clin Nutr ESPEN* 2022; **47**: 147-151.
11. Kruser JM, Prescott HC. Dysphagia after acute respiratory distress syndrome another lasting legacy of critical illness. *Ann Am Thorac Soc* 2017; **14**: 307-308.
12. Brodsky MB, Huang M, Shanholtz C, Mendez-Tellez PA, Palmer JB, Colantuoni E, Needham DM. Recovery from dysphagia symptoms after oral endotracheal intubation in acute respiratory distress syndrome survivors: a 5-year longitudinal study. *Ann Am Thorac Soc* 2017; **14**: 376-383.
13. Lindh MG, Mattsson G, Koyi H, Johansson MB, Razmi R, Palm A. Swallowing function in COVID-19 patients after invasive mechanical ventilation. *Arch Rehabil Res Clin Transl* 2022; **4**: 100177.
14. Reyes-Torres CA, Flores-López A, Osuna-Padilla IA, Hernández-Cárdenas CM, Serralde-Zúñiga AE. Phase angle and overhydration are associated with post-extubating dysphagia in patients with COVID-19 discharged from the ICU. *Nutr Clin Pract* 2022; **37**: 110-116.
15. de Lima MS, Sassi FC, Medeiros GC, Ritto AP, de Andrade CRF. Preliminary results of a clinical study to evaluate the performance and safety of swallowing in critical patients with COVID-19. *Clinics* 2020; **75**: 1-2.
16. Dawson C, Capewell R, Ellis S, Matthews S, Adamson S, Wood M, Fitch L, Reid K, Shaw M, Wheeler J, Pracy P, Nankivell P, Sharma N. Dysphagia presentation and management following coronavirus disease 2019: an acute care tertiary centre experience. *J Laryngol Otol* 2020; **134**: 981-986.
17. Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. *Crit Care* 2020; **24**: 1-4.
18. Khamis F, Al Awaidy S, Shaaibi M Al, Shukeili M Al, Chhetri S, Balushi A Al, Sulaimi S Al, Balushi A Al, Wesonga R. Epidemiological characteristics of hospitalized patients with moderate versus severe COVID-19 infection: a retrospective cohort single centre study. *Diseases* 2021; **10**: 1.
19. Bain W, Yang H, Shah FA, Suber T, Drohan C, Al-Yousif N, DeSensi RS, Bensen N, Schaefer C, Rosborough BR, Somasundaram A, Workman CJ, Lampenfeld C, Cillo AR, Cardello C, Shan F, Bruno TC, Vignali DAA, Ray P, Ray A, Zhang Y, Lee JS, Methe B, McVerry BJ, Morris A, Kitsios GD. COVID-19 versus Non-COVID-19 acute respiratory distress syndrome comparison of demographics, physiologic parameters, inflammatory biomarkers, and clinical outcomes. *Ann Am Thorac Soc* 2021; **18**: 1202-1210.
20. Krynytska I, Marushchak M, Birchenko I, Dovgalyuk A, Tokarskyy O. COVID-19-associated acute respiratory distress syndrome versus classical acute respiratory distress syndrome (a narrative review). *Iran J Microbiol* 2021; **13**: 737-747.
21. Bordejé Laguna L, Marcos-Neira P, de Lagrán Zurbano IM, Marco EM, Guisasola CP, Viñas Soria CD, Martí PR. Dysphagia and mechanical ventilation in SARS-COV-2 pneumonia: It's real. *Clin Nutr* 2021; https://doi.org/10.1016/j.clnu.2021.11.018.
22. Todi S, Ghosh S. A comparative study on the outcomes of mechanically ventilated COVID-19 vs non-COVID-19 patients with acute hypoxemic respiratory failure. *Indian J Crit Care Med* 2021; **25**: 1377-1381.
23. Kamal M, Naseer Khan A, Ali G. A comparison of APACHE II and APACHE IV scoring systems in predicting outcome in patients with acute lung injury (ALI) and the adult respiratory distress syndrome (ARDS) in intensive care unit (ICU). *Rawal Med J* 2013; **38**: 234-238.
24. Brault C, Zerbib Y, Kontar L, Fouquet U, Carpentier M, Metzelard M, Soupison T, De Cagny B, Maizel J, Slama M. COVID-19- versus non-COVID-19-related acute respiratory distress syndrome: differences and similarities. *Am J Respir Crit Care Med* 2020; **202**: 1301-1304.
25. Abdullah F, Myers J, Basu D, Tintinger G, Ueckermann V, Mathebula M, Ramlall R, Spoor S, Villiers TD, Walt ZVD, Cloete J, Rheeder P, Paruk F, Engelbrecht A, Lalloo V, Myburg M, Kistan J. Decreased severity of disease during the first global omicron variant COVID-19 outbreak in a large hospital in Tshwane, South Africa. *Int J Infect Dis* 2020; **116**: 28-42.