Received: 24 March 2023 | Accepted: 13 June 2023

DOI: 10.1002/ams2.868

ORIGINAL ARTICLE

ACUTE MEDICINE & SURGERY WILEY

Factors associated with the outcome of patients with COVID-19 requiring mechanical ventilation: A single-center observational study in Japan

Ryo Deguchi[1] | **Tetsuro Nishimura**[1] | **Kenji Matsuo**[1] | **Fumiaki Wakita**[1] | **Akihiro Kawamoto**[1] | **Kenichiro Uchida**[1] | **Hiromasa Yamamoto**[1] | **Koichi Yamada**[2] | **Hiroshi Kakeya**[2] | **Hiromichi Fujii**[3] | **Toshihiko Shibata**[3] | **Yasumitsu Mizobata**[1]

[1]Department of Traumatology and Critical Care Medicine, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan

[2]Department of Infection Control Science, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan

[3]Department of Cardiovascular Surgery, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan

Correspondence
Ryo Deguchi, Department of Traumatology and Critical Care Medicine, Osaka Metropolitan University Graduate School of Medicine, 1-5-7 Asahimachi, Abeno-ku, Osaka City, Osaka 545-8586, Japan.
Email: degu92@gmail.com

Abstract

Aim: Coronavirus disease (COVID-19) spread worldwide, and was declared as a pandemic by the World Health Organization. Despite numerous studies in the last few years, the factors associated with the outcomes of patients with COVID-19 requiring mechanical ventilation remain unclear. The prediction of ventilator weaning and mortality using the data obtained at the time of intubation could be beneficial for establishing appropriate treatment strategies and obtaining informed consent. In this study, we aimed to clarify the association between patient information at the time of intubation and the outcomes of intubated COVID-19 patients.

Methods: This retrospective observational study used single-center data from patients with COVID-19. Patients with COVID-19 who were admitted to Osaka Metropolitan University Hospital from April 1, 2020, to March 31, 2022, and under mechanical ventilation were included. The main outcome was defined as the factors related to ventilator weaning; a multivariate analysis was carried out to evaluate the association between patient information at the time of intubation and the outcome.

Results: In total, 146 patients were included in this study. The factors significantly associated with ventilator weaning were age (65–74 years old, adjusted odds ratio [OR], 0.168; 75 years and older, adjusted OR, 0.121), vaccination history (adjusted OR, 5.655), and Sequential Organ Failure Assessment (SOFA) respiration score (adjusted OR, 0.007) at the time of intubation.

Conclusion: Age, SOFA respiration score, and COVID-19 vaccination history at the time of intubation could be associated with outcomes in patients with COVID-19 requiring mechanical ventilation.

KEYWORDS
COVID-19, mechanical ventilation, prognostic factor, ventilator weaning

INTRODUCTION

Coronavirus disease (COVID-19) was declared as a pandemic on March 11, 2020 by the World Health Organization (WHO).[1] On December 2022, the WHO reported that the cumulative number of COVID-19 cases had exceeded 600 million, and the cumulative number of deaths had exceeded 6 million.[2] In Japan, more than 20 million people have been infected, and more than 50,000 deaths were reported.[3] Although the number of COVID-19 cases has shown a steady decline since the start of 2023, there is still a possibility of future increases. It is crucial that we

maintain vigilance and address the disease with continued caution.

Coronavirus disease can be complicated by acute respiratory dysfunction syndrome, which can lead to respiratory failure requiring mechanical ventilation. In addition, it can induce excessive inflammatory reactions throughout the body, damage the vascular endothelial cells, cause thrombosis in the lungs, heart, kidneys, and brain, and lead to multiple organ failure, thus increasing the severity of infection.[4]

Recently, numerous factors have been reported to be associated with COVID-19 outcomes. Previous studies reported a strong relationship between history of chronic respiratory disease,[5] history of chronic kidney disease,[6] coronary risk factors such as age, obesity, history of smoking, history of hypertension, and history of diabetes, and poor outcomes.[7] A history of vaccination against COVID-19 might also influence the outcome.[8]

Drugs such as steroids,[9] remdesivir,[10] baricitinib,[11] and molnupiravir[12] have been associated with favorable outcomes among patients treated for COVID-19. In addition, many cases of COVID-19-associated coagulopathy have been reported,[13] and antithrombotic drugs are often given in those with severe cases. These drugs are commonly used in many COVID-19 treatment facilities in Japan, including our hospital.

As described above, various factors could be related to the outcomes of COVID-19; however, most of the recommendations are based on the results of low-grade studies. In addition, only a few studies have examined the relationship between patient information at the time of intubation and outcomes of those with severe COVID-19 cases.[14] This study aimed to clarify the association between patient information at the time of intubation and outcomes of intubated COVID-19 patients. The prediction of outcomes using the information collected at the time of intubation will help determine the possibility of achieving successful weaning from mechanical ventilation and the survival status at the time of intubation, which might be beneficial for establishing appropriate treatment plans, such as early tracheostomy and information sharing.

METHODS

Study design, study participants, eligibility, and setting

This retrospective observational study was undertaken at a single center in Japan. We included patients with COVID-19 who were intubated and treated at Osaka Metropolitan University Hospital. This study cohort did not include patients who were intubated for illnesses other than COVID-19. Intubation was indicated among patients who experienced dyspnea after receiving 5 L/min of oxygen. Patients admitted to our hospital between April 1, 2020 and March 31, 2022 were included. We excluded those with missing data on the day of intubation, who experienced cardiopulmonary arrest upon arrival, or whose life-prolonging treatment was discontinued on the day of visit. We extracted the following data from the medical records, which could potentially influence the outcomes of COVID-19 (see "Data collection"), and carried out a univariate analysis using these variables. For the multivariate analysis, we included variables that showed significant differences in the univariate analysis, as well as variables that have been reported to be associated with outcomes in previous studies. The study results were reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.[15] An opt-out method was used on the website to obtain patient consent. This study was carried out with the approval of the Osaka Metropolitan University Hospital Ethics Review Committee (2022–140).

Treatment for COVID-19

Corticosteroids (methylprednisolone or dexamethasone), remdesivir, tocilizumab, baricitinib, molnupiravir, and antithrombotic drugs (low-molecular-weight or unfractionated heparin) were used for the treatment of COVID-19. None of the patients who received molnupiravir underwent intubation and were excluded from the study. As COVID-19 can be complicated by bacterial pneumonia, antibacterial drugs (mainly ceftriaxone) were concomitantly administered from the start of COVID-19 treatment in all patients.

Data collection

Data were collected at the initiation of mechanical ventilation. The collected data were patients' baseline information (age, categorized into three groups: <65, 65–74, and ≥75 years, sex, body mass index [BMI] above 30 kg/m^2,[16] ethnicity, smoking history, and COVID-19 vaccination history), medical history (diabetes, cardiovascular diseases including hypertension, chronic respiratory disease [asthma, chronic obstructive pulmonary disease, and interstitial pneumonia], chronic renal failure, end-stage renal disease [requiring dialysis or kidney transplant], hematopoietic disease, malignant tumor, and history of chemotherapy in the last 12 months), hemoglobin A1c level on the day of intubation, Sequential Organ Failure Assessment (SOFA) scores on the day of intubation (respiration, coagulation, liver, cardiovascular, central nervous system, and renal scores), drugs given (steroids [methylprednisolone or dexamethasone], remdesivir, tocilizumab, baricitinib, molnupiravir, and antithrombotic agents e.g., unfractionated heparin, low-molecular-weight heparin, and nafamostat), and patient outcomes (ventilator weaning, mortality, and ventilator-free days within 14 days after intubation).

Outcome

The factors related to ventilator weaning at our hospital were assigned as the primary outcome. The factors

associated with mortality and ventilator-free days within 14 days after intubation were assigned as the secondary outcomes. Successful weaning from the ventilator was regarded as a "favorable outcome," while other cases were regarded as "poor outcomes." We defined "ventilator weaning" as a combination of "extubation" and "removal of the mechanical ventilator from the tracheostomy tube". There were no specific criteria for ventilator weaning; this decision was left to the discretion of the attending physician. If the mechanical ventilator was reattached to the tracheostomy tube within 72 h after removal, or if reintubation occurred within 72 h after extubation, the weaning was considered invalid.

Statistical analyses

For the statistical analysis of the two groups, Student's *t*-test was used for normally distributed data and Mann–Whitney's *U*-test for nonnormally distributed data. The normally distributed values were expressed as mean (standard deviation), while the nonnormally distributed values were expressed as median (first quartile–third quartile). Pearson's χ^2-test or Fisher's exact test was used to analyze the proportions. The relationship between the dependent and independent variables was assessed using logistic and linear regression analyses (both forced-entry methods). The results of the logistic regression analysis were expressed as adjusted odds ratios (ORs), 95% confidence interval (CIs), and *p* values. The results of the linear regression analysis are expressed as beta, *t*, 95% CIs, and *p* values. All statistical analyses were undertaken using SPSS version 25.0 (IBM Corp). All tests were two-tailed, and a *p* value of less than 0.05 was considered significant.

RESULTS

Flowchart of patient selection process

A flowchart of the patient selection process is shown in Figure 1. A total of 163 patients with COVID-19 were included in this study. We excluded 10 patients with missing data, 6 patients who experienced cardiopulmonary arrest upon arrival, and 1 patient whose life-prolonging treatment was discontinued on the day of visit. The number of eligible patients was 146; among them, 98 patients had a favorable outcome, while 48 patients had a poor outcome.

Patients' characteristics

Table 1 shows the characteristics of the patients with COVID-19 who were admitted and intubated in our hospital. Significant differences were observed between favorable and poor outcomes in terms of age, cardiovascular diseases including hypertension, SOFA respiration, renal scores, and treatment with baricitinib. A total of 113 patients were discharged from our hospital alive, while 33 died. The median number of ventilator-free days within 14 days after intubation was 3.

Primary outcome

We examined the factors associated with weaning from mechanical ventilation using a multivariate logistic regression model (Table 2). In addition to age and male sex, existing cardiovascular diseases including hypertension, SOFA respiration scores, and renal scores at intubation were used as

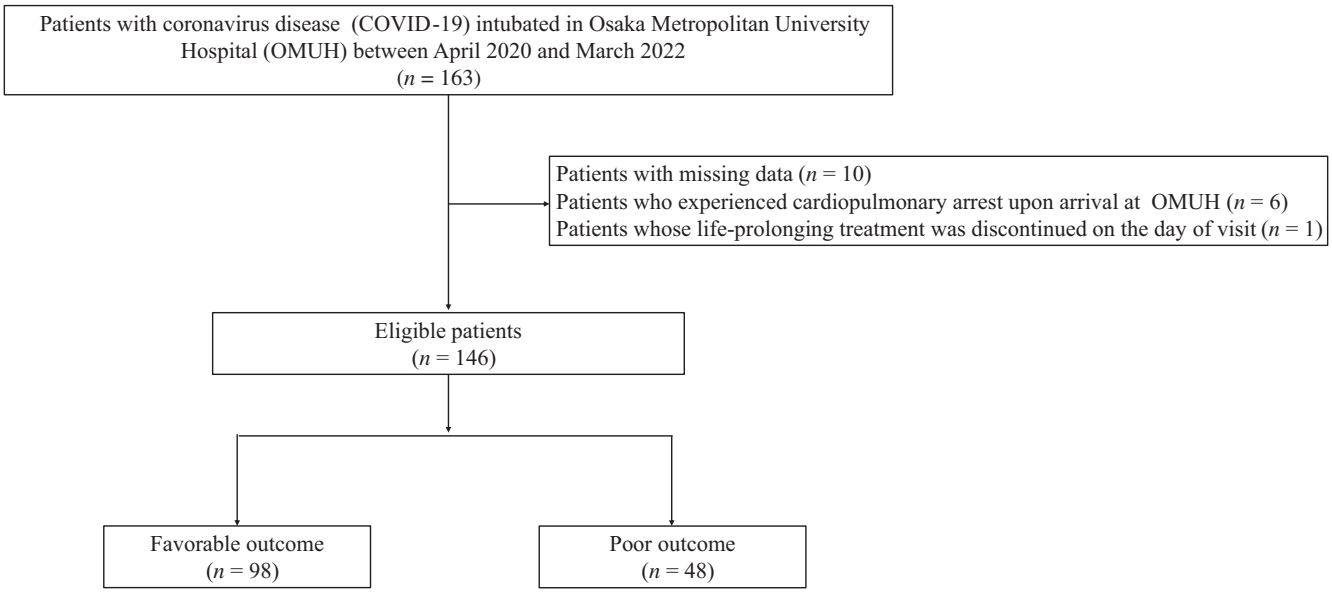

FIGURE 1 One hundred sixty-three patients with COVID-19 were included in this study. We excluded 10 patients with missing data, 6 patients who experienced cardiopulmonary arrest upon arrival, and 1 patient whose life-prolonging treatment was discontinued on the day of visit. The number of eligible patients was 146; among them, 98 patients had a favorable outcome, while 48 patients had a poor outcome.

TABLE 1 Baseline characteristics of patients with COVID-19 at the time of intubation and outcomes.

		Total		Favorable outcome		Poor outcome		
		(*n* = 146)		(*n* = 98)		(*n* = 48)		*p* value
Age, years	Median (IQR)	63	(55–74)	58	(53–70)	73	(64–79)	<0.001
<65	*n* (%)	77	(52.7)	65	(66.3)	12	(25.0)	<0.001
65–74	*n* (%)	35	(24.0)	19	(19.4)	16	(33.3)	0.064
≥75	*n* (%)	34	(23.3)	14	(14.3)	20	(41.7)	<0.001
Male	*n* (%)	123	(84.2)	85	(86.7)	38	(79.2)	0.238
Body mass index	Median (IQR)	24	(22.0–27.4)	24.4	(22.3–27.9)	23.5	(21.5–27.1)	0.420
≥30	*n* (%)	26	(17.8)	17	(17.3)	9	(18.8)	0.835
Ethnicity								
Japanese	*n* (%)	145	(99.3)	98	(100.0)	47	(97.9)	0.329
Others	*n* (%)	1	(0.7)	0	(0.0)	1	(2.1)	0.329
Smoking history	*n* (%)	41	(28.1)	26	(26.5)	15	(31.3)	0.551
Vaccination history	*n* (%)	16	(11.0)	13	(13.3)	3	(6.3)	0.145
Medical history								
Diabetes mellitus	*n* (%)	47	(32.2)	35	(35.7)	12	(25.0)	0.193
Cardiovascular diseases including hypertension	*n* (%)	83	(56.8)	50	(51.0)	33	(68.8)	0.042
Chronic respiratory disease	*n* (%)	22	(15.1)	14	(14.3)	8	(16.7)	0.706
Chronic kidney disease	*n* (%)	25	(17.1)	13	(13.3)	12	(25.0)	0.077
End-stage kidney disease[a]	*n* (%)	12	(8.2)	7	(7.1)	5	(10.4)	0.543
Hematopoietic disease	*n* (%)	5	(3.4)	3	(3.1)	2	(4.2)	0.664
Malignant neoplasm	*n* (%)	15	(10.3)	9	(9.2)	6	(12.5)	0.535
Receiving chemotherapy in the last 12 months	*n* (%)	2	(1.4)	1	(1.0)	1	(2.1)	0.551
SOFA score								
Respiration	Median (IQR)	2	(2–3)	2	(1–3)	3	(2–3)	<0.001
Coagulation	Median (IQR)	0	(0–1)	0	(0–1)	0	(0–0)	0.159
Liver	Median (IQR)	0	(0–0)	0	(0–0)	0	(0–0)	0.094
Cardiovascular	Median (IQR)	0	(0–0)	0	(0–0)	0	(0–0)	0.153
Central nervous system	Median (IQR)	0	(0–0)	0	(0–0)	0	(0–0)	0.306
Renal	Median (IQR)	0	(0–1)	0	(0–0)	0	(0–1)	0.020
Laboratory data								
HbA1c (%)	Median (IQR)	6.2	(5.8–7.2)	6.3	(5.8–7.3)	6.2	(5.9–7.0)	0.663
Therapeutic drug								
Steroid	*n* (%)	143	(97.9)	96	(98.0)	47	(97.9)	1.000
Remdesivir	*n* (%)	124	(84.9)	87	(88.8)	37	(77.1)	0.064
Tocilizumab	*n* (%)	16	(11.0)	9	(9.2)	7	(14.6)	0.327
Balicitinib	*n* (%)	45	(30.8)	37	(37.8)	8	(16.7)	0.010
Molnupiravir	*n* (%)	0	(0.0)	0	(0.0)	0	(0.0)	N/A[c]
Antithrombotic drug	*n* (%)	141	(96.6)	96	(98.0)	45	(93.8)	0.598
Outcome								
Weaning of mechanical ventilation	*n* (%)	98	(67.1)	98	(100.0)	0	(0.0)	
Mortality	*n* (%)	33	(22.6)	0	(0.0)	33	(68.8)	
Ventilator-free days within 14 days after intubation	Median (IQR)	3	(0–8)	7	(3–9)	0	(0–0)	

Abbreviations: HbA1c, hemoglobin A1C; N/A, not applicable; SOFA, Sequential Organ Failure Assessment.

[a]Requiring hemodialysis or kidney transplantation.

TABLE 2 Multivariate regression analysis of factors associated with weaning of patients with COVID-19 from mechanical ventilation.

Variable	Adjusted OR	95% CI	*p* value
Age, years			
<65	1.000	(reference)	
65–74	0.168	0.060–0.476	0.001
≥75	0.121	0.039–0.372	<0.001
Male	1.279	0.427–3.832	0.661
BMI ≥ 30	0.849	0.276–2.607	0.774
Vaccination history	5.655	1.030–31.054	0.046
Existing CVD including hypertension	1.086	0.437–2.701	0.859
Existing CKD	1.172	0.281–4.890	0.827
SOFA respiration score on intubation	0.007	0.337–0.839	0.007
SOFA renal score on intubation	0.708	0.444–1.130	0.148

Note: The forced-entry method was adopted as the variable imputation method for multivariate analysis. The *p* value for the analytical model was <0.001. Hosmer–Lemeshow test: $p = 0.088$; the model predictive value was 67.1%.

Abbreviations; BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; CVD, cardiovascular disease; OR, odds ratio; SOFA, Sequential Organ Failure Assessment.

TABLE 3 Multivariate regression analysis of factors associated with mortality among patients with COVID-19 requiring mechanical ventilation.

Variable	Adjusted OR	95% CI	*p* value
Age, years			
<65	1.000	(reference)	
65–74	5.405	1.643–17.786	0.005
≥75	6.531	1.884–22.637	0.003
Male	0.775	0.246–2.443	0.664
BMI ≥ 30	1.813	0.552–5.947	0.326
Vaccination history	0.404	0.070–2.342	0.312
Existing CVD including hypertension	0.962	0.351–2.633	0.940
Existing CKD	0.614	0.133–2.828	0.532
SOFA respiration score on intubation	2.384	1.362–4.173	0.002
SOFA renal score on intubation	1.491	0.929–2.394	0.098

Note: The forced-entry method was adopted as the variable imputation method for multivariate analysis. The *p* value for the analytical model was <0.001. Hosmer–Lemeshow test: $p = 0.290$; the model predictive value was 77.4%.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; CVD, cardiovascular disease; OR, odds ratio; SOFA, Sequential Organ Failure Assessment.

independent variables as they were significantly different in univariate analyses (Table 1), while BMI, vaccination history, and existing chronic kidney disease were used as independent variables; these variables were suggested to be associated with the outcomes in previous studies, as mentioned in the introduction. In this study, age, vaccination history, and SOFA respiration score were significantly associated with ventilator weaning.

Secondary outcome

We examined the factors associated with mortality and ventilator-free days within 14 days after intubation using multiple logistic regression and multiple linear regression models. The same primary outcome variables were used as independent variables. Age and SOFA respiration score were associated with mortality (Table 3). Higher age group and respiration and renal SOFA scores were significantly associated with a decreased number of ventilator-free days. Vaccination history was associated with increased number of ventilator-free days (Table 4).

DISCUSSION

In this study, we examined the association between information at the time of intubation and outcomes of patients with COVID-19 requiring mechanical ventilation using multivariate analysis and found significant associations between outcomes of age, vaccination history, and SOFA respiration score.

Previous studies have suggested a relationship between age, respiratory status at the time of intubation, and the outcome of COVID-19.[17,18] Additionally, this study found a significant association between COVID-19 vaccination history and COVID-19 outcomes in patients requiring mechanical ventilation. A meta-analysis reported that a history of COVID-19 vaccination was associated with the reduction in COVID-19 exacerbation and mortality.[19] Our study showed that COVID-19 vaccination can inhibit the progression of COVID-19 after the initiation of mechanical ventilation.

This study showed a significant association between renal function at the time of intubation and ventilator-free days within 14 days after intubation. During the PubMed database search, we were unable to find studies that examined the association between the outcomes of COVID-19 requiring mechanical ventilation and renal function on the day of intubation. The pathogenesis of kidney injury caused by COVID-19 can be explained by the following two possible mechanisms: ischemia of the kidney due to thrombogenesis[4] and entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into the body. The SARS-CoV-2 virus enters the body through the angiotensin converting enzyme-2 (ACE2) receptor. The lungs and proximal renal tubules express high levels of ACE2 receptors.[20] In patients with COVID-19, SARS-CoV-2 fragments were detected in the urine within 2–3 weeks after infection,[20] and histological changes in ACE2 receptors in the proximal tubules and podocytes were reported.[20–22] The SARS-CoV-2 virus could

TABLE 4 Multivariate regression of factors associated with ventilation-free days within 14 days of intubation of patients with COVID-19.

Variable	Beta	*t*	95% CI	*p* value
Age, years				
<65	(reference)			
65–74	−2.493	−3.468	−3.915 to −1.071	0.001
≥75	−2.449	−3.181	−3.972 to −0.927	0.002
Male	−0.717	−0.906	−2.282–0.848	0.366
BMI ≥ 30	0.426	0.541	−1.131–1.983	0.589
Vaccination history	2.175	2.296	0.302–4.047	0.023
Existing CVD including hypertension	−1.104	−1.778	−2.333–0.124	0.078
Existing CKD	0.538	0.521	−1.503–2.578	0.603
SOFA respiration score on intubation	−1.027	−0.253	−1.620 to −0.435	0.001
SOFA renal score on intubation	−0.803	−0.224	−1.482 to −0.124	0.021

Note: The forced-entry method was adopted as the variable imputation method for multivariate analysis. The *p* value of the regression equation was <0.001. *R*, 0.572; R^2, 0.327; adjusted R^2, 0.282.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; CVD, cardiovascular disease; SOFA, Sequential Organ Failure Assessment.

directly cause renal damage.[22] A previous study undertaken by the European Renal Association–European Dialysis and Transplantation Association showed that a history of chronic kidney disease might affect the outcome of patients with severe COVID-19.[6] However, the medical history of chronic kidney disease did not have a significant association with ventilator-free days in this study. The existence of acute kidney injury as a comorbidity in patients with COVID-19 might reflect the intensity of the infection. The occurrence of acute kidney injury could have exacerbated the outcome.

Although this was a single-center study in Japan, the variables related to the outcomes were not significantly different from those reported in other countries. No correlation was observed between obesity and cardiovascular disease in this study, which have been associated with outcomes in previous studies.[6] Racial differences and medications, as well as the lack of cases, might have influenced our results. If a larger number of cases were included, it might be possible to identify the accurate factors associated with the outcomes.

As most of the participants in this study were Japanese, it is difficult to generalize these results to other countries in terms of race and treatment policies. However, our results can be possibly generalized to medical institutions managing patients with COVID-19 requiring mechanical ventilation in Japan.

Limitations

This study has some limitations. First, we did not discuss the different variants of SARS-CoV-2, the type and number of times that COVID-19 vaccination was given, or the interval between vaccination and the onset of COVID-19. Second, the patients' treatments were not sufficiently recorded until they were admitted to our hospital. Third, we were unable to monitor the subsequent outcomes of the patients who were transferred to our hospital. Fourth, a significant but unadjustable difference was observed between favorable and poor outcomes associated with the use of baricitinib. Finally, as this was an observational study, confounding factors could have existed.

CONCLUSION

Age, SOFA respiration score, and COVID-19 vaccination history at the time of intubation could be associated with outcomes in patients with COVID-19 requiring mechanical ventilation.

ACKNOWLEDGMENTS

We thank Mari Shimokawa for her support in contributing to the acquisition of the data. We would like to thank Editage for English language editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

Approval of the research protocol: This study was approved by the Institutional Review Board of Osaka Metropolitan University Hospital (approval number: 2022–140).
Informed consent: We applied an opt-out method on the website to obtain patient consent.
Registry and registration no. of the study/trial: N/A.
Animal studies: N/A.

ORCID

Ryo Deguchi https://orcid.org/0000-0002-8831-2388
Kenichiro Uchida https://orcid.org/0000-0002-3673-6007

REFERENCES

1. WHO Director. General's opening remarks at the media briefing on COVID-19, 2020 [Internet]. [Cited: 2023 Jan 13]. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
2. WHO. Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data [Internet]. [Cited: 2023 Jan 13]. Available from: https://covid19.who.int
3. A specific website for COVID-19 [Internet] [Cited: 2023 Jan 13]. Available from: https://www3.nhk.or.jp/news/special/coronavirus/data-all/
4. Sastry S, Cuomo F, Muthusamy J. COVID-19 and thrombosis: the role of hemodynamics. Thromb Res. 2022;212:51–7.
5. Clark A, Jit M, Warren-Gash C, Guthrie B, Wang HHX, Mercer SW, et al. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study. Lancet glob. Health. 2020;8:e1003–17-e1017–7.
6. ERA-EDTA Council, ERACODA Working Group. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. Nephrol Dial Transplant. 2021;36:87–94.
7. Vasbinder A, Meloche C, Azam TU, Anderson E, Catalan T, Shadid H, et al. Relationship between preexisting cardiovascular disease and death and cardiovascular outcomes in critically ill patients with COVID-19. Circ Cardiovasc Qual Outcomes. 2022;15:e008942.
8. Drożdżal S, Rosik J, Lechowicz K, Machaj F, Szostak B, Przybyciński J, et al. An update on drugs with therapeutic potential for SARS-CoV-2 (COVID-19) treatment. Drug Resist Updat. 2021;59:100794.
9. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne JAC, Murthy S, Diaz JV, Slutsky AS, Villar J, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. JAMA. 2020;324:1330–41.
10. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the treatment of Covid-19 – final report. N Engl J Med. 2020;383:1813–26.
11. Lin Z, Niu J, Xu Y, Qin L, Ding J, Zhou L. Clinical efficacy and adverse events of baricitinib treatment for coronavirus disease-2019 (COVID-19): a systematic review and meta-analysis. J Med Virol. 2022;94:1523–34.
12. Jayk Bernal A, Gomes da Silva MM, Musungaie DB, Kovalchuk E, Gonzalez A, Delos Reyes V, et al. Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. N Engl J Med. 2022;386:509–20.
13. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. J Thromb Haemost. 2020;18:1559–61.
14. Domi H, Matsuura H, Kuroda M, Yoshida M, Yamamura H. Simple prognostic factors and change of inflammatory markers in patients with severe coronavirus disease 2019: a single-center observational study. Acute Med Surg. 2021;8:e683.
15. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. Int J Surg. 2014;12:1500–24.
16. Bellou V, Tzoulaki I, van Smeden M, Moons KGM, Evangelou E, Belbasis L. Prognostic factors for adverse outcomes in patients with COVID-19: a field-wide systematic review and meta-analysis. Eur Respir J. 2022;59:2002964.
17. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. BMC Infect Dis. 2021;21:855.
18. Sekihara K, Shibasaki T, Okamoto T, Matsumoto C, Ito K, Fujimoto K, et al. Poor prognosis of patients with severe COVID-19 admitted to an infectious disease intensive care unit during the pandemic caused by the Delta variant in Japan. Glob Health Med. 2022;4:122–8.
19. Huang YZ, Kuan CC. Vaccination to reduce severe COVID-19 and mortality in COVID-19 patients: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci. 2022;26:1770–6.
20. Ahmadian E, Hosseiniyan Khatibi SM, Razi Soofiyani S, Abediazar S, Shoja MM, Ardalan M, et al. Covid-19 and kidney injury: pathophysiology and molecular mechanisms. Rev Med Virol. 2021;31:e2176.
21. Su H, Yang M, Wan C, Yi LX, Tang F, Zhu HY, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. Kidney Int. 2020;98:219–27.
22. Akilesh S, Nast CC, Yamashita M, Henriksen K, Charu V, Troxell ML, et al. Multicenter clinicopathologic correlation of kidney biopsies performed in COVID-19 patients presenting with acute kidney injury or proteinuria. Am J Kidney Dis. 2021;77:82–93.e1.

How to cite this article: Deguchi R, Nishimura T, Matsuo K, Wakita F, Kawamoto A, Uchida K, et al. Factors associated with the outcome of patients with COVID-19 requiring mechanical ventilation: A single-center observational study in Japan. Acute Med Surg. 2023;10:e868. https://doi.org/10.1002/ams2.868