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Clinical epidemiology and outcomes of COVID-19 patients with extracorporeal membrane oxygenation support in Japan: a retrospective study

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A R T I C L E I N F O

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COVID-19
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A B S T R A C T

Objective: To elucidate the clinical epidemiology and outcomes of patients with COVID-19 who received extracorporeal membrane oxygenation (ECMO) in the Osaka Prefecture, Japan.

Methods: We conducted a retrospective study of COVID-19 patients who received ECMO. Among patients diagnosed with COVID-19 between January 29 and November 9, 2020, we targeted patients who received ECMO. The outcome was all-cause mortality. The baseline characteristics of the COVID-19 patients who received ECMO were summarized according to the outcome. A univariable logistic regression model was applied to evaluate the association of each factor (sex, age group, city of residence, presence of comorbidities, presence of close contact, use of dialysis, and wave) with all-cause mortality. Odds ratios (ORs) with 95% confidence intervals were calculated.

Results: Among the 14,864 patients diagnosed with COVID-19 during the study period, 39 patients received ECMO. Fourteen patients (35.9%) died. All patients aged 30–39 years survived, whereas all patients aged ≥80 years died. Higher mortality was observed among patients in the higher age group, and the *P* value for trend was significant (*P* value for trend: 0.04).

Conclusions: Of the 14,864 COVID-19 patients in Osaka Prefecture until November 2020, 39 underwent ECMO. Of these, 14 died.

Introduction

COVID-19 has spread to almost every country worldwide. In Japan, 419,015 COVID-19 cases were confirmed as of February 17, 2021 (Ministry of Health LaW 2021). The Osaka Prefecture, the largest metropolitan area in western Japan, has the second-highest number of COVID-19 patients in Japan (Hirayama et al., 2021, Takeuchi et al., 2020a, Takeuchi et al., 2020b). The cumulative number of confirmed COVID-19 cases in the Osaka Prefecture was 46,247 as of February 17, 2021 (Osaka Prefectural Government, 2021).

Some COVID-19 patients develop severe disease, including severe acute respiratory distress syndrome (ARDS) (Barbaro et al., 2020, Schmidt et al., 2020). Extracorporeal membrane oxygenation (ECMO) support is used to treat lung injury in these severe ARDS patients (Barbaro et al., 2020, Combes et al., 2018, Schmidt et al., 2020). Previous studies outside Japan have reported the characteristics and outcomes of COVID-19 patients who received ECMO (Barbaro et al., 2020, Bartlett et al., 2020, Biancari et al., 2021, Haiduc et al., 2020, Ma et al., 2020, Ramanathan et al., 2020, Schmidt et al., 2020, Shaefi et al., 2021, Zhu et al., 2021).

Although a previous study by the “Japan ECMOnet for COVID-19” (a nationwide registry of COVID-19 patients with ECMO) reported the characteristics of the first 14 COVID-19 cases that involved ECMO use (Takeda, 2020), details on the clinical epidemiology and outcomes of COVID-19 patients treated using ECMO in Japan are not fully understood. In this study, we aimed to elucidate the clinical epidemiology

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and outcomes of COVID-19 patients who received ECMO by conducting a retrospective study in the Osaka Prefecture, Japan.

Methods

Study design, data collection and patients

We conducted a retrospective study of COVID-19 patients who received ECMO in the Osaka Prefecture, Japan. Details of the data collection are described elsewhere (Hirayama et al., 2021, Katayama et al., 2021, Tanaka et al., 2021, Zha et al., 2021). In the Osaka Prefecture, in accordance with the Infectious Diseases Control Law (Osaka Prefectural Government, 2020c, Hirayama et al., 2021), an investigation was conducted to collect epidemiological information on COVID-19 patients (Osaka Prefectural Government, 2020c, Hirayama et al., 2021); therefore, the requirement for informed consent was waived. We targeted patients who received ECMO among COVID-19 patients registered in the system by the end of November 2020 and whose follow-up was complete. Of the COVID-19 cases enrolled by the data collection system from January to November 2020, we only considered those from Osaka Prefecture with a complete follow-up history. Our study was approved by the Osaka University Hospital Ethical Review Committee (reference no. 20397).

Measurements

Information on COVID-19 patients who received ECMO was collected, including sex, age, city of residence, comorbidities, cluster, close contact with infected individuals, use of dialysis, onset date, symptoms at diagnosis, date of medical treatment, date of hospital admission, date of discharge, reason for discharge, date a change in symptoms occurred, date of ECMO initiation, date of ECMO termination and date of death (for patients who died during the observation period). The onset date was defined as the date when symptoms appeared. If the onset date was missing, we substituted the onset date with the date of medical treatment, the date of hospital admission, or the date a change in symptoms occurred, whichever occurred first. The age groups were clustered for every 10 years in the available data. ECMO patients were defined as those with information on either the date of ECMO initiation or termination.

Following the definitions outlined by Osaka Prefecture, we defined COVID-19 infection waves according to the onset date as follows: the first wave (until 13 June 2020), the second wave (from 14 June to 9 October 2020), and the third wave (from 10 October 2020) (Osaka Prefectural Government, 2020a, Osaka Prefectural Government, 2020b). High-risk comorbidities, such as diabetes; heart failure; respiratory diseases, including chronic obstructive pulmonary disease; chronic kidney diseases requiring dialysis; and the use of immunosuppressants and anticancer drugs, were summarized in this database (Osaka Prefectural Government, 2020b). A cluster was defined as a group of 5 or more COVID-19 positive cases with an epidemiological link to the primary identified COVID-19 cases identified from various facilities, such as nursing homes, medical institutions and restaurants (National Institute of Infectious Diseases, 2021). Clusters were categorized as: no, medical institution and others. Local public health centers identified close contacts as those who lived with the confirmed cases or had prolonged contact with the patients; those who examined, nursed or cared for the confirmed cases without personal protection equipment; those who were likely to have had direct contact with contaminated materials; or those who had contact with confirmed cases for >15 min at a short distance (approximately 1 m) without personal protection equipment (National Institute of Infectious Diseases, 2021). Symptoms at diagnosis were classified as follows: asymptomatic, mild (cough only, without breathlessness or respiratory symptoms), moderate (breathlessness, pneumonia or necessity of oxygen therapy) and severe (necessity of stay in the intensive care unit or the use of mechanical ventilation) (Hirayama et al., 2021). Hospitalized patients were identified through having one of the following data items: date of hospitalization and/or discharge or reason for discharge.

Outcomes and follow-up period

The outcome was all-cause mortality. Follow-up started on the day of ECMO initiation and ended on the day of ECMO termination or the day the patient died, whichever occurred first. To deal with the situation where the day of ECMO initiation was equal to the day of ECMO termination, we added one day to the observation period for all the patients.

Statistical analyses

The baseline characteristics of the COVID-19 patients who received ECMO in the Osaka Prefecture, Japan, were summarized according to the outcome (survivors/non-survivors). Categorical variables were summarized by count and proportion, and continuous variables were summarized by median and interquartile range. The distribution of follow-up status (survivors under follow-up, subjects with discharged alive or released alive, deaths) of the study population was summarized by time since ECMO initiation (10 days, 20 days, 30 days, 40 days, 45 days). In this analysis, patients with missing information on the date of ECMO initiation were excluded. A univariable logistic regression model was used to evaluate the association of each factor (sex, age group, city of residence, presence of comorbidities, presence of close contact, use of dialysis, and wave) with all-cause mortality. The reference category was as follows: sex, male; age group, 60–69 years; city of residence, Osaka City; presence of comorbidities, without; presence of having a close contact, without; use of dialysis, without; and wave, first wave. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

All *P* values were two-tailed, and $P<0.05$ was considered statistically significant. All statistical analyses were conducted using STATA version 14.0 MP software (StataCorp LP).

Results

In the Osaka Prefecture, Japan, 14,864 patients were diagnosed with COVID-19 between January 29 and November 9, 2020. Among them, 39 patients received ECMO support (Figure 1). Table 1 describes the baseline characteristics of the 39 COVID-19 patients who received ECMO according to the outcome (survivors/non-survivors). Among the 39 patients, 25 (64.1%) survived, and 14 (35.9%) died. All female patients survived, whereas 39% of the male patients died. All patients in the youngest age group (30–39 years) survived, whereas all the patients in the highest age group (≥80 years) died. Fifty percent of patients with comorbidities died, whereas 26% of patients without comorbidities died. The median number of days from onset to ECMO initiation was shorter among patients who died (12 days) than among those who survived (14 days). The median days from ECMO initiation to ECMO termination were also shorter among patients who died (10 days) than among those who survived (15 days).

Table 2 shows the distribution of the follow-up status at each point (10 days, 20 days, 30 days, 40 days, 45 days) from ECMO initiation. In this analysis, 2 patients with missing information on the date of ECMO initiation were excluded. Table 3 shows the results of the univariable logistic regression analysis. Higher mortality was observed among patients in the higher age group, and the *P*-value for the trend was significant ($P=0.04$). Other factors were not significantly associated with mortality.

Discussion

To the best of our knowledge, the present study is the first in Japan to elucidate in detail the clinical epidemiology and outcomes of COVID-19

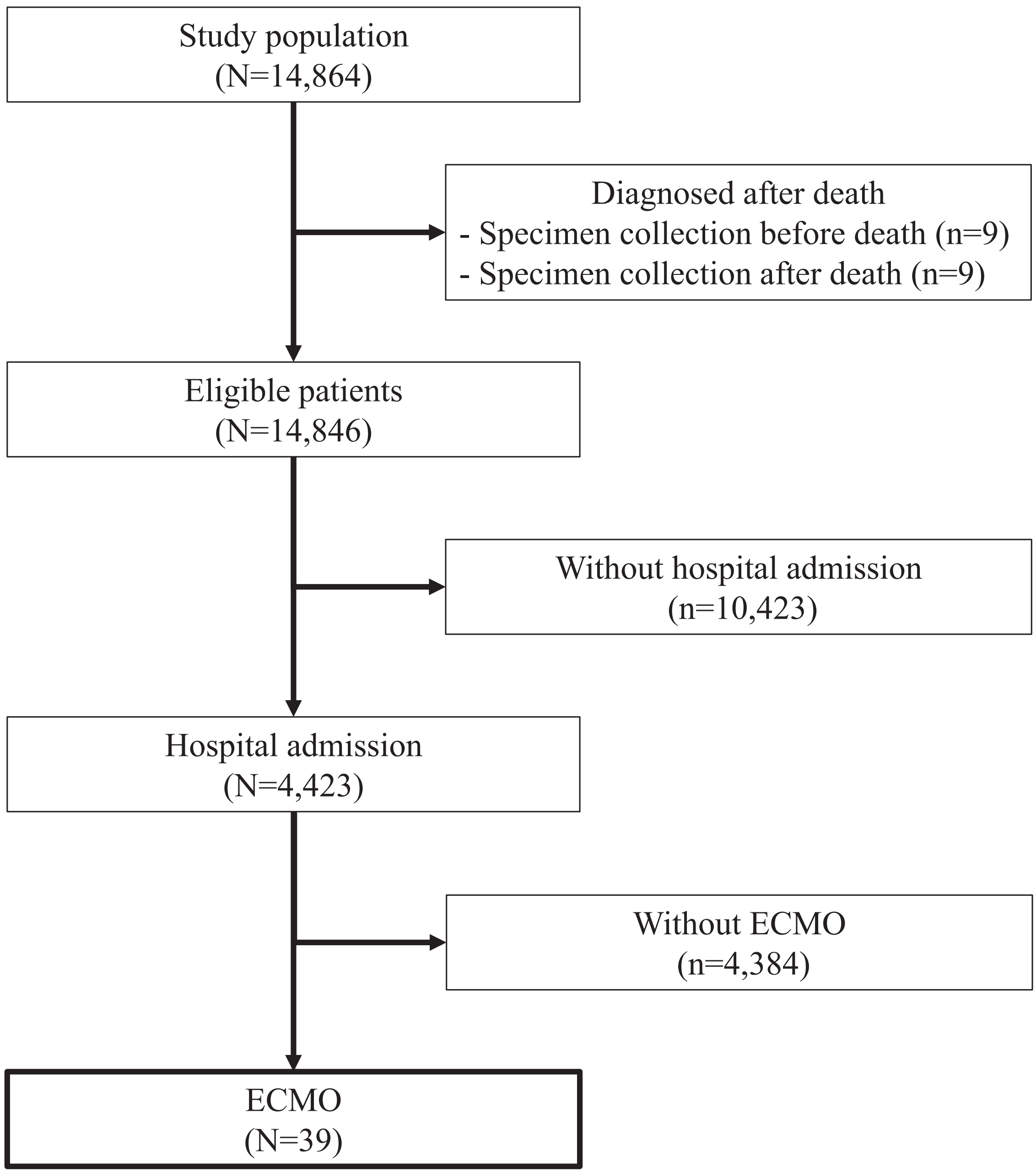

Figure 1. Flow diagram of patients with extracorporeal membrane oxygenation (ECMO).

patients treated using ECMO. Our retrospective analysis of 39 COVID-19 patients who received ECMO in the Osaka Prefecture, Japan, revealed a mortality rate of 35.9% (14 of 39 patients died). All patients aged 30–39 years survived, whereas all patients aged ≥80 died. The most noteworthy result of our findings is that 65% (13 of 20) of patients aged 60–79 years survived.

Studies conducted in other countries report a similar mortality rate for COVID-19 patients who received ECMO (Barbaro et al., 2020, Bartlett et al., 2020, Biancari et al., 2021, Haiduc et al., 2020, Ma et al., 2020, Ramanathan et al., 2020, Schmidt et al., 2020, Shaefi et al., 2021, Zhu et al., 2021). In the Extracorporeal Life Support Organization (ELSO) registry, the in-hospital mortality 30, 60 and 90 days after the initiation of ECMO support was estimated to be approximately 30%, 37% and 37%, respectively (Barbaro et al., 2020). A study using data from the Study of the Treatment and Outcomes in Critically Ill Patients with COVID-19 (STOP-COVID) reported that 34.6% of COVID patients who received ECMO died within 60 days from ECMO initiation (Shaefi et al., 2021). Although the mortality observed in the present study was similar to that of previous studies, a longer follow-up period is needed to determine the mortality of COVID-19 patients who received ECMO in Japan.

Similar to our findings, studies in other countries have reported that higher age was associated with higher mortality among COVID-19 patients who received ECMO. In a report from the ELSO registry (Barbaro et al., 2020), significantly higher mortality was observed among patients aged ≥60 years compared with patients aged 16–39. Another study from 5 European countries reported that the proportion of patients aged >60 years was higher among 6-month non-survivors than among 6-month survivors (Biancari et al., 2021). In a statement from a shared research group in Japan, higher age was known to be one of the adverse prognostic factors among COVID-19 patients who received ECMO (Shared Research Group in Ministry of Health, 2020). ECMO sup-

Table 1
Characteristics of the study population

	Survivors N = 25	Non-survivors N = 14	Total N = 39
Sex*			
Male	22 (61)	14 (39)	36 (100)
Female	3 (100)	0 (0)	3 (100)
Age group (years)*			
30–39	2 (100)	0 (0)	2 (100)
40–49	3 (75)	1 (25)	4 (100)
50–59	7 (78)	2 (22)	9 (100)
60–69	7 (58)	5 (42)	12 (100)
70–79	6 (75)	2 (25)	8 (100)
≥80	0 (0)	4 (100)	4 (100)
City of residence*			
Osaka city	10 (56)	8 (44)	18 (100)
Other cities	15 (71)	6 (29)	21 (100)
Comorbidities*			
Without	17 (74)	6 (26)	23 (100)
With	8 (50)	8 (50)	16 (100)
Having close contact*			
Without	22 (67)	11 (33)	33 (100)
With	3 (50)	3 (50)	6 (100)
Use of dialysis*			
Without	24 (69)	11 (31)	35 (100)
With	1 (25)	3 (75)	4 (100)
Wave*			
First wave (January 29, 2020 – June 13, 2020)	15 (63)	9 (38)	24 (100)
Second wave (June 14, 2020 – November 9, 2020)	10 (67)	5 (33)	15 (100)
Days from onset to extracorporeal membrane oxygenation initiation†	14 (10–18)	12 (9–14)	12 (10–16)
Days from extracorporeal membrane oxygenation initiation to ECMO termination†	15 (10–19)	10 (4–15)	12 (8–19)

*N (%) is shown.
†Median and interquartile range are shown.
ECMO with extracorporeal membrane oxygenation.

port may therefore not be recommended for COVID-19 patients aged ≥80 years because of the higher mortality among these patients.

Due to a lack of knowledge of the virus and clinical treatment experience at the beginning of the COVID-19 epidemic, the criteria to proceed to ECMO support in Japan were based on the respiratory status of progressive deterioration, with PEEP10 cmH_2O and P/F <100, and were final judged comprehensively by clinicians at each institution (Ministry of Health Labour and Welfare, 2021, ECMOnet, 2020, Shared Research Group in Ministry of Health, 2020). Therefore, there is no definite age cutoff for decisions to proceed with ECMO support in Japan. Asai et al. reported data on elderly patients with COVID-19 from Japan, describing ECMO introduction in patients aged into their 80s (Asai et al., 2022). In Badulak et al.'s study, no age cutoff of ECMO introduction is specified (Badulak et al., 2021). In the ELSO registry analysis, some patients appear to be >70 years old, and the results are similar to those of our study, indicating that proceeding to ECMO support for patients >75 years old does not effectively improve the prognosis of severe and critical patients with COVID-19 (Bartlett et al., 2020, Broman et al., 2021).

In our study, there was a small percentage of women (8% [3 of 39]), and there were no deaths among female patients receiving ECMO support. The present investigation revealed a gender difference in terms of whether women had a lower mortality, which was also found in the ELSO registry (Barbaro et al., 2020). Although the reason for the variation in mortality is unclear, it may be associated with the differences in the immunological response to COVID-19 between the genders. However, this study lacked information on smoking status, which may have obscured confounding factors in the gender difference (Tanaka et al., 2021). According to a recent study regarding smoking status and severe illness in hospitalized COVID-19 patients in Japan (Matsushita et al., 2021), smokers are more likely to develop smoking-related diseases such as cardiovascular disease, cancer and lung disease. These comorbidities contribute to the risk of severe and critical COVID-19, resulting in increased mortality. Moreover, a systematic review and meta-analysis reported that women were less likely to receive mechanical ventilation or renal replacement therapy than men and had shorter intensive care unit stays. This is the result of a complex interaction between physiological and societal factors (Asai et al., 2022). Additional research on gender differences in COVID-19 patients is needed in Japan and globally.

Potential limitations

This study had several limitations. First, as already mentioned, we did not provide detailed information on the types of comorbidities. Second, following active epidemiological investigation, the data did not include detail on the clinical characteristics of COVID-19 patients who received ECMO, such as the Sequential Organ Failure Assessment or Respiratory Extracorporeal Membrane Oxygenation Survival Prediction scores, ventilation parameters, laboratory parameters or blood gases. Our study also did not report whether ECMO was veno-venous or veno-arterial; no studies in Japan report this information. According to the literature from other countries, 99% of ECMO is veno-venous. Further large-scale observational studies to improve the prognosis of COVID-19 patients receiving ECMO support in Japan are needed. Third, unmeasured confounding factors might have affected the results of our study. Finally, we could not conduct multivariable analyses because of the limited sample size. However, while the sample size is limited, to our knowledge, the majority of papers focusing on ECMO support in Japan are case reports, and no investigations from population-based epidemiological data have been published. Given the scarcity of evidence from Japan, our study is essential and likely to be used as fundamental data that will connect to the next step of research on ECMO support in severe and critical COVID-19 patients.

Author contributions

TT, LZ and TK conceived the study design. TT drafted the manuscript, and TT, LZ and KT performed the statistical analyses. YK, TSo, AH, SK, TSh and TK provided clinical expertise and critically revised the

Table 2
Distribution of follow-up status at each point from ECMO initiation

Period	10 days	20 days	30 days	40 days	45 days
Survivors under follow-up, n (%)	26 (70)	8 (22)	4 (11)	1 (3)	1 (3)
Subjects with discharged alive or released alive, n (%)	4 (11)	18 (49)	20 (54)	23 (62)	23 (62)
Deaths, n (%)	7 (19)	11 (30)	13 (35)	13 (35)	13 (35)
Total, N	37 (100)	37 (100)	37 (100)	37 (100)	37 (100)

*Two patients with missing information on the date of ECMO initiation were excluded.
ECMO=extracorporeal membrane oxygenation

Table 3
Results of univariable logistic regression analysis

	Odds ratio	95% CI
Sex		
Male	Reference	
Female	Unconverged	
Age group (years)		
30–39	Unconverged	
40–49	0.47	0.04–5.90
50–59	0.40	0.06–2.80
60–69	Reference	
70–79	0.47	0.07–3.34
≥80	Unconverged	
P for trend	0.04	
City of residence		
Osaka city	Reference	
Other cities	0.50	0.13–1.88
Comorbidities		
Without	Reference	
With	2.83	0.73–10.95
Having close contact		
Without	Reference	
With	2.00	0.35–11.58
Use of dialysis		
Without	Reference	
With	6.55	0.61–70.23
Wave		
First wave (January 29 – June 13, 2020)	Reference	
Second wave (June 14 – November 9, 2020)	0.83	0.22–3.23

manuscript. All authors approved the version for publication. TK oversaw the writing of the manuscript.

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Ethical Approval

The study was approved by the Osaka University Hospital Ethical Review Committee (reference no. 20397).

Conflict of Interest

All authors declare no conflict of interest

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References

Asai Y, Nomoto H, Hayakawa K, Matsunaga N, Tsuzuki S, Terada M, et al. Comorbidities as Risk Factors for Severe Disease in Hospitalized Elderly COVID-19 Patients by Different Age-Groups in Japan. Gerontology 2022:1–11.
Badulak J, Antonini MV, Stead CM, Shekerdemian L, Raman L, Paden ML, et al. Extracorporeal Membrane Oxygenation for COVID-19: Updated 2021 Guidelines from the Extracorporeal Life Support Organization. Asaio j 2021;67(5):485–95.
Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. The Lancet 2020;396(10257):1071–8.
Bartlett RH, Ogino MT, Brodie D, McMullan DM, Lorusso R, MacLaren G, et al. Initial ELSO guidance document: ECMO for COVID-19 patients with severe cardiopulmonary failure. Asaio J 2020;66(5):472.
Biancari F, Mariscalco G, Dalén M, Settembre N, Welp H, Perrotti A, et al. Six-month survival after extracorporeal membrane oxygenation for severe COVID-19. J Cardioth and Vasc Anes 2021;35(7):1999–2006.
Broman LM, Eksborg S, Coco VL, De Piero ME, Belohlavek J, Lorusso R. Extracorporeal membrane oxygenation for COVID-19 during first and second waves. The Lancet Resp Med 2021;9(8) e80-e1.
Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. New Eng Jl of Med 2018;378(21):1965–75.
ECMOnet J. Introduction to Respiratory ECMO. 2020.
Haiduc AA, Alom S, Melamed N, Harky A. Role of extracorporeal membrane oxygenation in COVID-19: a systematic review. J of Card Surg 2020;35(10):2679–87.
Hirayama A, Masui J, Murayama A, Fujita S, Okamoto J, Tanaka J, et al. The characteristics and clinical course of patients with COVID-19 who received invasive mechanical ventilation in Osaka Japan. Int J of Infec Diseases 2021;102:282–4.
Katayama Y, Zha L, Kitamura T, Hirayama A, Takeuchi T, Tanaka K, et al. Characteristics and Outcomes of Pediatric COVID-19 Patients in Osaka Japan. Int J Environ Res and Public Health 2021;18(11):5911.
Ma X, Liang M, Ding M, Liu W, Ma H, Zhou X, et al. Extracorporeal membrane oxygenation (ECMO) in critically ill patients with coronavirus disease 2019 (COVID-19) pneumonia and acute respiratory distress syndrome (ARDS). Medical science monitor: international medical journal of experimental and clinical research 2020;26 e925364-1.
Matsushita Y, Yokoyama T, Hayakawa K, Matsunaga N, Ohtsu H, Saito S, et al. Smoking and severe illness in hospitalized COVID-19 patients in Japan. Int J Epidemiol 2021.
Ministry of Health LaW. COVID-19 Guide to Medical Treatment Version 5.3. 2021.
Ministry of Health LaWoJ. The Statistics of Patients with COVID-19.; 2021. Available from: https://www.mhlw.go.jp/stf/newpage_16794.html.
National Institute of Diseases. Guidelines for Conducting Active Epidemiological Surveillance of Patients with Novel. Coronavirus Infections 2021.
Osaka Prefectural Government. 27th Novel Coronavirus Response Headquarters. 2020a. Available from: http://www.pref.osaka.lg.jp/attach/38215/00371479/ikkatsu.pdf
Osaka Prefectural Government. Osaka Prefecture New Coronavirus Countermeasures Headquarters Meeting; 2020b. Available from: http://www.pref.osaka.lg.jp/kikaku_keikaku/sarscov2/.
Osaka Prefectural Government. The press release on providing COVID-19 patients data for academic research institutes; 2020c. Available from: http://www.pref.osaka.lg.jp/hodo/index.php?site=fumin&pageId=39707. [Accessed March 10 2021].
Osaka Prefectural Government. The Press Releases and Documents about COVID-19 Patients.; 2021. Available from: http://www.pref.osaka.lg.jp/iryo/osakakansensho/happyo.html.
Ramanathan K, Antognini D, Combes A, Paden M, Zakhary B, Ogino M, et al. Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases. The Lancet Respiratory Medicine 2020;8(5):518–26.
Schmidt M, Hajage D, Lebreton G, Monsel A, Voiriot G, Levy D, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. The Lancet Resp Med 2020;8(11):1121–31.
Shaefi S, Brenner SK, Gupta S, O'Gara BP, Krajewski ML, Charytan DM, et al. Extracorporeal membrane oxygenation in patients with severe respiratory failure from COVID-19. Inten care med 2021;47(2):208–21.
Shared Research Group in Ministry of Health LaWSRGfaRfRAoEaR-eIDaIoRM. Mechanical ventilation and extracorporeal membrane oxygenation for acute respira-

tory failure owing to COVID–19: basic concept. Nihon Kyu¯kyu¯ Igakkai Zasshi 2020;31(10):466–71.

Takeda S. Nationwide system to centralize decisions around extracorporeal membranous oxygenation use for severe COVID-19 pneumonia in Japan. Acute Med & Surg 2020;7(1).

Takeuchi T, Imanaka T, Katayama Y, Kitamura T, Sobue T, Shimazu T. Profile of patients with novel coronavirus disease 2019 (COVID-19) in Osaka Prefecture, Japan: a population-based descriptive study. Journal of Clinical Medicine 2020a;9(9): 2925.

Takeuchi T, Kitamura T, Hirayama A, Katayama Y, Shimazu T, Sobue T. Characteristics of patients with novel coronavirus disease (COVID-19) during the first surge versus the second surge of infections in Osaka Prefecture. Japan. Global Health & Medicine 2020b.

Tanaka K, Zha L, Kitamura T, Katayama Y, Takeuchi T, Komukai S, et al. Characteristics and outcomes of older patients with coronavirus disease 2019 in Japan. Geriat & Geron Int 2021.

Zha L, Sobue T, Takeuchi T, Tanaka K, Katayama Y, Komukai S, et al. Characteristics and Survival of Intensive Care Unit Patients with Coronavirus Disease in Osaka, Japan: A Retrospective Observational Study. J of Clin Med 2021;10(11):2477.

Zhu Y, Zhang M, Zhang R, Ye X, Wei J. Extracorporeal membrane oxygenation versus mechanical ventilation alone in adults with severe acute respiratory distress syndrome: A systematic review and meta-analysis. Int Jof Clin Prac 2021:e14046.