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## ORIGINAL ARTICLE

# Usefulness of the Yokohama Advanced Cardiopulmonary Help Team in patients with acute respiratory distress syndrome

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#### Abstract

Aim: To evaluate whether establishing an extracorporeal membrane oxygenation (ECMO) specialist team, termed the Yokohama Advanced Cardiopulmonary Help Team (YACHT), affected the outcomes and centralization of patients requiring ECMO in Yokohama-Yokosuka regions.

**Methods:** This retrospective observational study included patients aged  $\geq 18$  years and treated with venovenous-ECMO for severe acute respiratory distress syndrome (ARDS) from 2014 to 2023. The primary outcome was intensive care unit (ICU) mortality. The secondary outcomes included ICU-, mechanical ventilator-, and ECMOfree days and complications during the first 28 days.

Results: This study included 46 (12 without- and 34 with-YACHT) patients. Among with-YACHT patients, 24 were transferred to our hospital from other hospitals, 14 were assessed by dispatched ECMO physicians, and 9 were transferred after ECMO introduction. No without-YACHT patients were transferred from other hospitals. With-YACHT patients experienced coronavirus disease 2019-associated respiratory failure more frequently (0 vs. 27, p < 0.001) and had higher Acute Physiology and Chronic Health Evaluation II scores (19 vs. 24, p = 0.037) and lower Respiratory Extracorporeal Membrane Oxygenation Survival Prediction scores (4 vs. 2, p = 0.021). ICU mortality was not significantly different between the groups (2 vs. 4, p = 0.67). ICU- (14 vs. 9, p = 0.10), ventilator- (11 vs. 5, p = 0.01), and ECMO-free days (20 vs. 14, p = 0.038) were higher before YACHT establishment. The incidences of complications were not significantly different between the groups.

Conclusions: Mortality was not significantly different pre- and post-YACHT establishment; however, it helped promote regionalization and centralization in Yokohama-Yokosuka areas. We will collect more cases to demonstrate YACHT's usefulness.

#### **KEYWORDS**

acute respiratory distress syndrome, coronavirus disease 2019, extracorporeal membrane oxygenation network, venovenous extracorporeal membrane oxygenation, Yokohama Advanced Cardiopulmonary Help Team

# **INTRODUCTION**

Venovenous extracorporeal membrane oxygenation (VV-ECMO) is widely used for respiratory management of severe acute respiratory distress syndrome (ARDS)<sup>1,2</sup> and ARDS associated with coronavirus disease 2019 (COVID-19).<sup>3</sup> However, ECMO is a high-risk and highcost treatment that requires expertise for safe use. The

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Extracorporeal Life Support Organization (ELSO) recommends that patients requiring ECMO be centrally managed in respiratory ECMO centers.<sup>1,4</sup> The ELSO also advocates regionalization (establishment of local healthcare networks) and centralization (consolidation of patients) for safe performance and management of ECMO. In the United Kingdom,<sup>5</sup> Italy,<sup>6</sup> and Sweden,<sup>7</sup> studies have reported that centralized management in nationally designated respiratory ECMO centers has contributed to high survival rates.

In Japan, ECMOnet was established in April 2021 in response to the COVID-19 pandemic to share information regarding ECMO treatment and provide medical care beyond the boundaries of academic societies, hospitals, and local governments. This ECMOnet shared data of patients requiring ECMO with facilities accredited by the Japanese Society of Intensive Care Medicine, the Japanese Association for Acute Medicine, and others. The Japan ECMOnet provided a 24/7 consultation system assisting hospitals with ECMO management and educational simulation courses,<sup>8</sup> thus contributing to an increased survival rate of patients with severe ARDS, from 36%<sup>9</sup> during the 2009 H1N1 pandemic to 63%<sup>10</sup> during the 2020 COVID-19 pandemic.

Studies indicate that nationally designed ECMO centers lead to successful outcomes for patients requiring ECMO<sup>5-7</sup>; however, to the best of our knowledge, their impact in local regions in Japan remains unclear. Therefore, this study aimed to evaluate the impact of an ECMO specialist team in Yokohama by analyzing data reported before and after its establishment.

# **METHODS**

# Study design, setting, and patients

This retrospective before–after comparison study enrolled patients  $\geq$ 18 years and treated with VV-ECMO for severe ARDS at Yokohama City University Medical Center Advanced Critical Care Center from October 1, 2014, to March 31, 2023. Our facility is the only advanced emergency center in Yokohama and routinely receives critically ill patients from other emergency centers. It has 12 mixed ICU beds and treats approximately 1500 critically ill patients (trauma, burns, respiratory failure, and others) annually, providing emergency and critical care to the residents of Yokohama (population, ~3,700,000) and patients from the neighboring city of Yokosuka (population, ~400,000), thus covering a population of over 4 million. We are also the only facility in Yokohama and Yokosuka with vehicles capable of ECMO transport.

The inclusion criteria were as follows: age  $\geq$  18 years, admission to our ICU for treatment of severe ARDS caused by COVID-19, bacterial or viral infection, trauma, or others, initiation of VV-ECMO for refractory ARDS, and received ECMO for >24 h. Patients were excluded if they

ARDS was defined based on the Berlin criteria<sup>11</sup>: onset within 7 days of apparent triggers or new or worsening of respiratory symptoms; chest imaging (computed tomography [CT] scan or chest radiography) showing bilateral opacities unexplainable by pleural effusion, atelectasis, or nodules alone; pulmonary edema unexplainable solely by cardiac insufficiency or excessive infusion (objective evaluation such as echocardiography is needed if possible); and presence of hypoxemia—categorized as mild (200 mmHg  $\leq$  partial pressure of arterial oxygen [PaO<sub>2</sub>]/ fraction of inspiratory oxygen [FiO<sub>2</sub>]  $\leq$  300 mmHg), moderate (100 mmHg  $\leq$  PaO<sub>2</sub>/FiO<sub>2</sub> $\leq$  200 mmHg), and severe (PaO<sub>2</sub>/FiO<sub>2</sub>  $\leq$  100 mmHg).

This study was approved by the Institutional Review Board of Yokohama City University and conducted according to the principles of the Declaration of Helsinki. The requirement for patient consent was waived due to the retrospective nature of this study.

# Yokohama Advanced Cardiopulmonary Help Team (YACHT)

Our ECMO specialist team, called the Yokohama Advanced Cardiopulmonary Help Team (YACHT), was established in 2019 and functioned from January 2020 to centralize the treatment of patients receiving ECMO and establish a 24/7 consultation system in Yokohama and Yokosuka.

ELSO recommends that a dedicated ECMO team should be formed, but there is no clear definition of this. We defined a dedicated team as one that includes intensivists with at least 20 cases of ECMO experience. This team comprised four physicians—board-certified doctors from the Japanese Society of Intensive Care Medicine, Japanese Association for Acute Medicine, and Japanese Society of Respiratory Care Medicine—experienced in ECMO and respiratory management, four senior emergency medicine residents, five nurses working in the ICU, two medical engineers (MEs) experienced with ECMO, two drivers, and office workers.

The YACHT provided (1) a 24/7 consultation system with ECMO management to hospitals in the Yokohama-Yokosuka area and, sometimes, patient evaluation, (2) patient transfers to our hospitals and, sometimes, the introduction of ECMO at the referral hospital (primary transport), (3) monthly educational simulations (circuit exchange, hand crank, and troubleshooting), (4) monthly meetings (reviews of cases and update of latest findings of ECMO and respiratory failure), (5) ECMO transport simulations with affiliated hospitals, and (6) preparation of an in-hospital manual (Supplemental File 1). Patients admitted between October 1, 2014, and December 31, 2019 were assigned to the without-YACHT group, and those admitted from January 1, 2020, to March 31, 2023, to the with-YACHT group.

## Data collection

According to the ELSO registry guideline,<sup>12</sup> we collected data from electronic medical records on age, sex, nationality, body weight, body mass index, comorbidities (coronary artery disease, chronic cardiac disease, chronic obstructive pulmonary disease, stomach ulcer, peripheral vascular disease, liver disease, cerebrovascular disease, diabetes, dementia, chronic kidney disease, and malignancy), causes of respiratory failure, indices of disease severity (Acute Physiology and Chronic Health Evaluation [APACHE] II, Sequential Organ Failure Assessment, and Respiratory Extracorporeal Membrane Oxygenation Survival Prediction [RESP] scores), ventilator-free days, ECMO-free days, ICU-free days, and complications at 28 days after admission. Complications were patientderived (hemorrhagic, respiratory, or infectious) or machine-derived (circuit exchange or pump failure); these data were determined by physicians.

We also collected patient-specific information, including type of admission (direct or transfer), type of referral hospital (emergency and critical care center or not), transfer rates, and number of primary ECMO transports. In the Yokohama-Yokosuka area, 11 emergency and critical care centers cooperate and provide emergency medical care 24 h a day.

# Study outcomes

The primary outcome was ICU mortality. The secondary outcomes were ICU-, mechanical ventilator-, and ECMOfree days during the first 28 days and complication rate. For patients who died within 28 days, the number of ICU-, ventilator-, and ECMO-free days was set as 0. Additionally, the number of site visits before and after YACHT establishment was assessed as regionalization, and the transfer rate and number of primary transports as centralization. A site visit was defined as the YACHT visiting the other hospital to assess patients' respiratory status and the need for ECMO.

#### Statistical analyses

Continuous variables are expressed as means (standard deviations) or medians (interquartile ranges), as appropriate. Categorical variables are presented as frequencies (percentages). Analysis of variance (ANOVA) of continuous variables was performed using the Kruskal–Wallis test or two-way ANOVA for non-normally distributed data. Categorical variables were compared using the chi-squared test or Fisher's exact test. To estimate outcome predictors, all potential predictors were included in the univariate analyses (Mann–Whitney U test). All statistical analyses were performed using JMP<sup>®</sup>, Version 17 (SAS Institute Inc., Cary, NC, USA).

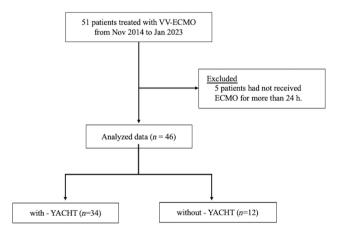
# RESULTS

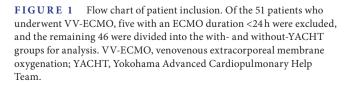
From October 1, 2014, to March 31, 2023, a total of 51 patients with severe refractory ARDS underwent VV-ECMO at our institution. Of them, 46 (12 in the without-YACHT group and 34 in the with-YACHT group) were included herein (Figure 1). Five patients were excluded because the ECMO duration was <24 h.

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Table 1 shows the characteristics of the 46 patients. All patients in the without-YACHT group were transported to our emergency room, whereas 24 of the 34 patients in the with-YACHT group were transferred from other hospitals, 14 were transferred from other emergency and critical care centers (in some cases, multiple patients were transferred from one hospital), and 10 from non-emergency and critical care care centers (Figure 2); there was an increase in the number of patients transported from other hospitals. For these 14 patients in the with-YACHT group, a physician affiliated with the YACHT visited the other hospital to evaluate the patient's respiratory status and necessity for ECMO.

Patient characteristics are presented in Table 2. The body mass index was higher in the with-YACHT group (23.7 [19.9–27.4] kg/m<sup>2</sup> vs. 29.5 [27.3–31.7] kg/m<sup>2</sup> p = 0.011), with no significant differences in age, sex, and Charlson comorbidity index. The indication for ECMO was mainly COVID-19 in the with-YACHT group (0 [0%] vs. 27 [79%], p < 0.001), with no significant differences among other indications (bacterial or viral infections [other than COVID-19], trauma, and others). The vital signs before ECMO showed lower percutaneous oxygen saturation (96% [94–99] vs. 91% [90–93] p = 0.003), and pre-ECMO glucocorticoids were administered more frequently (3 [25%] vs. 20 [58%], p = 0.04) in the with-YACHT group. The APACHE II (19 [15–23] vs. 24 [21–26] p = 0.037) and RESP (4 [3–5] vs. 2 [2–3] p = 0.021) scores were significantly





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	ing hospital	Non-emergency and critical care center	I	I	I	1	I	1				I		I	0	I		I	0	0	0	0	0	I	I	I	0	I		I	0
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dmission		Site visit	ī	Ι	Ι	Ι	Ι	Ι	I	I	I	I	Ι	T	Ι	I	Ι	I	0	0	I	I	0	I	0	I	0	0	0	0	0
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		APACHE II	28	25	23	13	20	20	35	6	31	6	28	29	33	14	25	38	28	18	18	20	17	23	31	30	27	27	26	22	19
		Cause of ARDS	Bacterial	Others	Bacterial	Bacterial	Bacterial	Bacterial	Viral	Others	Others	Trauma	Bacterial	Others	Viral	Viral	Viral	Viral	Bacterial	Viral	Viral	Viral	Others	Viral							
		ECMOnet	8 	Ι	I	Ι	Ι	Ι	I	I	I	I	I	I	I	I	I	I	0	0	I	I	0	Ι	I	Ι	I	I	I	I	1
		YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	Without-YACHT	With-YACHT																
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		Age (years)	55	54	32	49	13	39	52	36	65	31	80	62	70	63	70	72	51	43	57	59	72	67	66	54	56	57	57	49	51
		Year	2014	2015	2015	2016	2016	2016	2016	2016	2018	2018	2019	2019	2020	2020	2020	2020	2020	2020	2020	2020	2020	2020	2020	2021	2021	2021	2021	2021	2021
		No	1	2	3	4	5	9	7	8	6	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29

4 of 9 WILEY-ACUTE MEDICINE

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		Outcome	Discharged																
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ı	Type of referring hospital	Emergency and critical care center	0	0	Ι	Ι	Ι	Ι	Ι	0	0	0	Ι	0	0	0	I	Ι	I
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		2	2	6	6	1	4	2	2	2	4	9	2	1	1	1	6	0	
		APACHE II	24	22	17	11	18	17	24	22	19	22	20	20	21	24	30	20	19
		Cause of ARDS	Viral	Bacterial	Viral	Viral	Trauma	Others											
		ECMOnet				I												I	I
		YACHT	With-YACHT																
		Sex	Μ	Μ	Μ	Μ	ц	ц	н	ц	Μ	Μ	Μ	Μ	Μ	Μ	Μ	Μ	Μ
		Age (years)	60	61	48	49	61	47	53	52	57	56	39	70	49	56	45	25	37
		Year	2021	2021	2021	2021	2021	2021	2021	2021	2021	2021	2022	2022	2022	2022	2022	2022	2023
		No	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46

extracorporeal membrane oxygenation survival prediction score; YACHT, Yokohama Advanced Cardiopulmonary Help Team.

 $^{\rm ac}$ —" refers to something that is not related and has not been done.

 $^{\mathrm{b}\alpha}\mathrm{o}"$  refers to something that is related and has been done.

TABLE 1 (Continued)

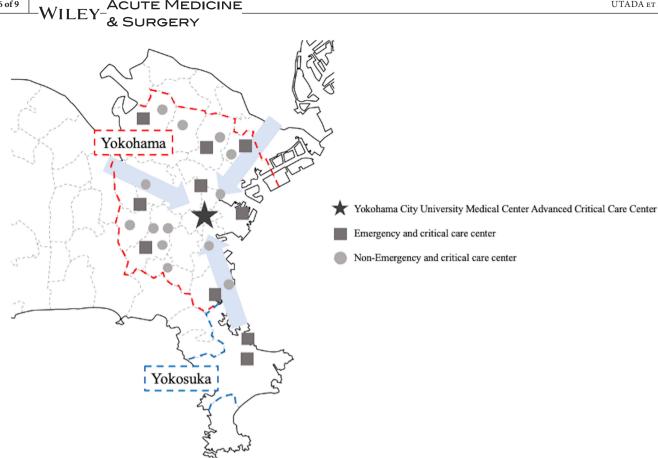


FIGURE 2 Location of our hospital and referral hospitals in Yokohama and Yokosuka. Patients receiving VV-ECMO were transferred to our hospital from emergency or non-emergency and critical care centers throughout the Yokohama-Yokosuka area. VV-ECMO, venovenous extracorporeal membrane oxygenation.

higher, and the predicted mortality rate was also higher in the with-YACHT group.

Table 2 shows the outcomes of patients in both groups. No significant difference was noted in ICU mortality between the two groups (2 [17%] vs. 4 [12%], p = 0.67). The numbers of ICU- (14 [9–18] vs. 9 [6–12] *p*=0.10), ventilator- (11 [7–16] vs. 5 [2-7] p=0.01), and ECMO-free days (20 [15-25] vs. 14 [11–17] p = 0.038) was higher in the without-YACHT group than in the with-YACHT group. The complication rates were not significantly different between the two groups.

# DISCUSSION

We assessed the efficacy of YACHT by comparing the 28day mortality rates of patients receiving ECMO before and after its establishment. YACHT establishment did not improve outcomes for patients receiving ECMO. However, the YACHT establishment has led to progress in regionalization and centralization in the Yokohama-Yokosuka area.

The Yokohama-Yokosuka area lacks facilities that meet the requirements presented by the ELSO. To achieve regionalization and centralization, a system of cooperation with local emergency medical service teams and neighboring hospitals is required. Our facility has been the only major

center involved in emergency medical care in the Yokohama-Yokosuka area since 1990. Therefore, we cooperate with healthcare institutes by providing emergency medical care.

In this study, no referrals were noted for severe respiratory failure before the YACHT establishment. After the YACHT establishment, patients with severe respiratory failure were referred to our institution from neighboring hospitals. Although initially after YACHT's establishment, consultations for severe respiratory failure were directed via the Japan ECMOnet, more recently, hospitals have contacted us directly outside the Japan ECMOnet. Our regionalization in the Yokohama-Yokosuka area benefited from the cooperative system established with neighboring hospitals. In cases of severe respiratory failure, we visited the hospital to evaluate the patient's respiratory condition before making decisions regarding transfers (14/34 cases). This face-to-face relationship may have benefited regionalization.

This regionalization facilitated centralization. As shown in Table 1, the number of patients requiring ECMO management who were transferred to our hospital from neighboring hospitals increased after YACHT establishment (from 0% to 70.6%). With the YACHT, an ambulance for patients requiring ECMO was deployed (Supplemental File 2), and a primary transport system was established, resulting in nine transfers (24 total transfers). We cooperated with a

TABLE 2 The clinical characteristics and outcomes of patients.

	1	01

Variable (frequency (%)/median [IQR])	Without	YACHT ( <i>n</i> = 12)	With YA	CHT ( <i>n</i> = 34)	<i>p</i> -value
Patients characteristics					
Age (years)	47	[39-54]	55	[51–59]	0.08
Male sex	11	[92]	26	[76]	0.22
Body mass index	23.7	[19.9–27.4]	29.5	[27.3-31.7]	0.01
Charlson Comorbidity Index	0.6	[0.1-1.1]	0.7	[0.3-0.96]	0.10
Cause of ARDS					
COVID-19	0	[0]	27	[79]	< 0.001
Bacterial pneumonia	5	[42]	1	[3]	0.003
Viral pneumonia (without COVID-19)	2	[17]	2	[5]	0.28
Trauma	1	[8]	1	[3]	0.45
Others	4	[33]	3	[9]	0.03
Treatment pre ECMO					
Neuromuscular blocker	1	[8]	3	[8]	0.95
Glucocorticoid therapy	3	[25]	20	[58]	0.04
Mean blood pressure before ECMO introduction	83	[69–97]	84	[75-93]	0.93
Respiratory rate before ECMO introduction	24	[19–27]	23	[20-26]	0.03
SpO <sub>2</sub> before ECMO introduction	96	[94-99]	91	[90-93]	0.003
PaO <sub>2</sub> before ECMO introduction	86	[67–107]	78	[65–90]	0.45
PaCO <sub>2</sub> before ECMO introduction	72	[49-94]	58	[43-72]	0.31
Murray score	3.1	[2.8-3.5]	3.3	[3.1–3.5]	0.42
Prediction					
APACHE II score at the time of ICU admission	19	[15-23]	24	[21–26]	0.04
SOFA score at the time of ICU admission	10	[8-12]	11	[10-12]	0.24
RESP score at the time of ECMO introduction	4	[3-5]	2	[2-3]	0.02
Outcomes					
ICU mortality (%)	2	(17)	4	(12)	0.67
ICU-free days	14	[9–18]	9	[6-12]	0.10
Ventilator-free days	11	[7-16]	5	[2-7]	0.01
ECMO-free days	20	[15-25]	14	[11-17]	0.04
Complication					
Bleeding (%)	4	(33)	4	(12)	0.18
Respiratory (%)	0	(0)	2	(6)	1.00
Infection (%)	0	(0)	1	(3)	1.00
Circuit replacement (%)	0	(0)	3	(9)	0.56
Pump failure (%)	0	(0)	3	(9)	0.56

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation; ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; PaCO<sub>2</sub>, partial pressure of arterial carbon dioxide; PaO<sub>2</sub>, partial pressure of arterial oxygen; RESP, respiratory extracorporeal membrane oxygenation survival prediction; SpO<sub>2</sub>, saturation of percutaneous oxygen; YACHT, Yokohama Advanced Cardiopulmonary Help Team.

neighboring hospital regarding costs and responsibilities in the event of transportation. We believe that this increase in the number of transfers from other hospitals and the ECMO primary transports has contributed to centralization in the Yokohama-Yokosuka area. Strong regionalization may allow safer and more effective centralization.

We believe that the YACHT establishment also had an educational effect. Although more patients with severe respiratory failure requiring ECMO were treated after the YACHT was established (APACHE II score: 19 [15–23] vs. 24 [21–26] p = 0.037; RESP score: 4 [3–5] vs. 2 [2–3] p = 0.021), mortality (2 [17%] vs. 4 [12%] p = 0.021) and complications did not increase (Table 2). The reason was possibly the YACHT conducted monthly in-hospital simulations for physicians, nurses, and MEs not affiliated with the YACHT (Supplemental File 1), enabling all staff working in the ICU to deal with troubleshooting. Primary transport simulations were conducted with neighboring hospitals,

with no problems during transport (Supplemental File 1). Consequently, the 28-day mortality rate after YACHT establishment in this study was 12%, below the overall mortality rate in Japan (35%)<sup>13</sup> and that reported by the ELSO (42%).<sup>14</sup>

This study has some limitations. First, differences were noted in patient characteristics. As the COVID-19 pandemic began around 2020, most patients with respiratory failure had COVID-19 in the with-YACHT group, while no patients had COVID-19 in the without-YACHT group. These differences in patient characteristics may have affected our results. Second, the sample size was small. Third, due to a beforeand-after comparative study design, eliminating the subjectivity of the observer was difficult. Finally, the study did not consider the long-term outcomes of the patients, except for death. Therefore, it was not possible to assess their long-term prognosis. Additionally, this study only included data from our hospital. However, considering the size of our hospital, we believe that the data from our hospital capture the trend of Yokohama as a whole.

The balance of supply and demand for ECMO varies regionally and nationally; therefore, regionalization and centralization advocated by the ELSO require regional assessment. The Japan ECMOnet promotes nationwide regionalization and centralization to improve outcomes of patients requiring ECMO, and the YACHT was established to promote regionalization and centralization in the Yokohama-Yokosuka area. This may be a catalyst for other regions of Japan to achieve greater regionalization and centralization of patients requiring ECMO.

# CONCLUSIONS

Herein, no significant difference was observed in mortality before and after YACHT establishment; however, it helped to promote regionalization and centralization in the Yokohama-Yokosuka area. In the future, we aim to collect more cases to demonstrate the usefulness of YACHT.

#### ACKNOWLEDGMENTS

We thank our colleagues at the Advanced Critical Care and Emergency Center of the Yokohama City University Medical Center.

FUNDING INFORMATION None.

**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 from the corresponding author upon reasonable request.

# ETHICS STATEMENT

Approval of the research protocol: This study was approved by the Institutional Review Board of Yokohama City University (approval number: B191100016).

Informed consent: The requirement for patient consent was waived due to the retrospective nature of this study.

Registry and the registration no. of the study/trial: N/A. Animal studies: N/A.

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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