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RESEARCH ARTICLE

Association between ICU quality and in-hospital mortality of V-V ECMO-supported patients—the ECMO quality improvement action (EQIA) study: a national cohort study in China from 2017 to 2019

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Abstract **This cohort study was performed to explore the influence of intensive care unit (ICU) quality on in-hospital mortality of veno-venous (V-V) extracorporeal membrane oxygenation (ECMO)-supported patients in China. The study involved all V-V ECMO-supported patients in 318 of 1700 tertiary hospitals from 2017 to 2019, using data from the National Clinical Improvement System and China National Critical Care Quality Control Center. ICU quality was assessed by quality control indicators and capacity parameters. Among the 2563 V-V ECMO-supported patients in 318 hospitals, a significant correlation was found between ECMO-related complications and prognosis. The reintubation rate within 48 hours after extubation and the total ICU mortality rate were independent risk factors for higher in-hospital mortality of V-V ECMO-supported patients (cutoff: 1.5% and 7.0%; 95% confidence interval: 1.05–1.48 and 1.04–1.45; odds ratios: 1.25 and 1.23; $P = 0.012$ and $P = 0.015$, respectively). Meanwhile, the V-V ECMO center volume was a protective factor (cutoff of ⩾ 50 cases within the 3-year study period; 95% confidence interval: 0.57–0.83, odds ratio: 0.69, $P = 0.0001$). The subgroup analysis of 864 patients in 11 high-volume centers further strengthened these findings. Thus, ICU quality may play an important role in improving the prognosis of V-V ECMO-supported patients.**

Keywords veno-venous extracorporeal membrane oxygenation; in-hospital mortality; high-volume centers; quality control; intensive care unit capacity parameters

Introduction

Extracorporeal membrane oxygenation (ECMO) has played vital roles in the treatment of severe COVID-19 pneumonia. A recent worldwide meta-analysis including 1896 critically ill patients with COVID-19 who received ECMO support showed that in-hospital mortality was reduced to 37% compared with 50%–80% in patients without ECMO support. However, the mortality rate

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differed greatly between different centers [1–4]. Heterogeneity of experience among ECMO centers may have played an important role [5]. The intensive care unit (ICU) is the main site in which ECMO-supported patients receive treatment. However, treatment in the ICU is associated with frequent adverse medical events because of the high intensity of therapeutic activities per day, the high quantity and complexity of medical data, and sudden changes in patients' clinical conditions. The quality of ICU has a crucial effect on patients' prognosis [6,7].

In 2015, the China National Critical Care Quality Control Center (China-NCCQC) released 15 specific national clinical quality control indicators for critical care medicine. These 15 quality control indicators were recently found to be good predictors of the prognosis of critically ill patients, and a quality scoring system was defined to further optimize the system [8]. In addition, certain capacity parameters of the ICU, such as patient-to-bed ratio and nurse-to-bed ratio, were proven to be substantially associated with the incidence of ventilator-associated pneumonia [9]. ECMO was treated as a high-tech salvage strategy for critically ill patients, and its performance and management were a comprehensive reflection of the ICU level. The authors hypothesized that quality control plays an important role in the prognosis of ECMO-supported patients. Therefore, China-NCCQC carried out the ECMO quality improvement action (EQIA) study to investigate the associations among ICU capacity parameters, quality control indicators, and in-hospital mortality of V-V ECMO-supported patients.

Methods

Study population

The NCIS database of the National Health Commission of the People's Republic of China was designed to collect detailed information of patients from 1700 tertiary hospitals. With reference to the authors' previous research [10], information from ECMO-supported patients included in the database from 1 January 2017, to 31 December 2019, were screened. The following indications for V-V ECMO initiation were in accordance with the Extracorporeal Life Support Organization (ELSO) guidelines [11,12]: severe acute respiratory distress syndrome and refractory hypoxemia (PaO_2/FiO_2 of < 60 mmHg for > 6 h or < 50 mmHg for > 3 h) or severe hypercapnic respiratory failure (pH of < 7.20 with $PaCO_2$ of > 80 mmHg for > 6 h) after maximizing traditional therapies, particularly the use of prone positioning. Patients with relative contraindications, such as central nervous system hemorrhage, systemic bleeding, and contraindications to anticoagulation, were rigorously excluded by intensivists. Among the 1700 tertiary hospitals in the database, 318 hospitals conducted V-V ECMO from 2017 to 2019. All these patients were enrolled in the study, and all information available in the database was recorded. The data collection was approved by the National Health Commission of China, and the study was approved by the Institutional Review Board of Peking Union Medical College Hospital (approval number: SK1828). A waiver for individual consent was granted by the research ethics board because of the retrospective and deidentified nature of the data.

Exposure variables

In this study, ICU quality was assessed by quality control and capacity indicators [6,7]. The 15 quality control indicators was classified into three categories: structural indicators, procedural indicators, and outcome indicators. The structural indicators were the percentage of ICU patients among all inpatients, the percentage of ICU bed occupancy of the total inpatient bed occupancy, and the percentage of patients with an Acute Physiology and Chronic Health Evaluation II (APACHE II) score of ⩾ 15 among all ICU patients. The procedural indicators were the 3- and 6-h Surviving Sepsis Campaign (SSC) bundle compliance rates, the rate of microbe detection before administration of antibiotics, the percentage of ICU patients receiving prophylaxis for deep vein thrombosis, the percentage of unplanned endotracheal extubation, the percentage of extubated patients reintubated within 48 h, the percentage of patients with unplanned ICU transfers, the 48-h ICU readmission rate, the incidence of ventilator-associated pneumonia, the incidence of catheter-related bloodstream infection, and the incidence of catheter-associated urinary tract infection (CAUTI). The outcome indicator was ICU mortality. The six capacity indicators assessed in this study were the ICU patient-to-bed ratio, severe patient-to-bed ratio, intensivist-to-bed ratio, nurse-to-bed ratio, intensivist-to-patient ratio, and intensivist-to-severe patient ratio. All parameters and their definitions are listed in Tables S1 and S2.

Study methods

The main outcome was in-hospital mortality, and the primary diagnosis at discharge was determined to be the reason for V-V ECMO initiation. The association between the center volume and prognosis was also assessed. On the basis of previous studies and the current ECMO situation in China, high-volume centers were defined as centers that performed ⩾ 50 V-V ECMO runs in 3 years [3,10,13,14]. The cutoff value of each indicator was identified in accordance with the quality control data in China from 2015 to 2020 and clinical practice experience [8]. Then, the patients were grouped in accordance with the quality indicators of their hospitals, and the in-hospital mortality rates of V-V ECMO-supported patients between hospitals with different qualities were compared. The association between ICU quality and in-hospital mortality was comprehensively explored.

In total, 31 provinces, municipalities, and autonomous regions in the Chinese mainland were included in the study (data from Hong Kong, Taiwan, and Macao were excluded). The age divisions and geographic and economic region divisions are listed in Table S3. Costs are expressed in USD after conversion using the annual average exchange rate between RMB and USD in 2019 (1 USD to 6.8985 RMB).

Statistical analysis

First, the baseline characteristics of all patients were stratified by time period and compared using Chi-square test and variance analysis for categorical and continuous variables, respectively. Univariate and multivariate logistic regression models with death during hospitalization as the dependent variable were applied to identify factors related to in-hospital mortality. The risk factors were screened in accordance with literature search, expert consensus, and expert experience. Factors of specific focus were the baseline characteristics (demographic characteristics, economic regions in which the hospitals were located, and season at admission) and patients' chronic underlying diseases and ECMO-related complications. The results are expressed as the odds ratio (OR) with 95% confidence interval (CI).

Second, generalized linear mixed models were performed with the quality-related parameters included in the models as the random variable to assess the association between ICU quality and in-hospital mortality. Variables that were statistically different in the first step, including patients' baseline characteristics, chronic underlying diseases, and ECMO-related complications, were adjusted in the models to eliminate potential confounding. The cutoff values for categorizing the quality-related parameters were assigned in accordance with the clinical implications and data distribution. The associations with in-hospital mortality were evaluated in separate models because of the multicollinearity among these parameters. A subgroup analysis of patients in high-volume centers was performed to reduce the bias caused by factors in low-volume centers. All P values presented were two-sided, with $P < 0.05$ considered statistically significant. All analyses were conducted using SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC, USA).

In addition, SPSS Modeler software version 18.0 (IBM Corp., Armonk, NY, USA) was used to conduct *apriori* association rule learning analysis and plot charts. This analysis conducted using the 17 most frequently used association rules, and the minimum requirements were determined as a support degree of ⩾ 10% and confidence of ⩾ 47%. Furthermore, the association rules were reported in accordance with descending support and confidence and lift values corresponding to the support of the association rules.

Results

Baseline characteristics of V-V ECMO-supported patients and identification of confounders for quality control association analysis

In total, 2563 V-V ECMO-supported patients in 318 hospitals from 2017 to 2019 were identified in the NCIS database. The number of V-V ECMO cases increased annually, totaling 386, 719, and 1458 cases in 2017, 2018, and 2019, respectively, whereas the in-hospital mortality remained constant (32.4%, 29.4%, and 27.4%, respectively; P = 0.137; Fig. 1). The baseline characteristics of these patients are listed in Table S4 and Figs. S1–S3. Univariate and multivariate regression analyses were performed to screen out factors significantly associated with in-hospital mortality. The results showed that lung cancer, intracranial hemorrhage, hypoxic–ischemic encephalopathy, multiple organ dysfunction syndrome, kidney injury, coagulation disorder, bacteremia, and shock were independently correlated with increased in-hospital mortality. By contrast, acute respiratory distress syndrome, age of 21–30 years, and location in a region with a mid-level gross domestic product were protective factors (Figs. 2 and 3; Tables S5 and S6). All these factors were treated as confounders in the subsequent analyses for quality control indicators.

Apriori association rule learning analysis was conducted to determine the risk factors for in-hospital mortality of V-V ECMO-supported patients by using the 17 most frequently used association rules. In accordance with the rule that a positive correlation was present between patient factors and in-hospital mortality and divided by the threshold of ⩾ 200 cases, the following seven factors were confirmed to be associated with in-hospital mortality of V-V ECMO-supported patients: received continuous renal replacement therapy (n = 640), received blood transfusion for hemorrhage (n = 601), received noninvasive ventilation (n = 599), underwent cardiopulmonary resuscitation (n = 597), complicated with bacteremia (n = 286), complicated with kidney injury (n = 274), and complicated with coagulation disorder (n = 268). The combination of coagulation disorder, kidney injury, and continuous renal replacement therapy was the most lethal risk factor for in-hospital mortality of V-V ECMO-supported patients (support, 11.08%; confidence, 48.59%; Fig. 4 and Table S7).

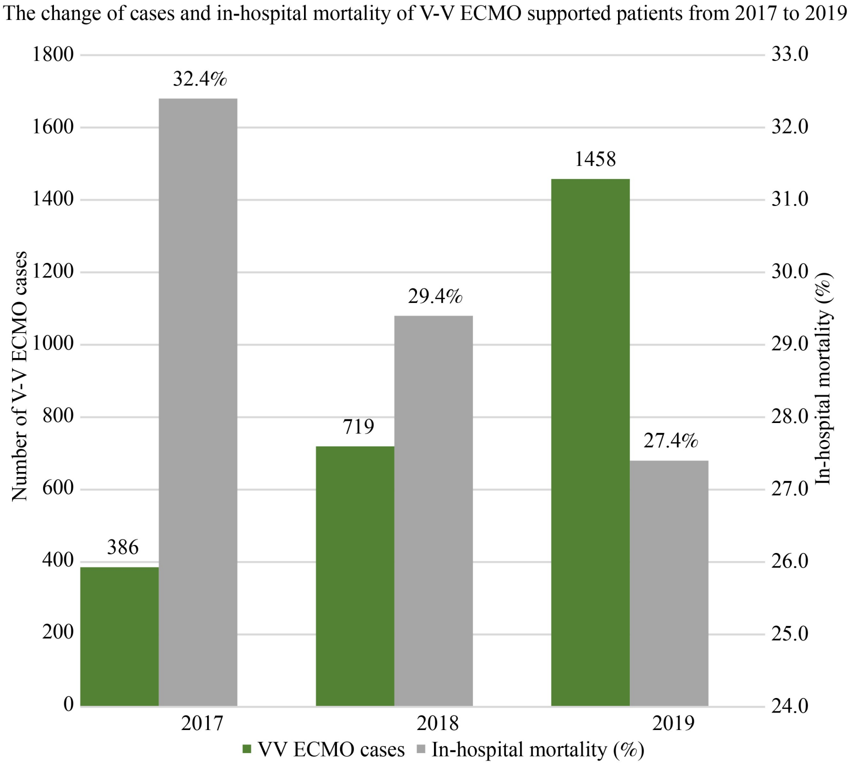

Fig. 1 Changes in patient number and in-hospital mortality of V-V ECMO-supported patients from 2017 to 2019. The number of V-V ECMO cases increased over time (n = 386 in 2017, n = 719 in 2018, and n = 1458 in 2019), whereas the in-hospital mortality rate decreased (32.4% in 2017, 29.4% in 2018, and 27.4% in 2019). V-V ECMO, veno-venous extracorporeal membrane oxygenation.

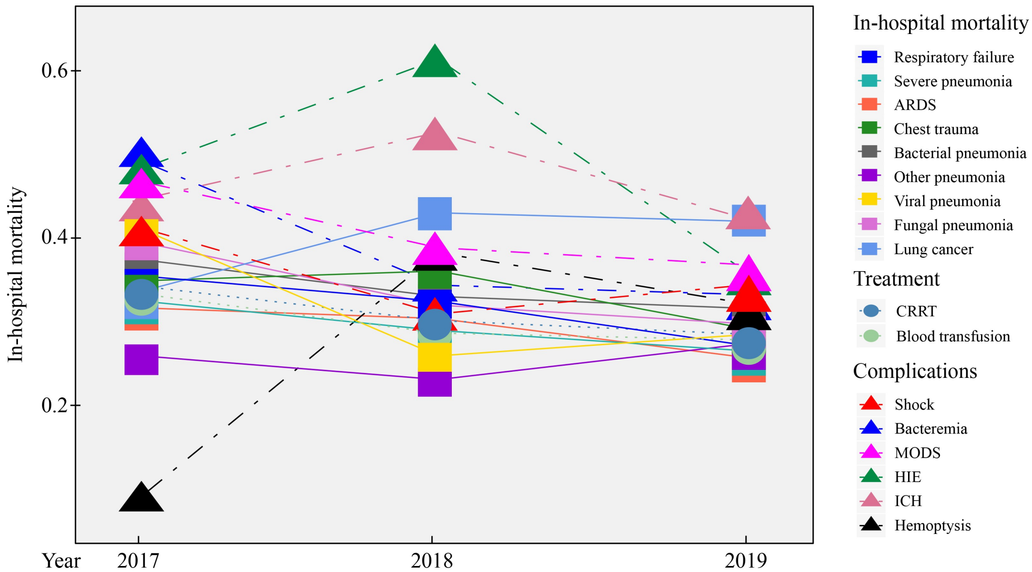

Fig. 2 Slope chart of associations of etiology, treatment, and complications with in-hospital mortality of V-V ECMO-supported patients. From 2017 to 2019, the in-hospital mortality rate showed a trend of decreasing year by year. Specifically, this included V-V ECMO-supported patients with respiratory failure, with severe pneumonia, with ARDS, with bacterial pneumonia, with fungal pneumonia, receiving CRRT, receiving blood transfusion, complicated with bacteremia, and complicated with MODS. Other factors showed an upward trend followed by a downward trend and vice versa. Square dot, etiology-related diagnosis. Circular dot, treatment. Triangular dot, complications. V-V ECMO, veno-venous extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; CRRT, continuous renal replacement therapy; MODS, multiple organ dysfunction syndrome; HIE, hypoxic–ischemic encephalopathy; ICH, intracerebral hemorrhage; bacteremia, bloodstream infection; hemoptysis, respiratory tract bleeding.

	OR	95%CI	*P*
Age (years) (Ref=0−13)			
14−20	0.88	0.51−1.51	0.641
21−30	0.58	0.38−0.90	0.014
31−40	0.69	0.47−1.03	0.069
41−50	0.70	0.48−1.02	0.060
51−60	0.85	0.59−1.23	0.394
61−70	0.89	0.61−1.28	0.516
71−	1.11	0.71−1.73	0.649
Gender (Ref=Male)			
Female	0.97	0.80−1.19	0.779
GDP (Ref=High)			
Middle	0.62	0.49−0.78	<0.001
Low	0.87	0.67−1.14	0.305
Season (Ref=Spring)			
Summer	0.97	0.73−1.29	0.844
Autumn	0.82	0.62−1.09	0.166
Winter	1.01	0.79−1.28	0.955
Comorbidities related diagnosis			
Hypertension	1.03	0.81−1.30	0.835
Diabetes Mellitus	1.25	0.96−1.64	0.100
Chronic cardiac dysfunction	1.21	0.99−1.48	0.069
Cerebral vascular disease	0.92	0.64−1.33	0.663
Digestive system disease	1.00	0.82−1.23	0.991
Etiology related diagnosis			
Viral pneumonia	1.04	0.81−1.34	0.740
Bacterial pneumonia	1.02	0.79−1.30	0.905
Fungal pneumonia	1.04	0.78−1.39	0.774
Severe pneumonia	0.87	0.70−1.07	0.179
Acute respiratory distress syndrome	0.80	0.65−0.98	0.034
Chest trauma	1.08	0.87−1.34	0.473
Lung cancer	2.07	1.27−3.37	0.003
Complications			
Cerebral hemorrhage	2.12	1.47−3.06	<0.001
Ischemic hypoxic encephalopathy	1.52	1.09−2.11	0.014
Multiple organ dysfunction	1.71	1.39−2.10	<0.001
Kidney injury	1.28	1.03−1.58	0.026
Coagulation disorder	1.56	1.26−1.93	<0.001
Bloodstream infection	1.44	1.18−1.76	<0.001
Shock	1.35	1.12−1.64	0.002
Respiratory tract bleeding	0.95	0.58−1.55	0.825

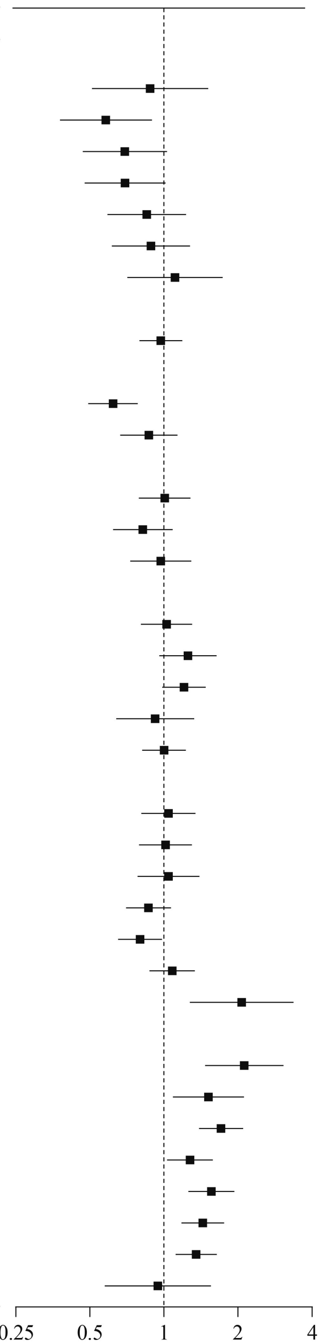

Fig. 3 Patient-related factors significantly associated with in-hospital mortality of V-V ECMO-supported patients. V-V ECMO support due to lung cancer diagnosis, complication with intracranial hemorrhage, hypoxic-ischemic encephalopathy, MODS, kidney injury, coagulation disorder, bacteremia, and shock was independently correlated with increased in-hospital mortality. By contrast, diagnosis with ARDS, age of 21–30 years, and hospital location in a middle GDP region were protective factors. V-V ECMO, veno-venous extracorporeal membrane oxygenation; MODS, multiple organ dysfunction syndrome; ARDS, acute respiratory distress syndrome; OR, odds ratio; 95% CI, 95% confidence interval; GDP, gross domestic product.

Association between ICU quality and in-hospital mortality of V-V ECMO-supported patients

All the quality control indicators and capacity parameters from hospitals where ECMO procedures were performed were collected, and mortality between hospitals with different qualities was compared. The results showed lower in-hospital mortality rates in V-V ECMO-supported patients who were treated in hospitals with a higher proportion of ICU patients among total inpatients (⩾ 1.5%), lower 3- and 6-h SSC bundle compliance rates (< 60% and < 90%, respectively), a lower reintubation

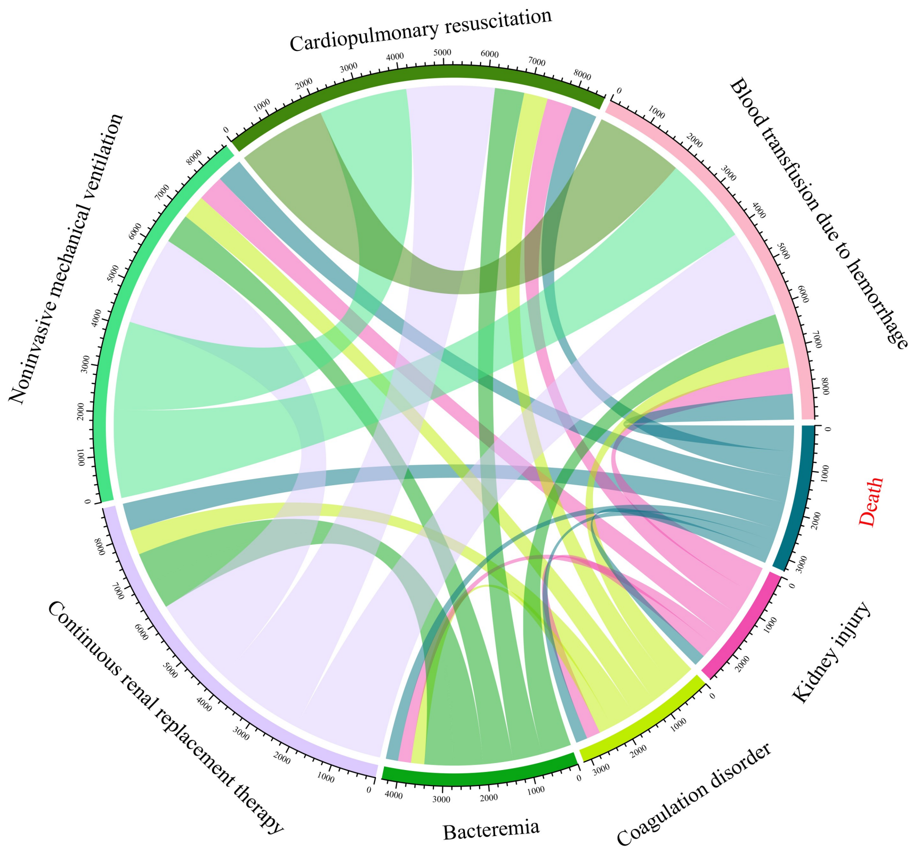

Fig. 4 *A priori* algorithm-based association rules between patient factors and in-hospital mortality of V-V ECMO-supported patients from 2017 to 2019. The association between patient factors and in-hospital mortality of 2563 V-V ECMO-supported patients was explored through *a priori* algorithm-based association rules. The strength of the correlation degree was indicated by the width of the ribbon, with a stronger association being associated with a wider ribbon. In accordance with the rule that a positive correlation was present between patient factors and in-hospital mortality and divided by the threshold of ⩾ 200 cases, the following seven factors were confirmed to be associated with in-hospital mortality of V-V ECMO-supported patients: received CRRT (n = 640), received blood transfusion for hemorrhage (n = 601), received noninvasive ventilation (n = 599), underwent CPR (n = 597), complicated with bacteremia (n = 286), complicated with kidney injury (n = 274), and complicated with coagulation disorder (n = 268). V-V ECMO, veno-venous extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy; CPR, cardiopulmonary resuscitation.

rate within 48 h after extubation (< 1.5%), a lower CAUTI incidence rate (< 1.5 per 1000 urinary catheter line days), and a lower total ICU mortality rate (< 7%; P = 0.045, 0.002, 0.0002, 0.007, 0.008, and 0.004, respectively). With respect to the ICU capacity parameters, the in-hospital mortality rate significantly decreased from 30.8% to 24.5% when the 3-year total number of V-V ECMO-supported patients exceeded 50 (P = 0.0009, Table 1).

Next, univariate and multivariate analyses were performed to examine the association between ICU quality and in-hospital mortality of V-V ECMO-supported patients. After adjustment for the patients' baseline characteristics, chronic underlying diseases, and other potential confounders that were screened out in the first step, the multivariate analysis showed that the reintubation rate within 48 h, CAUTI incidence rate, and total ICU mortality rate were independent risk factors for higher in-hospital mortality (OR [95% CI]: 1.25 [1.05–1.48], P = 0.012; 1.18 [1.01–1.39], P = 0.043; and 1.23 [1.04–1.45], P = 0.015, respectively), and treatment in a high-volume V-V ECMO center was a protective factor for the patients' prognosis (cutoff of ⩾ 50 cases within the 3-year period: OR, 0.69; 95% CI, 0.57–0.83; P = 0.0001; Table 2).

Subgroup analysis of V-V ECMO-supported patients in high-volume centers

In accordance with the division criteria, 864 patients (33.7% of the total patients) were treated in 11 high-volume V-V ECMO centers. The in-hospital mortality rate was significantly lower in high-volume centers than in low-volume centers (24.5% vs. 30.8%, respectively; P = 0.001; Table S8). The proportion of ICU patients among the total inpatients and the proportion of ICU bed occupancy among the total inpatient bed occupancy were significantly higher in high-volume centers than in

Table 1 Comparison of in-hospital mortality of V-V ECMO-supported patients between hospitals with different qualities

Indicators	Categories	All patients (*N*)	In-hospital mortality *n* (%)	$P^{¥}$
Quality control indicators				
Proportion of ICU in total inpatients (%)	< 1.5	655	208 (31.8)	0.045
	⩾ 1.5	1796	496 (27.6)	
Proportion of ICU in total inpatient bed occupancy (%)	< 1.2	513	151 (29.4)	0.655
	⩾ 1.2	1966	559 (28.4)	
Proportion of Apache II score > 15 in all ICU patients (%)	< 60	1554	429 (27.6)	0.115
	⩾ 60	781	240 (30.7)	
3-h SSC bundles compliance rate (%)	< 90	1204	310 (25.8)	0.002
	⩾ 90	1099	346 (31.5)	
6-h SSC bundle compliance rate (%)	< 80	976	238 (24.4)	0.0002
	⩾ 80	1320	417 (31.6)	
Microbiology detection before antibiotics (%)	< 80	490	139 (28.4)	0.960
	⩾ 80	1917	546 (28.5)	
Unplanned endotracheal extubation rate (%)	< 1.3	1813	527 (29.1)	0.739
	⩾ 1.3	603	171 (28.4)	
Reintubation rate within 48 h (%)	< 1.5	1375	367 (26.7)	0.007
	⩾ 1.5	983	313 (31.8)	
Rate of unplanned transfer to ICU (%)	< 2.5	1025	290 (28.3)	0.932
	⩾ 2.5	1230	350 (28.5)	
ICU readmission rate within 48 h (%)	< 1	1388	387 (27.9)	0.371
	⩾ 1	998	295 (29.6)	
VAP incidence rate (per 1000 ventilator days)	< 10	2060	588 (28.5)	0.506
	⩾ 10	411	124 (30.2)	
CRBSI incidence rate (per 1000 line days)	< 1.7	1878	533 (28.4)	0.585
	⩾ 1.7	582	172 (29.6)	
CAUTI incidence rate (per 1000 line days)	< 1.5	1456	388 (26.7)	0.008
	⩾ 1.5	1004	317 (31.6)	
ICU mortality rate (%)	< 7	1156	300 (26.0)	0.004
	⩾ 7	1316	410 (31.2)	
ICU capacity parameters				
Volume of centers (3 years' total cases of V-V ECMO)	< 50	1699	523 (30.8)	0.0009
	⩾ 50	864	212 (24.5)	
ICU patient-to-bed ratio	< 40	1030	314 (30.5)	0.155
	⩾ 40	1468	409 (27.9)	
Severe ICU patient-to-bed ratio	< 30	1819	508 (27.9)	0.159
	⩾ 30	511	159 (31.1)	
Intensivist-to-bed ratio	< 0.3	235	65 (27.7)	0.670
	⩾ 0.3	2291	664 (29.0)	
Nurse-to-bed ratio	< 1.5	313	80 (25.6)	0.169
	⩾ 1.5	2213	649 (29.3)	
Intensivist-to-ICU patient ratio	< 15	1514	449 (29.7)	0.325
	⩾ 15	981	273 (27.8)	
Intensivist-to-severe ICU patient ratio	< 20	557	176 (31.6)	0.074
	⩾ 20	1781	493 (27.7)	

$^{¥}P$ for comparison of in-hospital mortality under different values of each quality control indicator. V-V ECMO, veno-venous extracorporeal membrane oxygenation; ICU, intensive care unit; SSC, surviving sepsis campaign; VAP, ventilator-associated pneumonia; CRBSI, catheter-related bloodstream infection; CAUTI, catheter-associated urinary tract infection.

Table 2 Univariate and multivariate analyses of association between quality indicators and in-hospital mortality of all V-V ECMO-supported patients

	Univariate			Multivariate		
	OR	95% CI	*P*	OR	95% CI	*P*
Quality control indicators						
Proportion of ICU in total inpatients (⩾ 1.5%)	0.86	0.73–1.02	0.0841	0.85	0.71–1.01	0.065
Proportion of ICU in total inpatient bed occupancy (⩾ 1.2%)	0.95	0.77–1.18	0.6531	0.87	0.70–1.09	0.226
Proportion of Apache II score > 15 in all ICU patients (⩾ 60%)	1.09	0.95–1.27	0.2257	1.10	0.95–1.28	0.207
3-h SSC bundles compliance rate (⩾ 90%)	1.07	0.81–1.41	0.6493	0.97	0.72–1.32	0.862
6-h SSC bundle compliance rate (⩾ 80%)	1.02	0.92–1.13	0.7167	1.13	0.83–1.55	0.446
Microbiology detection before antibiotics (⩾ 80%)	1.01	0.81–1.25	0.9600	0.96	0.76–1.20	0.709
Unplanned endotracheal extubation rate (⩾ 1.3%)	0.97	0.79–1.18	0.7400	1.04	0.84–1.28	0.745
Reintubation rate within 48 h (⩾ 1.5%)	1.24	1.05–1.47	0.0115	1.25	1.05–1.48	0.012
Rate of unplanned transfer to ICU (⩾ 2.5%)	1.01	0.84–1.21	0.9321	1.03	0.86–1.25	0.743
ICU readmission rate within 48 h (⩾ 1%)	1.09	0.91–1.30	0.3711	1.11	0.92–1.33	0.285
VAP incidence rate (⩾ 10‰)	1.08	0.86–1.36	0.5062	1.03	0.92–1.14	0.620
CRBSI incidence rate (⩾ 1.7‰)	1.08	0.57–2.04	0.8136	1.05	0.55–2.03	0.876
CAUTI incidence rate (⩾ 1.5‰)	1.23	1.04–1.45	0.0141	1.18	1.01–1.39	0.043
ICU mortality rate (⩾ 7%)	1.25	1.06–1.47	0.0076	1.23	1.04–1.45	0.015
ICU capacity parameters						
Volume of ECMO centers (3 years' cases of V-V ECMO ⩾ 50)	0.75	0.63–0.90	0.0016	0.69	0.57–0.83	0.0001
ICU patient-to-bed ratio (⩾ 40)	0.94	0.83–1.06	0.3120	0.94	0.83–1.07	0.334
Severe ICU patient-to-bed ratio (⩾ 30)	1.08	0.93–1.25	0.3256	1.13	0.95–1.35	0.172
Intensivist-to-bed ratio (⩾ 0.3)	1.07	0.79–1.44	0.6699	1.06	0.78–1.45	0.701
Nurse-to-bed ratio (⩾ 1.5)	1.09	0.91–1.32	0.3362	1.05	0.91–1.21	0.543
Intensivist-to-ICU patient ratio (⩾ 15)	0.91	0.77–1.09	0.3255	0.95	0.85–1.07	0.399
Intensivist-to-severe ICU patient ratio (⩾ 20)	0.88	0.74–1.04	0.1420	0.85	0.71–1.02	0.090

V-V ECMO, veno-venous extracorporeal membrane oxygenation; ICU, intensive care unit; SSC, surviving sepsis campaign; VAP, ventilator-associated pneumonia; CRBSI, catheter-related bloodstream infection; CAUTI, catheter-associated urinary tract infection; OR, odds ratio; CI, confidence interval.

low-volume centers (3.9% vs. 1.8%, $P = 0.023$ and 3.2% vs. 1.6%, $P = 0.006$, respectively). Moreover, the proportion of patients with an APACHE II score of ⩾ 15 among all ICU patients was slightly lower (35.7% vs. 52.9%, $P = 0.065$), the reintubation rate within 48 h after extubation was significantly lower (0.8% vs. 1.6%, $P = 0.045$), and the ICU patient-to-bed and nurse-to-bed ratios were significantly higher (49.7 vs. 38.6, $P = 0.043$ and 2.63 vs. 2.05, $P = 0.037$, respectively; Table 3).

A subgroup analysis was performed on patients in high-volume centers only to eliminate the potential bias induced by center volume on the association between ICU quality and the in-hospital mortality of V-V ECMO-supported patients. Besides ECMO-related complications, the reintubation rate within 48 h and the ICU mortality rate were still independent risk factors for in-hospital mortality of V-V ECMO-supported patients (OR [95% CI]: 0.725 [0.625–0.84], $P < 0.0001$ and 1.219 [1.14–1.305], $P < 0.0001$, respectively). In high-volume centers, the ICU patient-to-bed ratio, intensivist-to-severe ICU patient ratio, and nurse-to-severe ICU patient ratio were significantly associated with the prognosis (OR [95% CI]: 0.985 [0.979–0.991], $P < 0.001$; 0.967 [0.944–0.991], $P = 0.007$; and 1.016 [1.006–1.026], $P = 0.002$, respectively; Table 4).

Discussion

This study comprehensively summarized the performance of V-V ECMO in China from 2017 to 2019. Furthermore, ICU quality was multifacetedly evaluated using structural indicators (capacity parameters), process indicators (quality control indicators), and outcome indicators (ICU mortality), and the association between ICU quality and the prognosis of V-V ECMO-supported patients was thoroughly analyzed. In addition to ECMO-related complications, the volume of ECMO centers and certain ICU quality control indicators were independently associated with in-hospital mortality.

The correlations between the indicators of quality

Table 3 Comparison of capacity parameters and quality control indicators in high- and low-volume V-V ECMO centers*

	High-volume centers (V-V ECMO ⩾ 50 cases)	Low-volume centers (V-V ECMO < 50 cases)	*P*
	N = 11	*N* = 307	
Quality control indicators (median, IQR)			
Proportion of ICU in total inpatients (%)	3.88 (1.92, 4.96)	1.8 (1.22, 3.19)	0.023
Proportion of ICU in total inpatient bed occupancy (%)	3.15 (1.99, 3.95)	1.64 (1.06, 2.54)	0.006
Proportion of patients with Apache II score ⩾ 15 in all ICU patients (%)	35.7 (19.5, 62.3)	52.9 (35.3, 72.0)	0.065
3-h SSC bundles compliance rate (%)	90.9 (79.9, 100)	90.7 (77.9, 100)	0.909
6-h SSC bundle compliance rate (%)	87.9 (63.0, 98.3)	83.2 (67.1, 98.5)	0.932
Microbiology detection before antibiotics (%)	97.4 (85.6, 100)	94.6 (80.3, 100)	0.334
DVT prophylaxis rate (%)	30.9 (17.3, 42.4)	34.1 (15, 60.2)	0.632
Unplanned endotracheal extubation rate (%)	0.39 (0.08, 0.9)	0.87 (0.26, 1.99)	0.095
Reintubation rate within 48 h (%)	0.77 (0.02, 2.03)	1.64 (0.8, 2.89)	0.045
Rate of unplanned transfer to ICU (%)	3.85 (1.47, 8.03)	3.1 (0.97, 10.5)	0.927
ICU readmission rate within 48 h (%)	0.58 (0.28, 1.48)	0.9 (0.43, 1.48)	0.355
VAP incidence rate per 1000 ventilator days (‰)	3.74 (1.81, 4.7)	5.39 (2.66, 9.37)	0.127
CRBSI incidence rate per 1000 lines days (‰)	1.09 (0.53, 2.25)	0.98 (0.42, 1.91)	0.636
CAUTI incidence rate (%) per 1000 lines days (‰)	0.93 (0.47, 2.32)	1.29 (0.5, 2.66)	0.671
ICU mortality rate (%)	6.56 (2.15, 11.12)	7.71 (3.99, 12.8)	0.262
Capacity parameters (median, IQR)			
ICU patient-to-bed ratio	49.7 (39.8, 61.1)	38.6 (28, 56.9)	0.043
Severe patient-to-bed ratio	17.1 (12.7, 28.2)	19.4 (11.9, 30.1)	0.628
Intensivist-to-bed ratio	0.63 (0.47, 0.81)	0.54 (0.4, 0.7)	0.300
Nurse-to-bed ratio	2.63 (1.84, 3.24)	2.05 (1.53, 2.52)	0.037
Intensivist-to-ICU patient ratio	13.7 (5.53, 16.9)	13.7 (9.45, 20.0)	0.482
Intensivist-to-severe ICU patient ratio	37.8 (24.7, 45.3)	26.9 (18.5, 40.5)	0.196

*The ECMO centers were divided into high- and low-volume centers in accordance with whether the total cases were > 50 from 2017 to 2019. IQR, interquartile range; SSC, surviving sepsis campaign; DVT, deep venous thrombosis; VAP, ventilator-associated pneumonia; CRBSI, catheter-related bloodstream infection; CAUTI, catheter-associated urinary tract infection.

control and the prognosis of V-V ECMO-supported patients were thoroughly explored. The unplanned reintubation rate and the ICU mortality rate were independently associated with in-hospital mortality in V-V ECMO-supported patients. Previous studies showed that after a successful spontaneous breathing test and extubation, 10%–25% of patients required reintubation, and reintubation increased the risk of ventilator-associated pneumonia and was associated with high mortality [15–17]. Ionescu et al. [18] recently found that older age, use of paralytics, and high positive end-expiratory pressure predicted reintubation. In the treatment of V-V ECMO-supported patients, ICU-acquired weakness caused by long-term application of sedatives and muscle relaxants and an inappropriate positive end-expiratory pressure setting may lead to an increase in the reintubation rate, which reflects the efficacy of respiratory therapy to a certain extent. The reintubation rate, together with the CAUTI rate and total ICU mortality rate, mirror the quality of care in the ICU, as confirmed by the study that showed patients with a high incidence rate had higher in-hospital mortality [19–21].

The volume of ECMO centers has been identified as an independent risk factor for patient outcomes [3,13], and the association between the center volume and prognosis of V-V ECMO-supported patients was first illustrated in a developing country. In the present study, V-V ECMO cases of > 50 runs within 3 years was confirmed to be a protective factor for patients' prognosis. Patients in high-volume centers were much older and had a higher rate of respiratory comorbidities than those in low-volume centers; however, they had a lower in-hospital mortality rate. Greater experience in the delivery of ECMO is of great importance for improving outcomes; however, given the complexity of ECMO, a better prognosis could be achieved by enhanced resources and personnel, and adherence to evidence-based care (all of which are ICU

Table 4 Multivariate analysis of association between quality indicators and in-hospital mortality of V-V ECMO-supported patients in high-volume centers

	B	SE	Wald	OR	95% CI	*P*
Quality control indicators						
Proportion of ICU in total inpatients	0.166	0.052	10.3	1.18	1.067–1.306	0.001
6-h SSC bundle compliance rate	0.015	0.004	13.52	1.015	1.007–1.023	< 0.0001
Microbiology detection before antibiotics	−0.028	0.01	7.338	0.972	0.952–0.992	0.007
Reintubation rate within 48 h	−0.332	0.075	18.37	0.725	0.625–0.84	< 0.0001
ICU mortality rate	0.198	0.035	33.02	1.219	1.14–1.305	< 0.0001
ICU capacity parameters						
ICU patient-to-bed ratio	−0.015	0.003	21.48	0.985	0.979–0.991	< 0.0001
Intensivist-to-severe ICU patient ratio	−0.034	0.012	7.275	0.967	0.944–0.991	0.007
Nurse-to-severe ICU patient ratio	0.016	0.005	9.688	1.016	1.006–1.026	0.002
V-V ECMO related complications						
Intracerebral hemorrhage	0.703	0.357	3.89	2.021	1.004–4.065	0.049
Hypoxic–ischemic encephalopathy	0.776	0.305	6.47	2.174	1.195–3.954	0.011
Multiple organ dysfunction syndrome	0.845	0.187	20.49	2.33	1.615–3.357	< 0.0001
Coagulation disorder	0.913	0.183	24.97	2.491	1.741–3.562	< 0.0001
Bacteremia	0.523	0.181	8.300	1.687	1.182–2.407	0.004

V-V ECMO, veno-venous extracorporeal membrane oxygenation; ICU, intensive care unit; SSC, surviving sepsis campaign; SE, standard error; OR, odds ratio; CI, confidence interval.

quality control indicators). A subgroup analysis of patients in high-volume centers was performed to rule out the potential influence of center volume, and the association between ICU quality and in-hospital mortality was further confirmed. Besides the reintubation rate and total ICU mortality rate, the intensivist-to-severe ICU patient ratio and nurse-to-severe ICU patient ratio were significantly associated with the prognosis of V-V ECMO-supported patients in high-volume centers.

A previous study showed that a high nurse-to-patient ratio was independently associated with a lower risk of in-hospital mortality [22]. The ELSO guidelines [12] recommend maintenance of a 1:1 patient-to-nurse ratio when patients are on ECMO support. The nurse-to-bed ratio in low-volume centers in the present study was 2.05, consistent with data in a nationwide survey showing a calculated patient-to-nurse ratio of approximately 2:1 [7]. However, this finding is far from adequate. Actually, the gap between medical human resources and ICU expansion was even greater, especially after the COVID-19 outbreak [4]. The number of trained personnel per center was an independent risk factor for the prognosis of ICU patients, especially critically ill patients, supported by the present study's finding of an association between the intensivist-to-severe ICU patient ratio and nurse-to-severe ICU patient ratio with in-hospital mortality of V-V ECMO-supported patients. Rational allocation of medical resources needs to be strengthened to further improve the prognosis of V-V ECMO-supported patients.

Limitations

This study had three main limitations. First, this was a retrospective observational study, and the observed differences may be subject to unobserved confounding factors. However, all available influencing factors, including indicators of ICU quality control, capacity parameters, and ECMO-related quality indicators, were analyzed to minimize the risk of bias. Second, some important information, such as the patient conditions requiring the initiation of ECMO support and the ECMO treatment details, could not be obtained because of limitations of the database. However, these problems were not the focus of this study. Finally, differences in treatment and heterogeneities among ICU management protocols could have biased the results because of the long observation window. However, the results from high-volume centers further strengthened the effect of ICU quality control on the prognosis.

Conclusions

The number of V-V ECMO cases increased and in-hospital mortality remained constant from 2017 to 2019. In addition to ECMO-related complications, the volume of ECMO centers and certain ICU quality control indicators (reintubation rate within 48 h after extubation and total ICU mortality) were independently associated with in-hospital mortality. The results of the subgroup analysis of 864 patients in 11 high-volume centers further strengthened these findings.

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Compliance with ethics guidelines

Conflicts of interest Wei Cheng, Jieqing Chen, Xudong Ma, Jialu Sun, Sifa Gao, Ye Wang, Longxiang Su, Lu Wang, Wei Du, Huaiwu He, Yujie Chen, Zunzhu Li, Qi Li, Jianhua Sun, Hongbo Luo, Jinbang Liu, Guangliang Shan, Bing Du, Yanhong Guo, Dawei Liu, Chang Yin, and Xiang Zhou declare that they have no conflict of interest.

This article does not contain any studies involving human or animal subjects. The data collection was approved by the National Health Commission of China, and the study was approved by the institutional review board of Peking Union Medical College Hospital (approval number: SK1828). Because of the retrospective and deidentified nature of the data, a waiver for individual consent was granted by the research ethics board.

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References

1. Ramanathan K, Shekar K, Ling RR, Barbaro RP, Wong SN, Tan CS, Rochwerg B, Fernando SM, Takeda S, MacLaren G, Fan E, Brodie D. Extracorporeal membrane oxygenation for COVID-19: a systematic review and meta-analysis. Crit Care 2021; 25(1): 211
2. Broman LM, Eksborg S, Lo Coco V, De Piero ME, Belohlavek J, Lorusso R; EuroECMO COVID-19 Working Group; Euro-ELSO Steering Committee. Extracorporeal membrane oxygenation for COVID-19 during first and second waves. Lancet Respir Med 2021; 9(8): e80–e81
3. Lebreton G, Schmidt M, Ponnaiah M, Folliguet T, Para M, Guihaire J, Lansac E, Sage E, Cholley B, Mégarbane B, Cronier P, Zarka J, Da Silva D, Besset S, Morichau-Beauchant T, Lacombat I, Mongardon N, Richard C, Duranteau J, Cerf C, Saiydoun G, Sonneville R, Chiche JD, Nataf P, Longrois D, Combes A, Leprince P; Paris ECMO-COVID-19 investigators. Extracorporeal membrane oxygenation network organisation and clinical outcomes during the COVID-19 pandemic in Greater Paris, France: a multicentre cohort study. Lancet Respir Med 2021; 9(8): 851–862
4. Li C, Hou X, Tong Z, Qiu H, Li Y, Li A; Chinese Society of Extracorporeal Life Support (CSECLS). Extracorporeal membrane oxygenation programs for COVID-19 in China. Crit Care 2020; 24(1): 317
5. Karagiannidis C, Strassmann S, Merten M, Bein T, Windisch W, Meybohm P, Weber-Carstens S. High in-hospital mortality rate in patients with COVID-19 receiving extracorporeal membrane oxygenation in Germany: a critical analysis. Am J Respir Crit Care Med 2021; 204(8): 991–994
6. Wang L, Ma X, He H, Su L, Guo Y, Shan G, Zhou X, Liu D, Long Y; China National Critical Care Quality Control Center Group. Analysis of structure indicators influencing 3-h and 6-h compliance with the surviving sepsis campaign guidelines in China: a systematic review. Eur J Med Res 2021; 26(1): 27
7. He H, Ma X, Su L, Wang L, Guo Y, Shan G, He HJ, Zhou X, Liu D, Long Y, Zhao Y, Zhang S; China-NCCQC group. Effects of a national quality improvement program on ICUs in China: a controlled pre-post cohort study in 586 hospitals. Crit Care 2020; 24(1): 73
8. Su L, Ma X, Gao S, Yin Z, Chen Y, Wang W, He H, Du W, Hu Y, Ma D, Zhang F, Zhu W, Meng X, Sun G, Ma L, Jiang H, Shan G, Liu D, Zhou X; China-NCCQC. Evaluation of ICUs and weight of quality control indicators: an exploratory study based on Chinese ICU quality data from 2015 to 2020. Front Med 2023; [Epub ahead of print] doi:10.1007/s11684-022-0970-x
9. Ding X, Ma X, Gao S, Su L, Shan G, Hu Y, Chen J, Ma D, Zhang F, Zhu W, Sun G, Meng X, Ma L, Zhou X, Liu D, Du B; China National Critical Care Quality Control Center Group. Effect of ICU quality control indicators on VAP incidence rate and mortality: a retrospective study of 1267 hospitals in China. Crit Care 2022; 26(1): 405
10. Cheng W, Ma XD, Su LX, He HW, Wang L, Tang B, Du W, Zhou YK, Wang H, Cui N, Long Y, Liu DW, Guo YH, Wang Y, Shan GL, Zhou X, Zhang SY, Zhao YP. Cross-sectional study for the clinical application of extracorporeal membrane oxygenation in the mainland of China, 2018. Crit Care 2020; 24(1): 554
11. Tonna JE, Abrams D, Brodie D, Greenwood JC, Rubio Mateo-Sidron JA, Usman A, Fan E. Management of adult patients supported with venovenous extracorporeal membrane oxygenation (VV ECMO): guideline from the Extracorporeal Life Support Organization (ELSO). ASAIO J 2021; 67(6): 601–610
12. Shekar K, Badulak J, Peek G, Boeken U, Dalton HJ, Arora L, Zakhary B, Ramanathan K, Starr J, Akkanti B, Antonini MV, Ogino MT, Raman L, Barret N, Brodie D, Combes A, Lorusso R, MacLaren G, Müller T, Paden M, Pellegrino V; ELSO Guideline Working Group. Extracorporeal Life Support Organization coronavirus disease 2019 interim guidelines: a consensus document from an international group of interdisciplinary extracorporeal membrane oxygenation providers. ASAIO J 2020; 66(7): 707–721
13. Barbaro RP, Odetola FO, Kidwell KM, Paden ML, Bartlett RH, Davis MM, Annich GM. Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. Am J Respir Crit Care Med 2015; 191(8): 894–901

14. Kirkland BW, Wilkes J, Bailly DK, Bratton SL. Extracorporeal membrane oxygenation for pediatric respiratory failure: risk factors associated with center volume and mortality. Pediatr Crit Care Med 2016; 17(8): 779–788
15. Li Y, Li H, Zhang D. Comparison of T-piece and pressure support ventilation as spontaneous breathing trials in critically ill patients: a systematic review and meta-analysis. Crit Care 2020; 24(1): 67
16. Jaber S, Quintard H, Cinotti R, Asehnoune K, Arnal JM, Guitton C, Paugam-Burtz C, Abback P, Mekontso Dessap A, Lakhal K, Lasocki S, Plantefeve G, Claud B, Pottecher J, Corne P, Ichai C, Hajjej Z, Molinari N, Chanques G, Papazian L, Azoulay E, De Jong A. Risk factors and outcomes for airway failure versus non-airway failure in the intensive care unit: a multicenter observational study of 1514 extubation procedures. Crit Care 2018; 22(1): 236
17. Gao F, Yang LH, He HR, Ma XC, Lu J, Zhai YJ, Guo LT, Wang X, Zheng J. The effect of reintubation on ventilator-associated pneumonia and mortality among mechanically ventilated patients with intubation: a systematic review and meta-analysis. Heart Lung 2016; 45(4): 363–371
18. Ionescu F, Zimmer MS, Petrescu I, Castillo E, Bozyk P, Abbas A, Abplanalp L, Dogra S, Nair GB. Extubation failure in critically ill COVID-19 patients: risk factors and impact on in-hospital mortality. J Intensive Care Med 2021; 36(9): 1018–1024
19. Patel PK, Gupta A, Vaughn VM, Mann JD, Ameling JM, Meddings J. Review of strategies to reduce central line-associated bloodstream infection (CLABSI) and catheter-associated urinary tract infection (CAUTI) in adult ICUs. J Hosp Med 2018; 13(2): 105–116
20. Clarke K, Hall CL, Wiley Z, Tejedor SC, Kim JS, Reif L, Witt L, Jacob JT. Catheter-associated urinary tract infections in adults: diagnosis, treatment, and prevention. J Hosp Med 2020; 15(9): 552–556
21. Duran Ramirez JM, Gomez J, Obernuefemann CLP, Gualberto NC, Walker JN. Semi-quantitative assay to measure urease activity by urinary catheter-associated uropathogens. Front Cell Infect Microbiol 2022; 12: 859093
22. Sakr Y, Moreira CL, Rhodes A, Ferguson ND, Kleinpell R, Pickkers P, Kuiper MA, Lipman J, Vincent JL; Extended Prevalence of Infection in Intensive Care Study Investigators. The impact of hospital and ICU organizational factors on outcome in critically ill patients: results from the Extended Prevalence of Infection in Intensive Care study. Crit Care Med 2015; 43(3): 519–526