

## Hospital expenses of nosocomial infection associated with extracorporeal membrane oxygenation in China: a retrospective cohort study

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**Background:** Extracorporeal membrane oxygenation (ECMO) is a highly invasive procedure and a highcost medical measure, but the economic impact of nosocomial infection after ECMO support remains largely uninvestigated.

**Methods:** We constructed a retrospective cohort of all patients hospitalized at the First Affiliated Hospital of Nanjing Medical University from 2013 to 2020 who had ECMO supported clinical samples. Propensity score matching (PSM) was used to control the impact of potential confounding variables, including demographics, commodities, and treatment, and to estimate the economic burden of nosocomial infection after ECMO support.

**Results:** There were 194 patients with ECMO support, 136 patients had no infection after ECMO, 38 patients had infection after ECMO, of which 97.4% was lower respiratory tract infection. Compared with patients among ECMO non infection group, the main reasons for ECMO treatment of patients among ECMO infection group were supportive treatment of cardiac dysfunction (63.16% vs. 42.31%, P=0.021) and longer use of catheter (13.74 $\pm$ 14.97 vs. 15.97 $\pm$ 14.33 days, P=0.034). The total hospital expenses for patients among ECMO infection group and ECMO non infection group were about \$55,878 and \$51,277 respectively. Patients with ECMO infection had significantly higher radiate expenses, operational expenses and anesthetic expenses than those among ECMO non infection group (\$119.06 vs. \$69.32, P=0.025; \$6,458.81 vs. \$4,882.49, P=0.034; \$331.62 vs. \$145.56, P=0.030).

**Conclusions:** Our study demonstrates that the incidence of nosocomial infection after ECMO support was relatively high, which did not lead to high total hospital expenses, but lead to higher radiate expenses, operational expenses and anesthetic expenses.

Keywords: Extracorporeal membrane oxygenation (ECMO); hospital expenses; nosocomial infection

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### Introduction

Extracorporeal membrane oxygenation (ECMO) is a novel technique for rescuing critically ill patients. It is a derivative of cardiopulmonary bypass in cardiac surgery. In the past decade, ECMO has gradually gained popularity as a rescue treatment for patients with severe acute respiratory distress syndrome (ARDS) and cardiogenic shock (1). It promotes gas exchange in the case of refractory hypoxemia or hypercapnia respiratory acidosis and also promotes reduced mechanical ventilation intensity (2). The technology itself can't treat the disease, but it can buy time for the drugs used to treat the disease, so as to improve the survival rate of patients. In some meta-analysis of individual patient data in severe ARDS, ECMO treatment has been demonstrated to significantly reduce 60- or 90-day mortality compared with conventional treatment (3,4). However, the ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) trial did not show a significant reduction in mortality in the ECMO group compared with treatment with conventional mechanical ventilation, who received conventional mechanical ventilation in combination with alternative rescue strategies (5). Therefore, there are still many controversies and doubts about whether the survival rate of patients receiving ECMO is improved. The outcomes varied due to the use of different participant selection criteria, protocols, and strategies, according to relevant regional emergency medical services and hospital response systems (6,7).

In addition, the reported risk of nosocomial infection among patients receiving ECMO ranged from 3.5% to 64% per extra corporeal membrane oxygenation run, while the incidence of nosocomial infection ranged from 10.1 to 116.2/1,000 ECMO days (8,9). Factors related to increased risk of nosocomial infection include adult patients, severity of potential diseases, immunosuppression, longer ECMO support and intensive care unit (ICU) hospitalization, and intravenous artery ECMO treatment. The presence of vascular equipment, such as large diameter ECMO cannula, central venous catheter and artery catheter, may pollute multiple entrances of these devices, and may increase the risk of hospital infection owing to the destruction of skin protection barrier (9-11).

This technology usually exposes patients to a variety of complications, so patients often have to pay high costs (12,13). With the discovery that antimicrobial prophylaxis in patients on ECMO could reduce nosocomial infection and showed lower mortality, some studies have found that antimicrobial prophylaxis and overuse have gradually emerged, so whether it is a cost-effective intervention is still undiscovered (14,15). Because of the extra cost of ECMOrelated nosocomial infection, it may bring more economic burden to the health system. However, the economic impact of ECMO-related nosocomial infections remains largely uninvestigated. Therefore, we proceeded to a retrospective cohort study to explore total hospitalization costs in ECMO-treated patients. We also compared resource usage (such as multiple treatments, hospital costs, and disposal)

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between the ECMO nosocomial infections and non-ECMO nosocomial infections groups, using a propensity score-matched analysis. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-1825/rc).

### Methods

### Study population

From January 1, 2013 to July 31, 2020, we enrolled 194 patients who were treated with ECMO in the First Affiliated Hospital of Nanjing Medical University. With 6,000 beds, the hospital is one of the main referral centers in eastern China. The First Affiliated Hospital of Nanjing Medical University has a perfect hospital information system. We retrieved patient characteristics from an electronic medical record. The data collected for each patient included demographic data, site of infection, underlying disease, microbiological data, clinical management, clinical outcomes (death or discharge alive) and various hospitalization expenses. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and the ethics committee of the First Affiliated Hospital of Nanjing Medical University approved the study (No. 2019-SR-075). Informed consent was taken from all the patients.

The nosocomial infection after ECMO was identified as the nosocomial infection from 24 hours after the use of ECMO to 48 hours after the end of ECMO (10). According to the diagnostic criteria for nosocomial infection (Trial) issued by the former Ministry of health in 2001, the patients were divided into ECMO infection group (n=38) and ECMO non infection group (n=156) according to whether there was nosocomial infection after ECMO. Patients with infection before ECMO support treatment and patients with weaning or death within 48 hours after ECMO support treatment were excluded.

### Study variables

Retrospective cohort study was used to extract and sort out the gender, age, hypertension, diabetes, ECMO treatment mode, treatment time, hospitalization time, antibiotics use, combination medication, ventilator use time, central venous intubation time, catheter intubation time and other factors of patients in ECMO infection group and ECMO

non infection group through hospital information system. The cost analysis of health economics in the two groups included the total cost of hospitalization, bed fee, nursing fee, western medicine fee, radiation fee, laboratory test fee, oxygen therapy fee, blood transfusion therapy fee, diagnosis and treatment fee, operational fee, anesthesia fee and other expenses.

Total hospitalization expenses include medicine, radiation, laboratory, diagnosis and treatment, operation, anesthesia, nursing, etc. All expenses are adjusted for inflation. Hospitalization expenses are settled in RMB and converted into US dollars according to the exchange rate issued by the Bank of China from 2013 to 2020 (2013: 1 US dollar =6.09 RMB; 2014: 1 US dollar =6.12 RMB; 2015: 1 US dollar =6.49 RMB; 2016: 1 US dollar =6.94 RMB; 2017: 1 US dollar =6.53 RMB; 2018: 1 US dollar =6.86 RMB; 2019: 1 US dollar =6.98 RMB; 2020: 1 US dollar =6.52 RMB) (https://srh.bankofchina.com/search/whpj/search\_cn.jsp).

### Propensity score matching (PSM)

To minimize the impact of potential confounding variables, we used Stata Version 15.0 for PSM. We did three rounds of PSM step by step. First, for the logistic regression model with ECMO infection group and ECMO non infection group as dependent variables, we input variables including the patient's demographics (age and gender), concomitant diseases (hypertension, diabetes, myocarditis, etc.), treatment (number of surgery and antibiotics), and clinical outcomes (length of stay, septic shock, cardiac arrest, respiratory failure, death, etc.) or infection type. We use predictive probabilities for each potential confounding variable of PSM. The propensity score was balanced between the two groups, so we used the nearest neighbor matching (1:1 match; 1:2 match; 1:3 match respectively) to obtain the matching between the subjects and the control group with the caliper value of 0.01. For the generated pairs, they matched all the included variables for further hospital expenses analysis.

### Statistical analysis

Demographic data were characterized using proportions for categorical variables and mean with standard deviations (SD). The PSM method was utilized to analyze the difference of hospitalization expenses of ECMO infection group *vs.* ECMO non infection group. After propensity score matches were generated, balance in baseline covariates of the two groups was assessed using reduce bias (%) or P value. All P values were two-sided with a significance threshold of P<0.05. Since the degree of data missing in this study was less than 5%, we deleted the missing data. All statistical analyses were performed using STATA ver. 15.0 (StataCorp LLC, College Station, TX, USA).

### **Results**

## Basic characteristics of the patients with ECMO infection group and ECMO non infection group before PSM

During the study period, 156 patients had no infection after ECMO, 38 patients had infection after ECMO, of which 97.4% was lower respiratory tract infection. Most of the patients (about 61.3%) were male, and the average age of two groups was 47.613 $\pm$ 17.294 and 46.895 $\pm$ 16.670 years respectively (*Table 1*). Compared with patients among ECMO non infection group, the main reasons for ECMO treatment of patients among ECMO infection group were supportive treatment of cardiac dysfunction (63.16% vs. 42.31%, P=0.021) and longer use of catheter (13.74 $\pm$ 14.97 vs. 15.97 $\pm$ 14.33 days, P=0.034), which may have an uncontrollable confounding effect in comparing medical costs between the two groups. However, there were no significant differences in comorbidity and other variables between the two groups (*Table 1*).

# Comparison of basic characteristics in both groups after PSM and equilibrium test results of PSM

We therefore used PSM (1:1 match; 1:2 match; 1:3 match respectively) to minimize the confounding effects impact and obtained 35 pairs matched for patient's demographic, comorbidity, and treatment. The results after 1:1 and 1:3 matching are similar to the results of 1:2. *Table 2* shows the comparison results of baseline characteristics before and after 1:2 matching. There were no significant differences in all baseline characteristics between the two groups after PSM. Depending on the results of equilibrium test, all variables between the two groups are balanced after PSM. The PSM matching results are shown in *Figure 1*. These pairs were submitted to analyses of medical expenses.

## Comparison of hospitalization expenses in both groups after PSM

The total hospital expenses for patients among ECMO

<b>Table 1</b> Basic characteristics of the patients with extracorporeal membrane oxygenation (ECMO) support	Table 1	Basic charact	eristics of the	patients with	extracorporeal	membrane	oxvgenation (	(ECMO) support
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Variables	ECMO infection group (n=156)	ECMO non infection group (n=38)	$t/\chi^2$	Р
Age	47.613±17.294	46.895±16.670	44.369	0.935
Sex, n (%)			0.237	0.627
Male	97 (62.18)	22 (57.89)		
Female	59 (37.82)	16 (42.11)		
Usage, n (%)			5.341	0.021
Cardiac dysfunction	66 (42.31)	24 (63.16)		
Cardiopulmonary resuscitation	90 (57.69)	14 (36.84)		
Year, n (%)			0.201	0.978
2017 and before	37 (23.72)	10 (26.32)		
2018	36 (23.08)	9 (23.68)		
2019	59 (37.82)	13 (34.21)		
2020	24 (15.38)	6 (15.79)		
Outcome, n (%)			1.235	0.26
Death	23 (14.74)	3 (7.89)		
Survival	133 (85.26)	35 (92.11)		
Preventive drugs before operation, n (%)			1.239	0.26
No	109 (69.87)	30 (78.95)		
Yes	47 (30.13)	8 (21.05)		
Diabetes, n (%)			0.023	0.88
No	134 (85.90)	33 (86.84)		
Yes	22 (14.10)	5 (13.16)		
Respiratory failure, n (%)			1.955	0.16
No	96 (61.54)	28 (73.68)		
Yes	60 (38.46)	10 (26.32)		
Renal damage, n (%)			0.002	0.96
No	135 (86.54)	33 (86.84)		
Yes	21 (13.46)	5 (13.16)		
Cardiac arrest, n (%)			1.113	0.29
No	119 (76.28)	32 (84.21)		
Yes	37 (23.72)	6 (15.79)		
Cardiac shock, n (%)			0.289	0.59
No	108 (69.23)	28 (73.68)		
Yes	48 (30.77)	10 (26.32)		

Table 1 (continued)

Table 1 (continued)

Variables	ECMO infection group (n=156)	ECMO non infection group (n=38)	$t/\chi^2$	Р
Carditis, n (%)			0.239	0.625
No	126 (80.77)	32 (84.21)		
Yes	30 (19.23)	6 (15.79)		
Atherosclerosis, n (%)			0.454	0.501
No	133 (85.26)	34 (89.47)		
Yes	23 (14.74)	4 (10.53)		
Liver injury, n (%)			0.018	0.893
No	141 (90.38)	34 (89.47)		
Yes	15 (9.62)	4 (10.53)		
Tumor, n (%)			1.928	0.165
No	145 (92.95)	32 (84.21)		
Yes	11 (7.05)	6 (15.79)		
Hypertension, n (%)			1.268	0.260
No	113 (72.44)	24 (63.16)		
Yes	43 (27.56)	14 (36.84)		
Length of stay	28.579±23.470	35.799±91.876	72.807	0.264
Fever days	4.010±7.158	4.947±7.082	27.443	0.238
Number of antibiotics	4.423±2.925	4.423±2.925	13.875	0.535
Days of antibiotic use	18.679±19.134	21.973±17.273	52.498	0.455
Number of abnormal blood routine	20.835±26.096	20.421±14.182	44.996	0.775
Days of ventilator use	7.969±9.470	8.921±9.143	37.696	0.263
Days of central venous catheter use	10.694±11.018	12.079±10.846	36.841	0.430
Days of catheter use	13.736±14.966	15.974±14.325	64.953	0.034

infection group and ECMO non infection group were about \$55,878 and \$51,277 respectively. Patients with ECMO infection had significantly higher radiate expenses, operational expenses and anesthetic expenses than those among ECMO non infection group (\$119.06 vs. \$69.32, P=0.025; \$6,458.81 vs. \$4,882.49, P=0.034; \$331.62 vs. \$145.56, P=0.030) (*Table 3*).

### Discussion

ECMO technique mainly involves the drainage of venous blood out of the body, oxygenated by artificial centrifugal pump and oxygenator, and then re-infuses blood into the body through veins and/or arteries to replace or partially replace the cardiopulmonary function, so as to maintain the perfusion and oxygenation of various organs in the body (16). ECMO can provide long-term cardiopulmonary support for patients with severe reversible circulatory and/or respiratory failure, providing valuable time for rescue treatment and cardiopulmonary function recovery (17). ECMO support rate of patients with cardiac arrest or cardiogenic shock is increasing. In this regard, although patient selection criteria have been expanded to include complex cases such as the elderly and multiple comorbidities, risk adjusted discharge survival rates was 29% overall (18). Despite advances in provision of ECMO care and increasing co-morbidities of patients, there has been no changes in risk adjusted survival over time. We examined 194 adult patients supported with

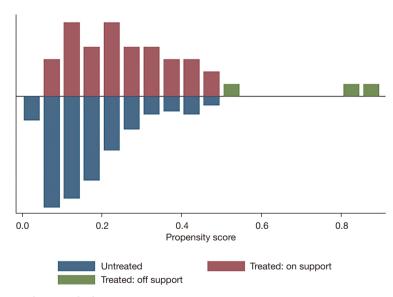
Variables	Status	ECMO infection group	ECMO non infection group	Bias (%)	Reduce bias (%)	t	Р
Age	Unmatched	46.378	47.967	-9.29	-5.07	-0.516	0.60
	Matched	46.314	48	-9.76		-0.408	0.684
Sex	Unmatched	1.405	1.382	4.84	-135.68	0.262	0.79
	Matched	1.4	1.457	-11.40		-0.477	0.63
Usage	Unmatched	0.378	0.566	-37.90	84.73	-2.075	0.04
	Matched	0.4	0.371	5.79		0.242	0.80
Year	Unmatched	2,018.351	2,018.178	13.25	-290.80	0.824	0.41
	Matched	2,018.429	2,018.857	51.77		2.166	0.23
Length of stay	Unmatched	29.108	38.48	-12.55	12.13	-1.018	0.31
	Matched	27.029	24.886	11.03		0.461	0.64
Fever days	Unmatched	5.081	3.862	16.95	6.89	0.929	0.35
	Matched	4.4	3.457	15.78		0.66	0.51
Preventive drugs before operation	Unmatched	0.811	0.711	23.48	69.14	1.337	0.18
	Matched	0.8	0.829	-7.25		-0.303	0.76
Number of antibiotics	Unmatched	5.027	4.395	21.51	-15.15	1.153	0.25
	Matched	4.771	4.171	24.77		1.036	0.30
Days of antibiotic use	Unmatched	21.973	17.954	21.77	59.01	1.235	0.22
	Matched	19.914	18.629	8.93		0.373	0.71
Number of abnormal blood routine	Unmatched	20.946	21.421	-2.12	-409.32	-0.146	0.88
	Matched	20.371	18.714	10.78		0.451	0.65
Days of ventilator use	Unmatched	9.162	7.888	13.59	30.17	0.753	0.45
	Matched	8.8	8	9.49		0.397	0.69
Days of central venous catheter use	Unmatched	12.405	10.559	16.87	96.12	0.927	0.35
	Matched	11.229	11.286	-0.66		-0.027	0.97
Days of catheter use	Unmatched	16.405	13.447	20.10	44.89	2.117	0.04
	Matched	14.657	16.171	-11.08		-0.463	0.64
Outcome	Unmatched	0.919	0.849	21.89	-94.94	1.3	0.19
	Matched	0.914	1	-42.68		-1.785	0.08
Hypertension	Unmatched	0.351	0.276	16.08	62.70	0.858	0.39
	Matched	0.314	0.343	-6.00		-0.251	0.80
Diabetes	Unmatched	0.135	0.138	-0.87	-976.90	-0.048	0.96
	Matched	0.114	0.086	9.40		0.393	0.69
Respiratory failure	Unmatched	0.243	0.375	-28.58	100.00	-1.614	0.11
	Matched	0.257	0.257	0.00		0	1

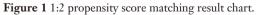
Table 2 Comparison of basic characteristics in both groups after PSM

Table 2 (continued)

Variables	Status	ECMO infection group	ECMO non infection group	Bias (%)	Reduce bias (%)	t	Р
Renal damage	Unmatched	0.135	0.132	1.04	-1,345.04	0.056	0.955
	Matched	0.143	0.2	-14.99		-0.627	0.533
Cardiac arrest	Unmatched	0.158	0.237	-19.86	32.40	-1.149	0.255
	Matched	0.158	0.211	-13.43		-0.585	0.56
Cardiac shock	Unmatched	0.263	0.308	-9.79	100.00	-0.548	0.586
	Matched	0.263	0.263	0.00		0	1
Carditis	Unmatched	0.158	0.192	-8.99	100.00	-0.508	0.614
	Matched	0.158	0.158	0.00		0	1
Atherosclerosis	Unmatched	0.105	0.147	-12.62	-53.31	-0.728	0.469
	Matched	0.105	0.053	19.35		0.844	0.402
Liver injury	Unmatched	0.105	0.096	3.00	100.00	0.163	0.871
	Matched	0.105	0.105	0.00		0	1
Tumor	Unmatched	0.158	0.071	27.46	100.00	1.379	0.175
	Matched	0.158	0.158	0.00		0	1

PSM, propensity score matching; ECMO, extracorporeal membrane oxygenation.





venoarterial ECMO from 2013 to 2020. Venoarterial ECMO was used for cardiac dysfunction in 90 patients (46.39%) and cardiopulmonary resuscitation in 104 patients (53.61%) respectively. Number of patients treated with ECMO increased annually, from a few cases to dozens per year. This

is explained by the fact that the First Affiliated Hospital of Nanjing Medical University is a high-level and high-capacity hospital in China, which can provide patients with highquality health care services or ECMO support services.

Studies have shown that ECMO support is linked

Table 3 Hospital e	xpenses in	patients with EC	MO support after PSM

Expenses (US dollars)	ECMO infection group (n=35)	ECMO non infection group (n=70)	t	Р
Nursing	308.20±284.28	337.99±328.02	0.440	0.661
Bed	616.37±556.51	672.47±500.70	0.494	0.622
Western medicine	14,872.36±14,335.52	15,757.57±12,198.94	0.312	0.756
Radiate	69.32±81.48	119.06±111.28	2.276	0.025
Laboratory	4,043.99±2,877.40	4,107.19±2,641.03	0.106	0.915
Oxygen-therapy	248.86±237.17	283.24±220.05	0.698	0.487
Blood-transfusion	1,337.22±1,199.64	1,181.12±1,660.42	-0.48	0.632
Therapy	21,285.49±13,129.13	22,725.53±11,836.62	0.537	0.593
Operation	4,882.49±2,571.98	6,458.81±4,326.17	2.154	0.034
Other inspectors	3,452.04±2,343.92	3,886.26±2,453.51	0.83	0.409
Anesthetic	145.56±226.28	331.62±549.19	2.216	0.030
Other	9.29±12.30	12.80±21.70	0.871	0.386
Total	51,277.48±31,753.36	55,878.04±31,908.46	0.666	0.507

ECMO, extracorporeal membrane oxygenation; PSM, propensity score matching.

to lower mortality. Within one year after matching and adjusting the covariates, the risk of mortality is reduced by 24–34% (19). In the propensity matching study, the risk differences of short-term survival rate and long-term survival rate were 14% and 13%, respectively consistently with our research (26/194, 13.4%) (7). However, other studies have shown that ECMO support increases the likelihood of in-hospital death (20). These results are not consistent with our results, which may be related to different selection criteria of patients supported by ECMO, different management methods of ECMO, demographic characteristics, comorbidity, medical insurance system and regional differences in medical culture.

ECMO requires a large number of medical resources, multidisciplinary cooperation, coordination of hospital systems, and has to be used in a limited time frame. It also associates with high medical costs (21). As a highly invasive procedure, ECMO provides more time and space for the identification of the etiology of cardiac arrest and maintenance of organ perfusion. However, due to the existence of multiple potential entrances, including ECMO intubation, standard invasive catheters, and open chest wounds, etc., patients who receive ECMO are at a high risk of healthcare-associated infection, especially blood stream infection (BSI), central line associated bloodstream infections (CLABSI) (22,23). Moreover, the artificial surfaces of the ECMO circuit, such as the membrane oxygenator (MO), drainage cannula, the return cannula, could be the target of microbial adhesion and colonisation, thereby facilitating the development of ECMO-related bloodstream infection (24). After 7 years of retrospective cohort study found that 38 patients developed nosocomial infection after ECMO support, and the incidence of nosocomial infection was about 19.59% (38/194). ECMO brings great mental and economic burden to the patient's family. If nosocomial infection after ECMO occurs again, it will be worse for the patients' families. Therefore, there is an urgent need to evaluate the cost-effectiveness of infection after ECMO support in order to obtain the best long-term results and reduce the burden, which will greatly help to strengthen the implementation of nosocomial infection prevention and control measures and increase the intensity of nosocomial infection surveillance.

Several cohort studies in the United States show that total inflation-adjusted hospitalization expenses of ECMO patients increased from \$732,349 in 2009 to \$134,573 in 2016 (25). The European cohort study showed that median in-hospital costs of the index hospitalization per ECMO patient were 129,967€ (about \$153,607) (26). According to the 2018 epidemiological survey of ECMO in mainland China, the average costs per case were \$36,334 (IQR, \$22,547–56,714) (27). The results of this study showed

that the total hospital expenses for patients among ECMO infection group and ECMO non infection group were about \$55,878 and \$51,277, respectively. It is clear that medical expenses of ECMO among patients in China were relatively low. Unfortunately, we do not find evidence of a significant increase in hospitalization expenses in patients with nosocomial infections after ECMO support. This may be linked with the following reasons. Firstly, nosocomial infection in patients supported by ECMO is highly likely to result in the death, which can cause significant underestimation of the hospital expenses due to nosocomial infection (28). Secondly, some studies have found that prophylactic antibiotics during ECMO could reduce nosocomial infection and showed lower mortality (29,30). Therefore, medical institutions usually increase the use of antibiotics in order to save lives for patients who need ECMO support, no matter whether nosocomial infection occurs or not, which can be reflected from the no statistically significant difference in the use of prophylactic antibiotics and the cost of antibiotics between ECMO infection group and ECMO non infection group. It may not be enough to only analyze the expenses of ECMO patients over their entire hospital period, and may even lead to misleading conclusions. Therefore, we analyzed the detailed expenses during hospitalization and found that patients with ECMO infection had significantly higher radiate expenses, operational expenses and anesthetic expenses than those among ECMO non-infectious group. It is not hard to explain that medical institutions often keep track of patients with nosocomial infections, which involves the increase in these costs. Study have found that ECMO patients are at high risk of hospitalization in the future, and a multidisciplinary team-based antimicrobial stewardship approach can significantly reduce the prophylaxis and overuse of antimicrobial in ECMO patients without increased risk of nosocomial infection (15,31). The ELSO ID TASK FORCE Recommendation Summary also suggests that cautious, aggressive use of antifungal prophylaxis in patients deemed to be at particularly high risk (32). Therefore, we call for the adhering to strict infection control measures in the life-saving process of ECMO support treatment, and antimicrobial prophylaxis follow standard guidelines.

This study presents several limitations. First, we only included pre-existing factors, such as patient characteristics, hospital factors and pre-existing comorbidities, before index hospitalization or at the beginning of index hospitalization in our database. We did not include variables associated with unavailable resuscitation and confounding variables for PSM. Therefore, these results may not be summarized and confirmed due to the limitations of the management database. Second, the cost of treatment for ECMO patients due to infection cannot be accurately calculated, such as the cost of antimicrobials, the cost of managing adverse effects from antimicrobials, etc. Therefore, this study only compares the total hospital expenses between ECMO infection group and ECMO non infection group, as well as detailed expenses such as bed expenses, nursing expenses, radiation expenses, and operational expenses, to evaluate the increased cost of ECMO patients after infection. Third, our sample size is relatively small and it may be impossible to accurately assess the increase in medical costs for nosocomial infection after ECMO support. Moreover, due to the significant differences in the cost indicators of different countries and healthcare systems, it is necessary to carry out multi-center cohort studies and randomized controlled trials for comparing hospital expenses among ECMO infection populations in different countries and systematically evaluate the economics burden of ECMO infection populations.

### Conclusions

In conclusion, our study demonstrates that nosocomial infection did not lead to superior hospital expenses, but lead to higher radiate expenses, operational expenses and anesthetic expenses for patients with ECMO support. The input of more resources to control nosocomial infection after ECMO could be justified not only for enhancing the clinical outcomes of hospitalized patients, but also for reducing hospital expenses.

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### Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and the ethics committee of the First Affiliated Hospital of Nanjing Medical University approved the study (No. 2019-SR-075). Informed consent was taken from all the patients.

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