



Current status of antimicrobial prophylaxis during extracorporeal membrane oxygenation in Japan: a national survey

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Abstract

Infection during extracorporeal membrane oxygenation (ECMO) is a common complication that leads to increased mortality. Thus, antimicrobial prophylaxis during ECMO is often performed to prevent nosocomial infections. However, the current status of antimicrobial prophylaxis during ECMO in Japan is unclear. Therefore, we conducted a national survey of members of the Japanese Society of Intensive Care Medicine (JSICM) to clarify the current status of antimicrobial prophylaxis during ECMO in intensive care units. An 11-question survey was devised to assess antimicrobial prophylaxis and surveillance practices during ECMO. A total of 253 hospitals responded. Of these, 235 hospitals were the JSICM-certified hospitals, and the response rate was 64%. A total of 96 hospitals (39%) administered antimicrobial prophylaxis during ECMO, and 17% of hospitals had a standardized protocol for antimicrobial prophylaxis during ECMO. Of these 96 hospitals, 79% used single agents. First-generation cephalosporins were the most commonly used (54%), followed by penicillins or penicillin-derived combinations (24%), second-generation cephalosporins (7%), and anti-methicillin-resistant *Staphylococcus aureus* agents (6%). In conclusion, our survey revealed 39% of hospitals administered antimicrobial prophylaxis during ECMO in Japan. First-generation cephalosporins were the agents most commonly used.

Keywords Antimicrobial prophylaxis · Extracorporeal membrane oxygenation · Survey

Introduction

Extracorporeal membrane oxygenation (ECMO) is a treatment for acute respiratory failure and has been of great interest during the COVID-19 pandemic. Infection during ECMO is a common complication that leads to increased mortality [1]. A previous review article described that about 20% of

adult patients receiving ECMO acquired a culture-proven infection during ECMO [2]. Therefore, prevention of nosocomial infections during ECMO is important [2]. A previous survey demonstrated that 74% of ECMO centers administered antimicrobial prophylaxis [3]. However, antimicrobial exposure is associated with adverse consequences, including microbial drug resistance and *Clostridioides difficile* infections [4]. A previous review described that current evidence did not support routine prophylactic antimicrobial use in patients receiving ECMO support [2]. The latest Extracorporeal Life Support Organization (ELSO) guidelines for the management of adults undergoing ECMO did not mention antimicrobial prophylaxis [5]. The current status of antimicrobial prophylaxis during ECMO in Japan is unclear. Therefore, we conducted a national survey of members of the Japanese Society of Intensive Care Medicine (JSICM) to clarify the current status of antimicrobial prophylaxis during ECMO in intensive care units (ICUs).

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Materials and methods

This study was approved by the Fujita Health University Ethics Committee (HM20-235). The JSICM Clinical Trial Group also approved the study protocol (No. 38).

An 11-question survey was devised to assess antimicrobial prophylaxis and surveillance practices during ECMO. The questions pertained to items based on a previous study [3] and included the following: number of ICU beds, number of ECMO runs, infection surveillance using cultures, use of antimicrobial prophylaxis, and use of a standardized protocol for antimicrobial prophylaxis (full survey items are shown in Supplemental File 1). First, requests for participation were sent to members of the JSICM based on the mailing lists on February 24, 2021. Responses were collected from February 24 to March 10, 2021, in an electronic survey format using a commercial website (www.surveymonkey.com). Second, we sent an invitation

letter on March 12, 2021 to the JSICM-certified hospitals that did not respond during the first time period. These responses were collected from March 15 to April 30, 2021, using an electronic survey system or by post.

Categorical data are presented as numbers (percentages), and continuous data as median (interquartile range).

Results

A total of 253 hospitals responded to the survey. Of these, 235 hospitals were JSICM-certified, and the response rate was 64%. A summary of the survey responses is shown in the Table 1. The median number of ICU beds was 10 [8, 14]. Eighty-nine hospitals (35%) performed ECMO on more than 6 cases per year, while 164 hospitals (65%) performed fewer than 5 ECMO runs per year.

A total of 127 hospitals (51%) performed routine surveillance. Most of the cultures were from samples obtained

Table 1 Responsiveness of each item

Survey item		<i>N</i> =253
Intensive care unit beds	<i>N</i>	10 [8, 14]
ECMO runs per year		
0	<i>N</i> (%)	43 (17)
1–5	<i>N</i> (%)	121 (48)
6–10	<i>N</i> (%)	49 (19)
11–	<i>N</i> (%)	40 (16)
Routine surveillance cultures		<i>N</i> =251
Yes	<i>N</i> (%)	127 (51)
Blood	<i>N</i> (%)	92 (72)
Sputum	<i>N</i> (%)	109 (86)
Urine	<i>N</i> (%)	68 (54)
How often do you perform routine surveillance cultures?		<i>N</i> =124
Every 24 h	<i>N</i> (%)	2 (2)
Every 48 h	<i>N</i> (%)	11 (9)
Every 72 h	<i>N</i> (%)	40 (32)
Other	<i>N</i> (%)	71 (57)
Routine prophylaxis, Yes	<i>N</i> (%)	96 (39)
What percentage of ECMO patients are administrated antimicrobial prophylaxis?	%	100 [100, 100]
Standardized protocol, Yes	<i>N</i> (%)	16 (17)
Monitor compliance, Yes	<i>N</i> (%)	10 (71)
Is the antimicrobial prophylaxis for ECMO patient single antimicrobial regimen?	<i>N</i> (%)	71 (79)
Yes		
Duration of prophylaxis		
Pre-cannulation only	<i>N</i> (%)	3 (3)
Pre-cannulation and for 24 h	<i>N</i> (%)	8 (9)
Limited number of days	<i>N</i> (%)	3 (3)
Duration of ECMO	<i>N</i> (%)	33 (37)
Other/Don't know	<i>N</i> (%)	42 (47)

N number, ECMO extracorporeal membrane oxygenation

from the sputum (86%), followed by those from the blood (72%) and urine (54%). The interval between of surveillance cultures varied, namely, every 24 h (2%), every 48 h (9%), every 72 h (32%), and other intervals (57%).

A total of 96 hospitals (39%) administered antimicrobial prophylaxis during ECMO, and 17% of hospitals had a standardized protocol for antimicrobial prophylaxis. Of these 96 hospitals, 79% used single agents. First-generation cephalosporins were the most commonly used (54%), followed by penicillins or penicillin-derived combinations (24%), second-generation cephalosporins (7%), anti-methicillin-resistant *Staphylococcus aureus* (MRSA) agents (6%), carbapenems (4%), third-generation cephalosporins (3%), and echinocandin antifungal agents (1%) (Fig. 1). Of the combined regimens, an anti-MRSA agent with a carbapenem was the most commonly used (82%). Anti-MRSA agents were used in all combined regimens.

About half the hospitals (47%) did not report the duration of antimicrobial prophylaxis. For the remainder of hospitals, duration of ECMO was the most common response.

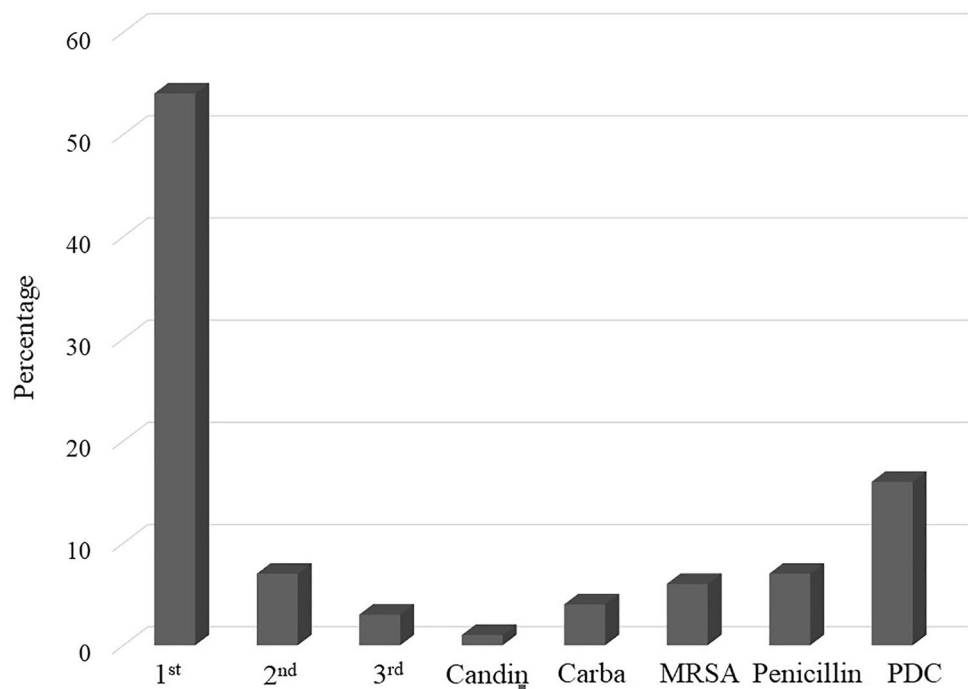
Discussion

Our survey revealed that 39% of hospitals administered antimicrobial prophylaxis during ECMO in Japan. We believe that these results represent the current status in Japan to a certain extent, because 64% of the JSICM-certified hospitals responded. In addition, this survey revealed that only 16% of hospitals run ECMO > 10 times per year, while a

previous international survey reported that 82% of centers use ECMO ≥ 10 times per year [1].

A 2010 ELSO survey of antimicrobial prophylaxis during ECMO reported that 74% of centers administered antimicrobial prophylaxis and 42% routinely administered antibacterial prophylaxis to all ECMO patients [3]. Forty-nine percent of the centers had a standardized protocol. Fewer than half the centers used a single agent, and first-generation cephalosporins were the most used in centers with a protocol, while vancomycin was the most used in those without a protocol. In centers using a combined regimen, none with a standardized protocol reported using carbapenems, whereas 14% of centers without a protocol reported using them. Routine infection surveillance was performed in 49% of the centers, and the cultures obtained were from blood (100%) and sputum (48%) samples. Another international survey performed in 2017 revealed that 55% of centers had a protocol for the use of prophylactic antibiotics and 61% had a protocol for infection surveillance, including cultures and inflammatory markers [1]. In our survey, 39% of hospitals administered antimicrobial prophylaxis and 79% of hospitals used single agents, unlike the results of previous surveys. On the other hand, only 17% of hospitals had a standardized protocol. Routine infection surveillance was performed in 51% of the centers, similar to the ELSO survey result. Despite the slow adoption of a standardized protocol in Japan, routine antimicrobial prophylaxis is not as popular as in other countries. As mentioned above, a previous review article and recent guidelines did not explicitly recommend routine antimicrobial prophylaxis. In addition, physicians

Fig. 1 Single-agent antimicrobial regimens. *1st* First-generation cephalosporin, *2nd* Second-generation cephalosporin, *3rd* Third-generation cephalosporin, *Candi* Echinocandin antifungal agent, *Carba* Carbapenem, *MRSA* Anti-MRSA agent, *Penicillin* Penicillin class, *PDC* Penicillin-derived combination



should consider the balance between individual and social risk/benefit ratios from the viewpoint of recent antimicrobial resistance patterns [6]. The 10-year lapse between the ELSO survey and our survey might affect the lower use of routine antimicrobial prophylaxis in Japan.

Recently, a single-center study showed that the protocol reduced the use of broad-spectrum antimicrobial agents such as cefepime, vancomycin, and carbapenem, while 30-day mortality and nosocomial infections did not change [7]. Another recent study evaluating the efficacy of prophylactic antibiotics using national data for 9615 ECMO patients from 2010 to 2017 in Japan revealed that 58% of patients were administered prophylactic antibiotics, and hospital mortality and nosocomial pneumonia in the prophylaxis group were significantly lower than those in the control group (56% vs. 60% and 13% vs. 15%, respectively) [8]. The effectiveness of antimicrobial prophylaxis and the optimal methods during ECMO remain unclear because of a lack of large prospective studies on this subject. Our study revealed that duration of antimicrobial prophylaxis was not determined in 47% of hospitals. We believe that the lack of evidence and the absence of a standardized protocol might be a reason for this result.

In terms of routine infection surveillance, our survey indicated that the proportion of blood and sputum samples obtained for cultures in Japan were 72 and 86%, respectively, while they were 100 and 48%, respectively, in the ELSO survey. A previous international survey reported that infection surveillance differed according to geographical region [1]. In Japan, routine blood culture was not as popular as in other countries. Physicians might perform infection surveillance as needed based on their experience because of a lack of evidence regarding optimal surveillance [1, 3]. Further high-quality studies are needed to eliminate regional and inter-hospital disparities.

This study has several limitations. First, we did not collect outcomes data. Thus, we could not draw a conclusion on whether antimicrobial prophylaxis and standardized protocols influenced outcomes. Second, the subjects of this survey were intensivists and hospitals belonging to the JSICM. Therefore, we did not include all hospitals that administer ECMO in Japan. In addition, different intensivists had unique opinions, even in the same hospital, because many hospitals did not have a standardized protocol.

Conclusions

Our survey revealed that 39% of hospitals administered antimicrobial prophylaxis during ECMO in Japan. In addition, first-generation cephalosporins were the agents most

commonly used. However, only 17% of hospitals have a standardized protocol. Prospective multicenter observational studies about the relationship between antimicrobial prophylaxis and outcomes are required to create a guideline.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10047-021-01291-3>.

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