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Review

Infections during extracorporeal membrane oxygenation: epidemiology, risk factors, pathogenesis and prevention

Stefano Biffi^{a,*}, Stefano Di Bella^b, Vittorio Scaravilli^c, Anna Maria Peri^b, Giacomo Grasselli^c, Laura Alagna^b, Antonio Pesenti^c, Andrea Gori^b^a School of Medicine and Surgery, University of Milan–Bicocca, Via Cadore 48, Monza, Italy^b Infectious Diseases Division, 'San Gerardo de' Tintori' Hospital, via Pergolesi 33, 20900 Monza, Italy^c Fondazione IRCCS Cà Granda–Ospedale Maggiore Policlinico, Milan, Italy

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ABSTRACT

Extracorporeal membrane oxygenation (ECMO) is a life support technique used in patients with respiratory and/or cardiac failure. The ECMO circuit consists of vascular cannulae, a pump and an artificial lung. Infections are among the most common complications associated with ECMO and have a significant impact on the mortality rate. Here we present a narrative literature review regarding the epidemiology, risk factors, pathogenesis and prevention of infectious complications during ECMO support. The prevalence of hospital-acquired infections during ECMO is 10–12% and their occurrence is likely to be more frequent compared with other critically ill patients. Coagulase-negative staphylococci, *Candida* spp., Enterobacteriaceae and *Pseudomonas aeruginosa* are the most frequently involved pathogens. A high incidence of ventilator-associated pneumonia was reported (24.4 cases/1000 ECMO days), with a major role unexpectedly played by Enterobacteriaceae. The infectious risk was shown to increase along the duration of the ECMO run, which represents the most important risk factor for the development of infections. Other ECMO-specific factors predisposing to infections include the severity of illness in ECMO patients, the high risk of bacterial translocation from the gut, and ECMO-related impairment of the immune system. Another important issue could be microbial colonisation of catheters, ECMO cannulae and the oxygenator, which is consistent with most commonly observed aetiologies.

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1. Introduction

Extracorporeal membrane oxygenation (ECMO) is a life support technique used in patients with respiratory and/or cardiac failure. During ECMO, blood is drained, diverted to an artificial lung and then returned to the patient, providing respiratory and/or haemodynamic support. The ECMO circuit consists of a venous drainage cannula, a blood pump, an oxygenator and a re-infusion cannula. The re-infusion cannula may be positioned in either the arterial or venous

circulation. In the former case the circuit is called venoarterial ECMO and guarantees both cardiac and respiratory support, whereas in the latter case it is called venovenous ECMO and provides only respiratory assistance [1,2]. Recently, double-lumen catheters for single-site (jugular) cannulation have been developed [3]. In addition, an arteriovenous ECMO setup devoid of the need for a blood pump is available as well [4].

Bleeding, renal failure and infections are the most common complications associated with ECMO [5]. Hospital-acquired infections occur in a large proportion of ECMO patients and have a significant impact on their morbidity and mortality.

The purpose of this article is to review the available literature on infectious complications in ECMO patients, to provide an epidemiological overview and to summarise the underlying risk factors and pathogenesis.

2. Methods

MEDLINE/PubMed was searched for sources using the following search pattern: (ecmo OR ecls OR els OR (extracorporeal AND ((membrane AND oxygenation) OR (life AND support)))) AND (infection OR nosocomial OR sepsis OR vap). This research was updated

Abbreviations: ECMO: extracorporeal membrane oxygenation; VA-ECMO: venoarterial extracorporeal membrane oxygenation; VV-ECMO: veno-venous extracorporeal membrane oxygenation; AV-ECMO: arterio-venous extracorporeal membrane oxygenation; ELSO: Extracorporeal Life Support Organization; BSI: bloodstream infection; UTI: urinary tract infection; VAP: ventilator-associated pneumonia; MDR: multi-drug resistant; SOFA: sequential organ failure assessment; CR-BSI: catheter-related blood stream infection; CoNS: coagulase negative Staphylococci; ICU: intensive care unit; NHSN: National Healthcare Safety Network; CA-BSI: catheter-associated bloodstream infection; CBP: cardiopulmonary by-pass; PK: pharmacokinetics.

* Corresponding author. School of Medicine and Surgery, University of Milan–Bicocca, Via Cadore 48, Monza, Italy. Fax: +39 039 233 9327.

E-mail address: s.biffi8@campus.unimib.it (S. Biffi).

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on 2 August 2016. Papers regarding the epidemiology, aetiology, risk factors and pathogenesis of infectious complications of ECMO were selected by abstract review. Articles published in languages other than English were not included. All selected papers were included regardless of the study design, publication date, sample composition and sample size. References from selected studies were manually searched for additional publications. On-line publications of the Extracorporeal Life Support Organization (ELSO) Infectious Disease Task Force were also taken into account. Further searches were performed examining the role and mechanisms of immune impairment in ECMO patients. Average incidence rates of various kinds of infection were calculated using data from studies with the same single-centre retrospective cohort design. Mean incidence rates have been pooled with regard to the duration of the ECMO run.

3. Epidemiology of nosocomial infections in extracorporeal membrane oxygenation

3.1. Incidence and prevalence

The ELSO registry collects epidemiological data submitted by ECMO centres. Data submission is voluntarily carried out by ELSO members through a standardised form. Reported data include demographic and clinical characteristics of ECMO patients, details of their ECMO runs, and information on complications and clinical outcome. According to two reviews of the ELSO registry performed by Vogel et al and Bizzarro et al, the prevalence of hospital-acquired infections during ECMO is 10–12% [6,7] (Table 1). This percentage mostly reflects the prevalence of infections in neonates and children, which mainly represents the population of the registry, whereas the prevalence is reported to be higher in the adult subgroup (21%) [6,7]. In the studies analysing data from the ELSO registry, prevalence is expressed as the number of infected patients to the overall number of ECMO patients. The ELSO registry collects data from all ELSO members worldwide but does not report the number of infectious episodes affecting each patient; therefore, the incidence rate cannot be extracted.

Table 1
Prevalence^a of nosocomial infection during extracorporeal membrane oxygenation (ECMO) as reported by the Extracorporeal Life Support Organization (ELSO) registry.

Study	Years reviewed	Adults	Paediatrics	Neonates	No. of patients	Prevalence (%)
Meyer et al [8]	1987–1993			√	5,123	4
Douglass et al [9]	1988–1993			√	5,001	3
Vogel et al [6]	1987–2009	√	√	√	38,661	10
				√	26,382	7
			√		9,283	16
		√			2,996	21
Bizzarro et al [7]	1998–2008	√	√	√	20,741	12
				√	12,311	8
			√		6,132	16
		√			2,298	21

^a Expressed as number of infected patients to the overall number of ECMO patients.

Table 2
Prevalence^a and incidence^b of hospital-acquired infections (HAIs) and bloodstream infections (BSIs) in adult extracorporeal membrane oxygenation (ECMO) patients.

Study	Year	No. of patients	Prevalence of HAIs (%)	Incidence of HAIs (cases/1000 ECMO days)	Prevalence of BSIs (%)	Incidence of BSIs (cases/1000 ECMO days)
Burket et al [10]	1999	71	45	57.57	n/a	18.77
Hsu et al [11]	2009	114	9	11.92	3	2.98
Sun et al [15]	2010	334	13	21.48	n/a	14.84
Pieri et al [12]	2012	46	39	n/a	17	31.06
Schmidt et al [13]	2012	220	65	75.46	18	15.98
Aubron et al [14]	2013	146	25	39.38	14	20.55

n/a, not available.

^a Expressed as number of infected patients to the overall number of ECMO patients.

^b Expressed as number of infectious episodes to the overall duration of the ECMO course.

According to other studies with a single-centre retrospective design, the prevalence and incidence of infectious episodes among adults range from 9 to 65% and from 12 to 75 cases per 1000 ECMO days, respectively [10–15] (Table 2). These rates are lower in the neonatal and paediatric population (Table 3). The reported variability reflects: (i) differences within the study designs (i.e. discrepancies in the definition of ‘infection’ and in the types of infections analysed by different studies); (ii) different patient cohort characteristics (i.e. patients with cardiac versus respiratory involvement, surgical versus medical admitted patients); and (iii) variability in the management of patients (i.e. microbiological surveillance, prophylaxis strategies, infection control policies).

Whilst the ELSO registry does not report the site of infectious episodes, the abovementioned single-centre retrospective studies provide data regarding the epidemiology of different types of infection (Table 4).

The prevalence of bloodstream infections (BSIs) during ECMO ranges from 3 to 18% and the incidence ranges from 2.98 to 20.55 episodes per 1000 ECMO days in adults [10–15] (Table 2). In paediatric and neonatal patients the prevalence is 6–18% [16–20,22] (Table 3).

The incidence of lower respiratory tract infections is very high in adults (i.e. 24.4 episodes/1000 ECMO days) [10–14]. The prevalence is 1–3% in the neonatal population [17,19] and 5% in the paediatric population [19], with an incidence rate of 1.45–4.5 and 5.5 episodes/1000 ECMO days, respectively [17,19].

A smaller role is played by urinary tract infections (UTIs), with a reported prevalence of 1–2% [12,13] and a reported incidence of 1–13.8 cases per 1000 ECMO days [10,11,14,15].

3.2. Impact of infections on mortality rate and extracorporeal membrane oxygenation complications

Infectious complications of ECMO have been associated with increased mortality and morbidity (Table 5), especially in the case of sepsis [8]. Among ECMO patients, nosocomial infections increase the risk of death by 38–63% [6,7].

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