Journal of Infection (2015) xx, 1—10

BIAM British Infection Association

www.elsevierhealth.com/journals/jinf

REVIEW

Early-onset pneumonia after out-of-hospital cardiac arrest

S. Kakavas [a,e,*], N. Mongardon [b,f], A. Cariou [c,g], A. Gulati [d], T. Xanthos [a,d]

[a] *Hellenic Society of Cardiopulmonary Resuscitation, Athens, Greece*
[b] *Université Paris Est, Faculté de Médecine, Service d'Anesthésie et des Réanimations Chirurgicales, Hôpitaux Universitaires Henri Mondor, Assistance Publique des Hôpitaux de Paris, Créteil, France*
[c] *Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, Service de Réanimation Médicale, Hôpital Cochin, Hôpitaux Universitaires Paris Centre, Assistance Publique des Hôpitaux de Paris, Paris, France*
[d] *Midwestern University, Downers Grove, IL, USA*
[e] *Pulmonary Department, Evangelismos, General Hospital of Athens, Greece*
[f] *Service d'Anesthésie et des Réanimations Chirurgicales, Hôpitaux Universitaires Henri Mondor, Assistance Publique des Hôpitaux de Paris, Université Paris Est, Faculté de Médecine, INSERM U955, Equipe 3, physiopathologie et pharmacologie des insuffisances coronaires et cardiaques, Créteil, France*
[g] *Service de Réanimation Médicale, Hôpital Cochin, Hôpitaux Universitaires Paris Centre, Assistance Publique des Hôpitaux de Paris, Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine; INSERM U970, Paris Cardiovascular Research Centre (PARCC), European Georges Pompidou Hospital, Paris, France*

Accepted 24 January 2015
Available online ■ ■ ■

KEYWORDS
Out-of-hospital cardiac arrest;
Resuscitation;
Pneumonia;
Therapeutic hypothermia;
Aspiration

Summary Early-onset pneumonia (EOP) is a common complication after successful cardiopulmonary resuscitation. Currently, EOP diagnosis is difficult because usual diagnostic tools are blunted by the features of post-cardiac arrest syndrome and therapeutic hypothermia itself. When the diagnosis of EOP is suspected, empiric antimicrobial therapy should be considered following bronchopulmonary sampling. The onset of EOP increases the length of mechanical ventilation duration and intensive care unit stay, but its influence on survival and neurological outcome seems marginal. Therapeutic hypothermia has been recognized as an independent risk factor for this infectious complication. All together, these observations

* Corresponding author. Hellenic Society of Cardiopulmonary Resuscitation, Patision 89, 10434 Athens, Greece. Tel.: +30 211 0121756; fax: +30 211 0121758.
E-mail addresses: sotikaka@yahoo.com (S. Kakavas), nicolas.mongardon@hmn.aphp.fr (N. Mongardon), alain.cariou@cch.aphp.fr (A. Cariou), dr.anil.gulati@gmail.com (A. Gulati), theodorosxanthos@yahoo.com (T. Xanthos).

http://dx.doi.org/10.1016/j.jinf.2015.01.012

Please cite this article in press as: Kakavas S, et al., Early-onset pneumonia after out-of-hospital cardiac arrest, J Infect (2015), http://dx.doi.org/10.1016/j.jinf.2015.01.012

underline the need for future prospective clinical trials to better delineate pathogens and risk factors associated with EOP. In addition, there is a need for diagnostic approaches serving the accurate diagnosis of EOP.

Introduction

Return of spontaneous circulation is just the first step toward the ultimate goal of resuscitation from cardiac arrest and favorable neurological outcome.[1,2] Unfortunately, only a small percentage of patients with return of spontaneous circulation will survive to hospital discharge, despite major advances in both pre-hospital and in-hospital treatments. Recent epidemiological data suggest that less than 8% of out-of-hospital cardiac arrest (OHCA) patients are discharged from hospital.[2] Indeed, patients have to face post-cardiac arrest syndrome, a complex association of hypoxic brain injury, cardio-circulatory dysfunction, and systemic ischemia/reperfusion lesions.[3] Moreover, infections may complicate the post-cardiac arrest period, leading to potential secondary insults in highly unstable patients.[4] Early-onset pneumonia (EOP) appears to be the leading form of infectious complications shortly after OHCA.[5] Despite the highly reported frequency and the obvious clinical and economic burden of EOP, there are remarkably few data addressing the characteristics of this complication. Meanwhile, an accurate and timely diagnosis of EOP remains a challenge, because of the myriad of confounding factors. In this review, we aim to define this recently highlighted form of pneumonia and to present the main information concerning its epidemiology, aetiology, diagnosis, impact, prevention and treatment. Emerging issues, gaps of knowledge and future researches requirement will be at least discussed throughout the sections.

Methodology

Literature search was conducted following a systematic approach. A search in the Pubmed database was carried out using the search terms 'cardiac arrest pneumonia' and 'post resuscitation pneumonia'. The electronic literature search included studies published between 1980 and September of 2014 and returned 377 citations. Only articles in English were retained. The inclusion criteria were studies concerning pneumonia during the post-resuscitation period after cardiac arrest. There were no restrictions on the type of study design. Following the initial screening, the references of all eligible studies were examined to identify any other potentially relevant articles. Collectively, 23 articles were included. Eight of them concerned prospective or retrospective cohort studies providing information about the incidence and microbiology of pneumonia after cardiac arrest.

Pathophysiology, risk factors and definition

Although diagnostic criteria are not clearly delineated, EOP has been defined based on the timing of its onset in relation to cardiac arrest occurrence. Thus, EOP can be defined as a pneumonia that develops within 5 days after cardiac arrest, while a pneumonia occurring during the further course of mechanical ventilation is considered to be late-onset pneumonia after cardiac arrest.[6] This threshold, albeit sometimes perceived as arbitrary, is based on the changes in the relative distribution of causative pathogens that has been recorded in earlier studies.[5,7–9] Consequently, ventilator-acquired pneumonia (VAP) comprises only part of the temporal spectrum of EOP. Although this may seem confusing, it is the result of the unclear diagnostic criteria for EOP and underlines the need of further epidemiological studies that would clarify the issue. Notably, even in the case of an "older" entity like VAP, a lack of consensus is still present: for some authors the fifth day in the intensive-care unit is considered to be the last day of an early onset,[10] while others regard the seventh[11–13] day as the final temporal threshold. There is also a great uncertainty whether the aforementioned time limits account to the number of days of hospitalization or mechanical ventilation.[10] The heterogeneity of the temporal and clinical definition of EOP is obvious in Table 1 that summarizes the studies focusing on pneumonia after OHCA.

In patients admitted to the intensive care unit after cardiac arrest, EOP is attributed to multiple mechanisms that render lungs prone to early infection.[4,14] First of all, EOP after OHCA may be primarily considered to be a consequence of the combination of aspiration pneumonitis and aspiration pneumonia.[15,16] In fact, the distinction between these two entities is largely artificial, both being a continuum.[17] In the specific setting of cardiac arrest, they are both promoted by the loss of airway protection due to abrupt coma, mouth-to-mouth or bag ventilation, and chest compressions. Furthermore, a sepsis-like systemic ischemic-reperfusion response occurs after the return of spontaneous circulation. In most severe cases, clinical manifestations culminate in multi-organ failure, which itself increases susceptibility to infection.[2] It is now also well established that critically ill patients develop a phase of immunosuppression, which occurs earlier than previously assumed.[18] Pulmonary contusions due to chest compressions may pave the way for secondary infection, through mechanical injuries.[19] Patients admitted after OHCA are frequently exposed to multiple either inter-hospital or intra-hospital transfers for diagnostic or therapeutic purposes within the first hours of admission. This represents another potential risk factor of aspiration and EOP.[22]

EOP might share some etiologic factors with VAP,[20–22] such as the insertion and/or contamination of the endotracheal tube during emergency airway access.[23,24] Endotracheal tube insertion may inoculate endogenous oropharyngeal bacteria in the lower respiratory tract.[23] In addition, a bacterial biofilm forms on inner surface of the tube and represents a significant source of bacterial

Please cite this article in press as: Kakavas S, et al., Early-onset pneumonia after out-of-hospital cardiac arrest, J Infect (2015), http://dx.doi.org/10.1016/j.jinf.2015.01.012