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Clinical and laboratory predictors of Infectious Complications in patients after Out-of-Hospital Cardiac Arrest

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ABSTRACT

Purpose: Identification of clinical and laboratory predictors related to Infectious Complications (ICs) in patients after Out-of-Hospital Cardiac Arrest (OHCA).
Methods: Patients, aged >18, after an OHCA between 9/2013 and 11/2015, surviving >24 h, were studied.
Results: Study group consisted of 42 patients (mean age 63.4 years, 88.1% men). Forty percent of patients had IC; lower respiratory tract infections were most common (87.5% of cases). ICs were more common in patients receiving Targeted Temperature Management (50% vs. 10%; p = 0.032).
Antibiotics were used in 85.7% of patients. The mean time to therapy initiation was 9.6 (SD 7.1) hours after admission. The mean course of treatment was 9.0 (SD 6.2) days. Fifty-three percent of patients receiving early antibiotic treatment didn't have IC. Initial antibiotic therapy was changed more often in patients with IC (75% vs. 38.9%; p = 0.045).
C-Reactive Protein, Procalcitonin, Troponin and White Blood Cell count values were higher in patients with IC.
Conclusion: Early initiated antibiotic treatment is overused in patients after OHCA. This practice is associated with necessitating antibiotic change in the majority of patients with IC. Assessment of clinical and laboratory parameters in the first days after OHCA increases the likelihood of appropriate ATB therapy.

1. Introduction

Infectious Complications are common among Out-of-Hospital Cardiac Arrest (OHCA) survivors with incidence reaching 70% [1,2]. The most common are lower respiratory tract infections referred in up to 65% of patients after OHCA [3].

Survivors of OHCA represent a specific subgroup which cumulates a lot of risk factors for development of infection. These factors begin to manifest themselves at the time of collapse, when airway protection is suddenly lost. This situation is compounded by the ensuing chest compressions and ventilation via non-definitive airway devices - both of which increase the risk of aspiration of oropharyngeal or gastric contents. The possibility of lung tissue contusion during resuscitation also plays a role. This continuum of increasing risk factors proceeds after achieving Return of Spontaneous Circulation (ROSC) due to Post-Cardiac Arrest Syndrome. This state has many components, but the most relevant in this context is systemic ischemia-reperfusion injury.

Furthermore, therapeutic approaches involved in critical care bring with them further risk – e.g. indwelling catheters, mechanical ventilation, and Targeted Temperature Management [4,5,6].

Diagnosing Infectious Complications in these patients is not as simple as may first be thought.

Commonly used clinical and laboratory parameters start to fail [7,8,9,10,11]. At this point a physician faces a problem: whether to administer antibiotics, and if so - when? Prophylactic antibiotic use could reduce the incidence of severe infections [12]. It could also have some benefit in reducing length of stay in the ICU and possibly mortality. On the other hand, however, this approach may not be reasonable in this age of increasing frequency of multi-resistant strains of pathogens [13]. Until quality evidence is available prophylactic antibiotic use for all OHCA survivors can't be recommended. The timing of antibiotic therapy remains on the shoulders of the physician and the team responsible for a patients care.

Although new biomarkers such as Presepsin have been tested as predictors of Infectious Complications in critically ill patients [15,16], their widespread adoption into daily practice is still some time away.

The aim of this analysis is to identify clinical and laboratory predictors significantly related to Infectious Complications in patients after OHCA, who have been admitted to the Coronary Care Unit (CCU) of Tertiary Care Institution (TCI).

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2. Methods

2.1. Patient population and hospital setting

Patients, aged >18 years, who suffered an OHCA between 9/2013 and 11/2015 and who survived >24 h, were studied. Patients were admitted to the CCU of a Tertiary Care Institution (2400 admissions/160 mechanically ventilated patients/40 OHCA patients annually) with coronary intervention facilities that are available 24 h a day, 7 days a week (2500 procedures/250 primary PCIs annually). The majority of patients were a part of a local, prospective, observational study. The study was conducted according to the Declaration of Helsinki.

2.2. Procedures

Patients treated after OHCA by Emergency Medical Services (EMS) personnel (usually including a physician), in whom cardiac origin was presumed, were transferred directly to the CCU. Based on the instruction of the attending cardiologist, patients with presumed Acute Coronary Syndrome or suspected myocardial ischemia were transferred directly to the catheterisation laboratory to undergo an emergent coronary angiography. The other patients were admitted to the CCU for an expeditious differential diagnosis and appropriate therapy.

All patients treated at the CCU received guideline-based therapy, including Targeted Temperature Management in non-contraindicated comatose survivors. Antibiotic therapy (administration, time of initiation, drug choice and treatment course) was based on the decision of the physician coordinating the patient's care.

Laboratory tests, including assessment of the commonly used inflammatory parameters (C-Reactive Protein, Procalcitonin, White Blood Cell count) were performed on admission and then every 24 h up to and including 72 h after admission. Microbial cultivation tests and chest radiographs were performed according to the physician's indication.

2.3. Database

Patient data were entered into a preformed database and included baseline characteristics, cardiac arrest related information, clinical parameters at admission, treatment data (ATB therapy, TTM, coronary angiography, ventilation parameters, etc.), hospitalization parameters, laboratory and outcome data (cerebral performance category, in-hospital and one-month mortality).

2.4. Definition and diagnosis of Infectious Complication

Definition of Infectious Complications was based on the criteria published by International Sepsis Forum Consensus Conference [17] and final diagnosis was made by the team treating the patient (at least two experienced physicians) and retrospectively revised by one other single experienced physician (JK).

2.5. Statistical analysis

All data were collected and analysed using both Microsoft Excel and SPSS software. The Fisher Test was used for qualitative parameters and the Mann-Whitney Test for quantitative parameters. Statistical tests used a significance level of $p = 0.05$. Comparison of patients with and without Infectious Complications and specific subgroups was performed.

3. Results

3.1. Population

Forty-two patients (88.1% men) suffering from cardiac OHCA, surviving >24 h, were enrolled. The mean age of the study population was 63.4 (SD 12.0) years.

All patients were treated by EMS personnel, 94.9% ($n = 37/39$) of them received bystander CPR at the scene. The other three patients were resuscitated by EMS personnel who witnessed the OHCA. The mean time to ROSC was 17.3 (SD 8.5) minutes. Ventricular fibrillation/pulseless ventricular tachycardia was present in 78.6% of cases. The most common cause of OHCA was ST Elevation Myocardial Infarction (STEMI) in 61.9%. The average length of ICU stay was 6.5 (SD 6.3) days. Seventy-three percent of patients were discharged with CPC scale 1–2. In-hospital mortality was 11.9% ($n = 5$).

All parameters and comparison between subgroups of patients with and without Infectious Complications are summarised in Table 1. In two cases we were not able to distinguish with certainty if an Infectious Complication was present, therefore these 2 patients were not included in the final comparison. No significant difference was found in baseline characteristics between patients with and without Infectious Complications.

3.2. Treatment

At admission 90.5% of patients were mechanically ventilated. The mean systolic blood pressure was 120.6 (SD 37.2) mmHg and 52.4% of patients needed catecholamine support (62.5% of patients with and 45.8% without Infectious Complication, $p = 0.349$). Subsequent use of norepinephrine in patients reached 78.6% overall (87.5% with and 70.8% without Infectious Complication, $p = 0.272$).

Targeted Temperature Management to either 32–34 °C or 36 °C was used in 76.2% of all patients, with half of these having an Infectious Complication. Hyperpyrexia occurred in 21.9% of patients after rewarming. In two patients induction of TTM started in the pre-hospital setting. Most patients (95.2%) received gastroprotection, principally Proton Pump Inhibitors (3 patients received H2 blockers). Coronary angiography was performed in 95.2% of patients.

3.3. Infectious Complications and antibiotic treatment

Forty percent ($n = 16/40$) of patients had an Infectious Complication. Lower respiratory tract infections (bronchitis and pneumonia) were most common, presenting in 87.5% of cases. Catheter related sepsis and blood stream infections both presented in 6.3% of cases. Infectious Complications were more common in patients receiving Targeted Temperature Management (50% vs. 10%; $p = 0.032$).

All Infectious Complications recorded were present in mechanically ventilated patients, none of the four patients who did not receive mechanical ventilation had Infectious Complication ($p = 0.136$).

We observed a trend for longer time of sedation (62.6 vs. 41.6 h, $p = 0.657$), longer time to extubation (51.3 vs. 44.2 h, $p = 0.688$), longer ICU stay (8.6 vs. 5.2 days; $p = 0.199$) and longer length of hospitalization in TCI (10.7 vs. 7.4 days; $p = 0.629$) in patients with Infectious Complication.

3.4. Antibiotic treatment

Antibiotic therapy was administered in 85.7% of all patients. The mean time to therapy initiation was 9.6 (SD 7.1) hours. Empiric drug therapy was the mode of choice, and was dependent upon the clinical judgement of the physician coordinating the patient's care. Amoxicillin-Clavulanate and Ampicillin-Sulbactam were used most often - both in 47.2% of patients, 5.6% of patients received Ampicillin-Sulbactam in combination with Metronidazole.