Clinical paper

Delayed return of spontaneous circulation (the Lazarus phenomenon) after cessation of out-of-hospital cardiopulmonary resuscitation

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Introduction: The delayed return of spontaneous circulation (ROSC) after cessation of cardiopulmonary resuscitation (CPR), also known as the Lazarus phenomenon, is a rare event described in several case reports. This study aims to determine the incidence and the time of occurrence of the Lazarus phenomenon after cessation of out-of-hospital CPR.

Methods: This prospective observational cohort study was conducted in the Helsinki Emergency Medical Service in Finland from 1 January 2011 through 31 December 2016. All out-of-hospital CPR attempts were carefully monitored for 10 min after the cessation of CPR in order to detect delayed ROSC.

Results: Altogether, 2102 out-of-hospital cardiac arrests occurred during the six-year study period. CPR was attempted in 1376 (65.5%) cases. In 840 cases (61.0% of all attempts) CPR attempts were terminated on site. The Lazarus phenomenon occurred five times, with an incidence of 5.95/1000 (95% CI 2.10–14.30) in field-terminated CPR attempts. Time to delayed ROSC from the cessation of CPR varied from 3 to 8 min. Three of the five patients with delayed ROSC died at the scene within 2–15 min while two died later in hospital within 1.5 and 26 h, respectively.

Conclusions: We observed that the Lazarus phenomenon is a real albeit rare event and can occur a few minutes after the cessation of out-of-hospital CPR. We suggest a 10-min monitoring period before diagnosing death. CPR guidelines should be updated to include information of the Lazarus phenomenon and appropriate monitoring for it.

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Introduction

The delayed return of spontaneous circulation (ROSC) after the cessation of cardiopulmonary resuscitation (CPR) is also called the Lazarus phenomenon or autoresuscitation. It was first reported in 1982 [1] and, thereafter, numerous case reports and three surveys have been published [2–8]. However, no prospective studies of the Lazarus phenomenon have been conducted and, hence, its true incidence remains unknown. Similarly, the exact time to delayed ROSC is not known since signs of life may not have been monitored continuously after the cessation of CPR.

Recommendations for how long monitoring should continue after stopping CPR are heterogeneous [3,9] or completely lacking. Current European Resuscitation Council (ERC) guidelines do not include any recommendation regarding whether patients should be monitored, or for how long, following unsuccessful CPR before declaring them dead [10].

This study aimed to determine the incidence and the time of occurrence of the Lazarus phenomenon after the cessation of out-of-hospital CPR.

Methods

Study setting and type

This prospective observational cohort study was conducted in the Helsinki Emergency Medical Service (EMS) in Finland from 1 January 2011 through 31 December 2016. EMS uniformly serves the entire capital city of Helsinki, with a population of 615 700. The
Department of Surgery at the Helsinki University Hospital approved the study plan. No informed consent was required from patients or their representatives due to the nature of the study.

**EMS**

The EMS system is three-tiered consisting of emergency medical technician–manned basic life support (BLS) ambulances, paramedic-manned advanced life support (ALS) ambulances, and a physician-manned unit. Fire engines used as first-response units are classified as BLS and the senior paramedic–manned medical supervisor unit serves as ALS. Cardiac arrest calls are attended by at least two units—that is, the nearest ambulance and a physician-manned unit (medical supervisor unit if a physician unit is not available). A first-responding fire engine is dispatched if it is likely to reach the patient first.

**CPR**

CPR adhered to the 2010 and 2015 ERC guidelines [10,11]. During the study period, no devices for mechanical chest compression were used. All patients received closed-chest CPR, that is, emergency thoracotomies were not performed. Following unsuccessful CPR, patients were pronounced dead on scene except for a few cases of accidental hypothermia which were transported under continuous CPR allowing them to receive invasive warming in the hospital operating theatre. CPR by EMS was recommended to continue for up to 35 min accompanying ventricular fibrillation and up to 20 min accompanying asystole and pulseless electrical activity (PEA). The EMS order of when not to initiate CPR has been described elsewhere [12]. This do-not-attempt-resuscitation (DNAR) order was revised in November 2015 to better address traumatic cardiac arrests and to simplify decision-making during asystole and PEA. In case of the initial rhythms of asystole and PEA, the maximum time to the initiation of ALS was removed from the DNAR order leaving the time to initiate CPR the only point allowing for a decision to be taken. Case-by-case decision-making was added to the order to account for EMS-witnessed traumatic cardiac arrests or traumatic cardiac arrests with a short ambulance response time.

**Monitoring after cessation of CPR**

In Helsinki routine EMS monitoring after the cessation of CPR was introduced in 2010 following a malpractice case in another part of Finland that gained much media attention. All out-of-hospital CPR attempts were carefully monitored for 10 min after the cessation of CPR in order to detect delayed ROSC of any duration. The Lazarus phenomenon was defined as delayed ROSC after the cessation of CPR. Post-CPR monitoring followed cases when the patient was intubated, alternative airway devices were used, adrenaline (or any other intravenous medication) was administered, the patient was defibrillated, or received prolonged (>10 min) basic CPR, that is, chest compressions and bag-mask ventilation. Monitoring included ECG, capnography, and visual observation of the patient to detect signs of life such as breathing, swallowing, or movement. Cardiac ultrasound (US) was used when appropriate by the physician-manned unit. A ventilation bag or ventilator was ordered disconnected from the intubation tube at the beginning of the monitoring period in order to prevent the development of auto-PEEP (positive end-expiratory pressure). Following a 10-min monitoring period, patients were declared dead if no signs of life were detected.

**Data collection and analysis**

EMS has had an Utstein style–based cardiac arrest registry since 1994 [13,14]. All out-of-hospital cardiac arrests are prospectively entered into the registry. If a Lazarus phenomenon occurred, the on-duty physician or the medical supervisor completed a separate Lazarus study form in addition to a standard cardiac arrest data form. In addition to the structured data, the Lazarus study form included a section where the entire CPR process was described in chronological order. The physician responsible for the cardiac arrest registry validated data on a case-by-case basis. Electronic patient reports from EMS (Merlot Medi®, CGI Finland), hospital patient records, and autopsy reports were retrieved.

For normally distributed continuous variables, the mean and standard deviation (SD) were presented. The median and interquartile range (IQR) were presented for non-normally distributed data. We calculated the 95% confidence interval (CI) for the incidence of the Lazarus phenomenon. Statistical testing was neither planned nor performed due to the small number of cases with delayed ROSC.

**Results**

During the six-year study period a total of 2102 out-of-hospital cardiac arrests occurred in Helsinki. CPR was attempted in 1376 (65.5%) cases. In 840 cases (61.0% of all attempts), CPR attempts were terminated on scene.

**Incidence and time of occurrence**

The Lazarus phenomenon occurred five times, with an incidence of 5.95/1000 (95% CI 2.10–14.30) in field-terminated CPR attempts and 2.38/1000 (95% CI 0.80–5.70) among all out-of-hospital cardiac arrests. Time to delayed ROSC from the cessation of CPR varied from 3 to 8 min (3 min in three cases, 6 min in one case, and 8 min in one case).

**Case features**

None of the five Lazarus cases presented as classic sudden out-of-hospital cardiac arrest with strictly guideline–based CPR. Two patients (cases 1 and 4) were permanent nursing home residents of an advanced age. One patient (case 2) suffered massive external bleeding and, therefore, fluid resuscitation was a priority over adrenaline administration during CPR. In case 4, major bleeding from the lungs or the trachea to the intubation tube predisposed the patient to auto-PEEP. Four of the five cases presented with PEA both as an initial rhythm and as the rhythm recorded when CPR was stopped.

Although cardiac US was not routine during every CPR attempt it was used in three of four cases to confirm no mechanical cardiac activity was present when CPR was stopped accompanying PEA.

There were two protocol deviations. In case 2, the ventilation bag was not immediately disconnected from the intubation tube when CPR ceased. In addition, in case 5, noradrenaline infusion initiated before cardiac arrest was not discontinued when CPR stopped.

Detailed descriptions of the five Lazarus cases are presented in Tables 1 and 2.

**Outcome**

All five patients remained deeply comatose after delayed ROSC. In two patients, prehospital advanced life support was continued (cases 2 and 3). In three cases, patients were allowed to breathe spontaneously and were only observed due to the dismal situation.
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