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Organ support therapy in the intensive care unit and return to work in out-of-hospital cardiac arrest survivors–A nationwide cohort study

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ABSTRACT

Aim: With increased survival after out-of-hospital cardiac arrest (OHCA), impact of the post-resuscitation course has become important. Among 30-day OHCA survivors, we investigated associations between organ support therapy in the Intensive Care Unit (ICU) and return to work.

Methods: This Danish nationwide cohort-study included 30-day-OHCA-survivors who were employed prior to arrest. We linked OHCA data to information on in-hospital care and return to work. For patients admitted to an ICU and based on renal replacement therapy (RRT), cardiovascular support and mechanical ventilation, we assessed the prognostic value of organ support therapies in multivariable Cox regression models.

Results: Of 1087 30-day survivors, 212 (19.5%) were treated in an ICU with 0-1 types of organ support, 494 (45.4%) with support of two organs, 26 (2.4%) with support of three organs and 355 (32.7%) were not admitted to an ICU.

Return to work increased with decreasing number of organs supported, from 53.8% (95% CI: 49.5–70.1%) in patients treated with both RRT, cardiovascular support and mechanical ventilation to 88.5% (95% CI: 85.1–91.8%) in non-ICU-patients. In 732 ICU-patients, ICU-patients with support of 3 organs had significantly lower adjusted hazard ratios (HR) of returning to work (0.50 [95% CI: 0.30–0.85] compared to ICU-patients with support of 0-1 organ. The corresponding HR was 0.48 [95% CI: 0.30–0.78] for RRT alone.

Conclusions: In 30-day survivors of OHCA, number of organ support therapies and in particular need of RRT were associated with reduced rate of return to work, although more than half of these latter patients still returned to work.

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Introduction

Survival of out-of-hospital cardiac arrest (OHCA) has increased during the last decade [1]. Several studies have shown that prehospital interventions and the clinical condition at hospital admission are associated with both short and long-term outcome [1–3]. Further, recent studies have shown how pre-hospital interventions (e.g. bystander interventions) are related to functional outcome measures [4,5]. However, knowledge of the prognostic value of the post-resuscitation in-hospital care and related interventions is sparse, and the long-term prognosis of patients with multiple organ failure following OHCA is unknown.

Cardiac arrest causes a degree of general ischemia, which leads to the complex post-cardiac arrest syndrome in patients who gain return of spontaneous circulation [6]. The syndrome resembles the systemic inflammatory response syndrome (SIRS), and severity depends on the cause of cardiac arrest, the degree of reperfusion

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injury, the underlying pathology, the extent of myocardial dysfunction and co-morbidity burden [6]. However, it has not been investigated whether the post arrest syndrome reflects only temporary damage or if it is a reflection of underlying permanent injuries leading to long-term disabilities.

Early interventions are hypothesized to decrease the duration of the no- or low-flow period, and hereby decrease the risk of anoxic tissue injury caused by the cardiac arrest. In line with this, bystander interventions have previously been shown to be associated with reduced hospital length of stay and risk of admission to an ICU as a proxy for reduced morbidity following OHCA [7]. Furthermore, in the ICU, number and severity of organ failures are well-known predictors of mortality [8,9]. Still, little is known on how the in-hospital treatment and the need of organ support therapy following OHCA predicts the long-term prognosis and in particular function in survivors.

Return to work indicates a favourable prognosis without major functional deficits [5] and previous studies of 30-day survivors after OHCA have shown rates of return to work of up to 76% [5,10]. Therefore, we investigated associations between need of organ support therapy, as a proxy for multiple organ failure, before day 30 after cardiac arrest and return to work in 30-day survivors.

Methods

Study setting

This cohort study used data from the Danish Cardiac Arrest Registry, to which emergency medical services (EMS) personnel have reported every case of OHCA where a resuscitation attempt was initiated since June 1st, 2001 [1].

In Denmark, basic life support-trained ambulance personnel are dispatched to all OHCA emergencies, and advanced life support-trained mobile emergency care units staffed with paramedics or anesthesiologists are dispatched to rendezvous with the ambulance personnel. Access to pre- and in-hospital health care in Denmark including admission to an ICU is tax financed and thereby available for all patients. However, the indication for admission to and treatment in an ICU is a clinical decision. All admissions to and major treatments at Danish ICUs are reported to the Danish National Registry of Patients and used by the Danish Intensive Care Database [11].

Study population

We identified 30-day survivors between 18 and 65 years, employed prior to the OHCA incident. Before 2005, ICU admission was not completely registered [11], and therefore we only included patients during 2005–2014. Patients not receiving any social benefits, as well as patients on maternity leave, leave-of-absence or public state education grants in a five-week span before cardiac arrest were defined as working at baseline [5]. As we assessed renal replacement therapy (RRT) as part of the need of organ support, we excluded patients treated with dialysis in the year before OHCA.

Study design

From the Danish Cardiac Arrest Registry, we included information on date and location of arrest, whether a bystander initiated CPR and/or defibrillated the patient, witness status, time interval between recognition of arrest/emergency dispatch center call and ambulance arrival and whether the patient was awake at hospital arrival. Status at arrival(comatose or awake) was recorded by ambulance personel and did hereby not include whether the patient woke up in the emergency department. The unique civil personal registration number given to all Danish residents at birth or upon immigration was used to gather data from other Danish nationwide registries. We retrieved data on age, sex and civil status from the Danish Civil Personal Registration registry and presumed cause of arrest (cardiac vs. non-cardiac) was determined using data from the Danish National Patient Registry and the Danish Cause of Death Registry [1,5]. Data on date of death was retrieved from the Danish Cause of Death Registry. Data on comorbidities were obtained from the Danish National Patient registry as well as the Danish National Prescription Registry (eTable 1) [12,13]. We retrieved data on organ support and 'simplified Acute Physiology Score' (SAPS II) from the Danish National Patient Registry [11,13], however SAPS II was only sufficiently registered from 2011 and onwards. Employment status was obtained from a registry administered by the Danish Labor Market Authority (DREAM registry) and was available on a weekly basis until July 2016. We obtained information on educational level from Statistics Denmark [14,15].

Exposures

Main exposure was number of severe organ failures within 30 days after OHCA among patients admitted to an ICU. We defined organ failure according to organ-support therapy in the ICU, identifying three types of organ support: 1. Mechanical ventilation defined by invasive ventilator support; 2. Cardiovascular support, defined by need of inotropic agents or vasopressors; and 3. RRT defined by renal support in the ICU. Based on the accumulated number of organ support therapies, and whether the patient was admitted to an ICU before day 30, we divided the patients into four groups: 1. Non-ICU-patients, 2. ICU-patients with support of 0-1 organ, 3. ICU-patients with support of two organs and, 4. ICU-patients with support of three organs.

In secondary analyses, we assessed the impact of the individual types of organ support and frequent combinations of organ support on return to work.

Outcomes

Outcome was return to work. We defined return to work as the first 2-week-span from day 30, during which no social benefits except from maternity leave, leave-of-absence and state education fund codes occurred. 30-day-survivors were followed from day 30 after OHCA for return to work, death, emigration or end of study (June 30, 2016).

Statistics

We presented categorical variables using percentages and frequencies, and continuous variables using medians and 25th and 75th percentiles. For return to work with mortality as competing risk, we depicted cumulative incidences using the Aalen-Johansen estimator. We calculated time to death and return to work for 30-day-survivors counting from day 30. Among patients admitted to an ICU we performed Cox regression models to assess the association between individual and number of organ support therapies and outcomes. We created a directed acyclic graph (DAG) [16] to identify covariates for our multivariable models. Covariates included patient age, sex, comorbid conditions, and calendar year of arrest, as well as status of living alone and patient educational level (eFigure 2). To ensure that the need of organ support is not driven or confounded by prehospital variables (bystander CPR, bystander defibrillation and witness status) or only reflected cognitive status at arrival, we added these in twofinal separate multivariable models.Missing data were imputed using multiple imputation methods (using the Substantive Model Compatible Fully Conditional Specification package in R). Data was missing at random (MAR). Assumption of proportional hazards was checked

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