Resuscitation xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Prognostic value of reduced discrimination and oedema on cerebral computed tomography in a daily clinical cohort of out-of-hospital cardiac arrest patients

Sandra Langkjær[a], Christian Hassager[a], Jesper Kjaergaard[a], Idrees Salam[a], Jakob Hartvig Thomsen[a], Freddy K. Lippert[b], Michael Wanscher[c], Lars Køber[a], Niklas Nielsen[d], Helle Søholm[a,*]

[a] Department of Cardiology 2142, The Heart Centre, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[b] Emergency Medical Services, Copenhagen, The Capital Region of Denmark, Denmark
[c] Department of Cardiothoracic Anaesthesiology 4142, The Heart Centre, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[d] Department of Anaesthesiology and Intensive Care, Skåne University Hospital, Lund University, Lund, Sweden

ARTICLE INFO

Article history:
Received 26 January 2015
Received in revised form 13 March 2015
Accepted 26 March 2015

Keywords:
Out-of-hospital cardiac arrest (OHCA)
Cerebral computed tomography (CT)
Prognosis
Prognostication
Mortality

ABSTRACT

Purpose: Assessment of prognosis after out-of-hospital cardiac arrest (OHCA) is challenging. Cerebral computed tomography (cCT) scans are widely available, but the use in prognostication of comatose OHCA-patients is unclear. We evaluated the prognostic value of cCT in a clinical cohort of OHCA-patients.
Method: A total of 1120 consecutive OHCA-patients with cardiac aetiology and successful or on-going resuscitation at hospital arrival were included (2002–2011). Utstein-criteria for registration of pre-hospital data and review of patient-charts for post-resuscitation care including cCT results were used. The primary endpoint was 30-day mortality analysed by log-rank and multivariate Cox-regression analyses.
Results: A cCT scan was performed in 341(30%) of the clinical OHCA-cohort, and an early CT (<24 h) was performed in 188 patients. The early CT was found 'normal' in 163(89%) and with reduced discrimination in 7(4%) of patients, which was independently associated with higher 30-day mortality compared with OHCA-patients with an early cCT ($HR_{adjusted}$ = 3.5 (95%CI: 1.0–11.5), p = 0.04). A late CT (≥24 h) was performed in 153 patients in a median of 3 days (IQR: 2–5) and was 'normal' in 89(60%), 'cerebral bleeding' in 4(3%), 'new cerebral infarction' in 10(7%), and 'reduced discrimination between white and grey matter and/or oedema' in 45(30%) patients. 'Reduced discrimination and/or oedema' by late cCT was independently associated with higher 30-day mortality compared to patients with a normal late CT ($HR_{adjusted}$ = 2.6 (95%CI: 1.4–4.8, p = 0.002).
Conclusion: Our observations suggest that a cCT may be useful as part of the neurological prognostication in patients with OHCA. 'Reduced discrimination between white and grey matter and/or oedema' on cCT was independently associated with a poor prognosis.

1. Introduction

The number of survivors from out-of-hospital cardiac arrest (OHCA) has significantly improved during the recent 10 years, however OHCA is still associated with a poor outcome with only 10% surviving to 30 days of those with attempted resuscitation.[1–3] The reasons for the increase in survival have been attributed to enhanced pre-hospital treatment, advanced life support and increased focus on post-resuscitation care.[1,4,5]

Assessment of cerebral outcome and estimation of prognosis in comatose OHCA-patients are challenging especially after the introduction of mild hypothermia.[6] Prognostication in comatose patients is recommended performed no earlier than 72 h after end of sedation,[7–9] and a multi-modal approach to prognostication is used by combining neurophysiological examination (electroencephalography/somatosensory-evoked potentials), biomarkers, neuroimaging, and repeated physical examination by dedicated physicians.[10–12]

Cerebral Computed Tomography (CT) scans are widely used, and the use as a prognostic tool has been suggested, but the modality is not thoroughly validated. Acute cerebral CT in daily clinical practice is used for ruling out intra-cranial haemorrhages, or new

* Corresponding author.
E-mail address: helle.soholm@gmail.com (H. Søholm).

http://dx.doi.org/10.1016/j.resuscitation.2015.03.023
0300-9572/

cerebral infarction as the cause of OHCA, and the modality may thereby influence the clinical decision-making.[13,14] Cerebral CT performed later during the admission after OHCA are often used in comatose patients or in case of clinical signs of anoxic brain injury. A late cerebral CT may therefore provide important information in the multi-modal prognostication after OHCA.[7] Predicting outcome with cerebral CT in OHCA patients has previously been investigated.[15–19] However, assessment of the prognostic value of early and late cerebral CT in large unselected clinical cohorts is, to our knowledge, still lacking.

In this study we aimed to evaluate the prognostic value of cerebral CT performed early (<24 h) and late cerebral CT (≥24 h) after OHCA in a daily clinical cohort.

2. Methods

2.1. Patients and study area

The study included patients with OHCA from June 2002 through 2011. OHCA patients with cardiac aetiology with return-of-spontaneous circulations (ROSC) or with on-going cardiopulmonary resuscitation (CPR) at hospital arrival in the greater Copenhagen area were included. All patients were treated by the Copenhagen Emergency Medical Services (EMS). All patients were included through their unique Danish personal identification number, CPR (The Central Person Register). We excluded patients younger than 18 years of age, patients with definite signs of death (e.g. *rigor/livor mortis*) and non-Danish residents due to unavailable outcome data.

Copenhagen, the capital of Denmark, is inhabited by a metropolitan population of approximately 1.2 million people and covers an area of 675 km^2 (260 Mi^2). The EMS consists of an emergency ambulance with Basic Life Support equipment, with a defibrillator and the treatment protocol adherent to the advanced life support guidelines from the European Resuscitation Council.[1,20] In another response unit a paramedic and attending physician (anaesthesiologist) also attend all patients with assumed OHCA. The attending physician used an Utstein registration sheet as documentation, and after dispatch entered the data into the OHCA-database.[21]

2.2. Post-resuscitation care

Patients were admitted for post-resuscitation care at one of eight hospitals in the greater Copenhagen area. A single investigator reviewed all individual patient charts with focus on the in-hospital post-resuscitation care. The attending radiologist assessed all CT scans and description and results of the cerebral CT scans were retrieved from the patient files. The CT reports were classified as the following: no acute abnormalities (including old cerebral infarction), cerebral bleeding, new cerebral infarction, or reduced discrimination between white and grey matter and/or oedema. The CT reports were furthermore divided into time of performance: early (<24 h) or late (≥24 h) after ROSC. Mild hypothermia was gradually implemented during the study period from 2002 to 2004. Co-morbidity was assessed by the Charlson Comorbidity Index that takes the severity of 22 conditions into account, and the index is commonly used for prediction of short-term mortality.[22,23] Reasons for withdrawal of active therapy was achieved from patient charts from the attending physician: circulatory failure, presumed anoxic brain damage, living will stating no wish for extended active life support, futile treatment, or pre-existing comorbidity (more than one may apply).

The regional ethics committee approved waiver of informed consent for the study with the reference number H-2-2012-053.

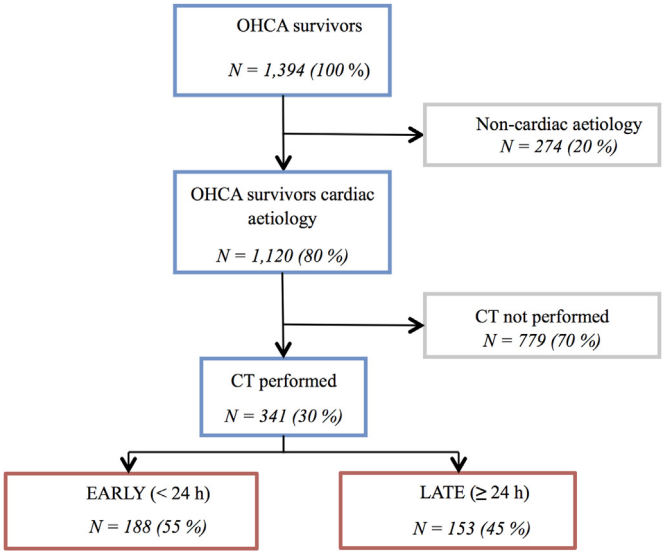

Fig. 1. Flowchart of included patients with out-of-hospital cardiac arrest (OHCA) successfully resuscitated or with on-going cardiopulmonary resuscitation (CPR) at hospital arrival. Cerebral computed tomography (CT) scans were stratified in early (<24 h) and late (≥24 h) after OHCA.

2.3. Outcome

The primary endpoint of the study was all-cause 30-day mortality, with data acquired from the Danish National Patient Registry, which holds vital status on all Danish citizens. Secondary endpoint was neurological outcome at hospital discharge assessed by the Cerebral Performance Category scale and favourable neurological outcome was defined as CPC 1 or 2, non-favourable as 3–4 and dead as CPC-score 5.[24]

2.4. Statistics

Continuous variables are presented as mean ± standard deviation (SD) for normally distributed data and as median and interquartile ranges (IQR) for non-normally distributed data. Differences between two groups were analysed with Student's unpaired t-test or Wilcoxon rank sum test as appropriate. Chi-squared test was used for categorical variables. 30-day mortality is presented as Kaplan-Meier plots and differences are tested using the log-rank test. Univariate and multiple proportional hazard regression analysis (Cox-regression) were performed with estimation of hazard ratios (HR) and 95% confidence intervals (CI) adjusting for potential confounders (age at arrest, sex, primary rhythm, witnessed arrest, bystander CPR, time to ROSC, mild hypothermia, and OHCA in public) after checking for the underlying assumptions of proportionality and interactions. Calendar year was used to estimate the temporal trends during the study period and differences were tested by the Mantel–Haenszel chi square test (trend test). All statistical analyses were carried out in SAS Statistics version 9.3 (Cary, NC, USA) with a level of significance defined as $p < 0.05$.

3. Results

From June 2002 through 2011 a total of 1120 patients with successful resuscitation or with on-going CPR at hospital arrival, who suffered from OHCA of cardiac aetiology, were included in the study (Fig. 1). Among the total population 30% ($n = 341$) of patients had a cerebral CT performed with 55% ($n_{early} = 188$) performed early (<24 h) and 45% ($n_{late} = 153$) performed late (≥24 h). Overall 30-day mortality in the cohort was 56%.

Please cite this article in press as: Langkjær S, et al. Prognostic value of reduced discrimination and oedema on cerebral computed tomography in a daily clinical cohort of out-of-hospital cardiac arrest patients. Resuscitation (2015), http://dx.doi.org/10.1016/j.resuscitation.2015.03.023