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Clinical paper

The optic nerve sheath diameter as a useful tool for early prediction of outcome after cardiac arrest: A prospective pilot study[☆]

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ABSTRACT

Introduction: Optic nerve sheath diameter (ONSD) measurement could detect increased intracranial pressure, and might predict outcome in post-cardiac arrest (CA) patients. We assessed the ability of bedside ONSD ultrasonographic measurement performed within day 1 after CA occurrence to predict in-hospital survival in patients treated with therapeutic hypothermia (TH).
Methods: In two French ICUs, a prospective study included all consecutive patients with CA without traumatic or neurological etiology, successfully resuscitated and TH-treated. ONSD measurements were performed on day 1, 2, and 3 ($ONSD_{1,2,3}$ respectively) after return of spontaneous circulation. All records were registered according to Utstein style.
Results: $ONSD_{1,2,3}$ were assessed in 36, 21, and 14 patients respectively. 19/36 patients (53%) were discharged alive from hospital, including 14/36 (39%) with favorable neurological outcome (Cerebral Performance Category [CPC] score 1–2). Survivors and non-survivors were similar regarding age, sex, cardiovascular risk factors, location and etiology of CA, simplified acute physiology score II, occurrence of post-CA shock, and clinical parameters collected during ONSD measurements. Median $ONSD_1$ was significantly larger in non-survivors versus survivors (7.2 mm [interquartile: 6.8–7.4] versus 6.5 mm [interquartile: 6.0–6.8]; $p = 0.008$). After adjustment on predictive factors, $ONSD_1$ was significantly associated with in-hospital mortality (OR 6.3; 95%CI [1.05–40] per mm of $ONSD_1$ above 5.5 mm; $p = 0.03$), and CPC score (OR for 1 point increase in CPC score: 3.2; 95%CI [1.2–9.4] per mm of $ONSD_1$ above 5.5 mm; $p = 0.03$). $ONSD_1$ was significantly correlated with brain edema assessed by the cerebrum gray matter attenuation to white matter attenuation ratio, measured by the brain computed tomography scan performed on admission in 20 patients (Spearman rho = −0.5, $p = 0.04$).
Conclusions: ONSD seems a promising tool to early assess outcome in post-CA patients treated with TH.

Introduction

In resuscitated cardiac arrest (CA) patients, early prognostication within the first days after admission in the intensive care unit (ICU) remains difficult, especially among patients treated with therapeutic hypothermia (TH). Clinical examination, neurological biomarkers, and electrophysiological evaluations can be used, mainly in combination.[1–3] The out-of-hospital cardiac arrest

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(OHCA) score has also been used to predict outcome.[4] According to recent guidelines, a multimodal neuroprognostication approach is recommended, but no specific combination of predictors is sufficiently supported by available evidence.[1,5]

In CA as in traumatic brain injury (TBI), anoxic and/or ischemic brain injuries can induce brain edema and increase intracranial pressure (ICP), reducing cerebral perfusion pressure and finally influencing neurological outcome.[6–10] The dural sheath that surrounds the optic nerve can inflate if pressure in the cerebrospinal fluid raised, as it occurs in brain edema or intracranial hypertension.[11] As invasive ICP monitoring showed a good correlation with optic nerve sheath diameter (ONSD) measurement, ONSD measurement has been used to detect increased ICP level in TBI.[12,13] Two retrospective studies observed that ONSD measured between 12 and 72 h after CA might be used for assessing neurological outcome.[14,15] The relationship between an early ONSD ultrasonographic measurement and CA outcome has never been prospectively evaluated after adjustment on known predictive factors. The aim of this prospective clinical pilot study was to assess the ability of ONSD ultrasonographic measurement performed within day 1 after CA occurrence to correctly predict in-hospital mortality in post-CA patients treated with TH.

Materials and methods

This prospective observational study was performed in two French ICUs from November 2011 to September 2013. All unconscious (Glasgow Coma Scale ≤6) patients ≥18 years old, admitted in ICU after successful resuscitation from CA, and treated with TH were screened. Exclusion criteria were as follows: unavailable ONSD measurement within 24 h after CA (unavailable investigator, early death, or major hemodynamic instability), CA of traumatic or neurological origin, previous cerebrovascular disease, facial trauma affecting the orbits and/or eyeballs, and previous history of ocular pathology such as exophthalmia, glaucoma or cataract. This study was conducted according to the principles of the Declaration of Helsinki of the World Medical Association and approved by the Ethics Committee of the *French Intensive Care Society* (approval No. 13-25). All surviving patients, or their next of kin if necessary, gave their written informed consent.

Patient management and data collection

Post-CA management was similar in both centers, in accordance with international guidelines,[5] and has been described in the supplemental digital content – Appendix 1. All data were prospectively collected according to Utstein recommendations.[16] Resuscitation intervals were defined as no-flow duration (time from collapse to first cardiopulmonary resuscitation), and low-flow duration (time from first cardiopulmonary resuscitation to return of spontaneous circulation), using emergency medical team data collected on scene. The French prehospital healthcare system has been described elsewhere.[17] Biological parameters, S-100B protein and neuron specific enolase (NSE) levels were measured on ICU admission, day 1, 2 and 3. OHCA score (supplemental digital content – Appendix 2), simplified acute physiologic score II (SAPS II) were calculated[4,18] and Cerebral Performance Category (CPC) score was prospectively collected at hospital discharge.[19]

Study protocol

ONSD measurement has been described in the supplemental digital content – Appendix 3 according to previous studies.[20] For each patient, ONSD measurements were performed at 24, 48 and 72 h after CA (ONSD at day 1, 2, and 3 or $ONSD_{1,2,3}$ respectively), with the head elevated to 30° as recommended, by an investigator per center trained in ocular ultrasonography, independently to post-CA management. Clinical and biological parameters, such as core temperature, mean arterial pressure, hemoglobin level, and partial pressure of arterial CO_2 values were collected during each measurement. Early brain computed tomography (CT) scan was performed at ICU admission (Brightspeed®, GE Medical System, Phoenix, AZ, USA) at the discretion of the physician in charge and according to CA history.[21] Cerebral edema was then assessed using the gray matter attenuation to white matter attenuation ratio (GWR). An independent investigator specialized in neuro-radiology and blinded to clinical outcome secondarily evaluated the GWR. As previously described,[10] increased cerebral edema results in lower GWR. ONSD was also measured on the initial brain CT scan, blindly to ultrasonographic measurements.

Statistical analysis

The primary endpoint was the ability of $ONSD_1$ value to predict in-hospital mortality after CA. Considering the results of other small retrospective series,[14,15] based on a mean (±standard deviation) ONSD value of 5.6 (±0.6) mm in patients with good outcome and 6.3 (±0.6) mm in patients with bad outcome, power calculations yielded that 32 evaluable patients were needed to achieve the power of 0.90 at the significance level of 0.05 (two-sided test). Continuous variables were expressed as median (interquartile range) and their relationship to other predictors was evaluated using Spearman correlation tests. Categorical variables were expressed as *n* (%), and compared using chi-square and Fisher's exact tests. Continuous and categorical variables were compared using nonparametric Mann and Whitney tests. Values of $p < 0.05$ were considered significant. Survivors (CPC 1–4) were compared with non-survivors (CPC 5). Variables where included in logistic regression models after analysis using a locally weighted scatterplot smoothing (LOWESS) function to identify proportional relationships and alternatively suggest thresholds. The relationship between in-hospital mortality and ONSD was evaluated using logistic regression, whereas the relationship between CPC score and ONSD was evaluated using ordered logistic regression with or without adjustment on OHCA score. The ability of $ONSD_1$ above the median value of the overall studied population to predict in-hospital mortality was evaluated after adjustment to OHCA score using a multiple logistic regression analysis. Odds ratios (OR) were expressed with their 95% confidence intervals (CI). Receiver-operating characteristic curves were plotted and areas under the curve (AUC) were estimated using Stata 12.0® (Statacorp College Station, USA).

Results

Patients' characteristics

Ninety-four patients were assessed for eligibility and 58 were excluded (Fig. 1). Among the 36 enrolled patients, 19 patients (53%) were discharged alive from hospital, with favorable neurological outcome occurring in 14 patients (39%). Among the 17 patients who died in ICU, 11 patients died from withdrawal or limitation of life-sustaining treatments (WLST) because of severe neurological impairment. Three other patients evolved to brain death, and the three remaining patients died from multiple organ failure (MOF). Baseline patients' characteristics according to outcome are described in Table 1. No statistical differences were observed between survivors and non-survivors regarding age, sex, body mass index, cardiovascular risk factors, location and etiology of CA. Characteristics of patients after ICU admission and according to outcome