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Prognostic performance of early absence of pupillary light reaction after recovery of out of hospital cardiac arrest

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ABSTRACT

Introduction: Loss of pupillary light reactivity (PLR) three days after a cardiorespiratory arrest is a prognostic factor. Its predictive value upon hospital admission remains unclear. Our objective was to determine the prognostic value of the absence of PLR upon hospital admission in patients with out-of-hospital cardiac arrest.
Methods: We prospectively included all out-of-hospital cardiac arrests occurring between July 2011 and July 2017 treated by a mobile medical team (MMT) based on data from a French cardiac arrest registry database. PLR was evaluated upon hospital admission and the outcome on day 30. The prognosis was classified as good for Cerebral Performance Category (CPC) 1 or 2, and poor for CPC 3–5 or in case of death.
Results: Data from 10151 patients was analysed. The sensitivity and specificity of the absence of PLR for a poor outcome were 72.2% (71.2–73.2) and 68.8% (66.7–70.1), respectively. We identified several variables modifying the sensitivity values and the false positive fraction of a factor, ranging from 0.49 (0.35–0.69) for the Glasgow Coma Scale to 2.17 (1.09–2.48) for pupillary asymmetry. Among those living with CPC 1 or 2 on day 30 (n = 1990; 19.6%), 621 (31.2% (29.2–33.3)) had no PLR upon hospital admission. In the multivariate analysis, loss of PLR was associated with a poor outcome (OR = 3.1 (2.7–3.5)).
Conclusions: Loss of pupillary light reactivity upon hospital admission is predictive of a poor outcome after out-of-hospital cardiac arrest. However, it does not have sufficient accuracy to determine prognosis and decision making.

Introduction

When assessed three days after a cardiorespiratory arrest, loss of pupillary light reactivity (PLR) is predictive of poor neurological outcome, with sensitivity ranging from 18% to 43% and specificity being close to 100% [1–7]. The American Academy of Neurology and the European Resuscitation Council and the European Society of Intensive Care Medicine recommend assessing PLR on the third day after cardiac arrest (CA), without sedation and hypothermia [8,9]. Drugs frequently used during and after cardiopulmonary resuscitation, i.e. adrenaline (epinephrine) and noradrenaline (norepinephrine), may disrupt the interpretation of this reflex [10]. On the other hand, the absence of this reflex at hospital admission has been less well-studied. A systematic review, performed in 1998 including 491 patients in four studies, found sensitivity values between 30 and 50% and specificity values between 69 and 100% for a poor neurological outcome [11]. According to data from more recent studies, this sensitivity would be between 27% to 87% and the specificity between 50%–92% [5,7,12–14]. The high variability of sensitivity and specificity across studies calls into question the exact prognostic performance of loss of PLR upon hospital admission.

Our objective was to assess the prognostic performance of the absence of PLR upon hospital admission for the neurological prognosis in a large series of patients with out-of-hospital cardiac arrest (OHCA).

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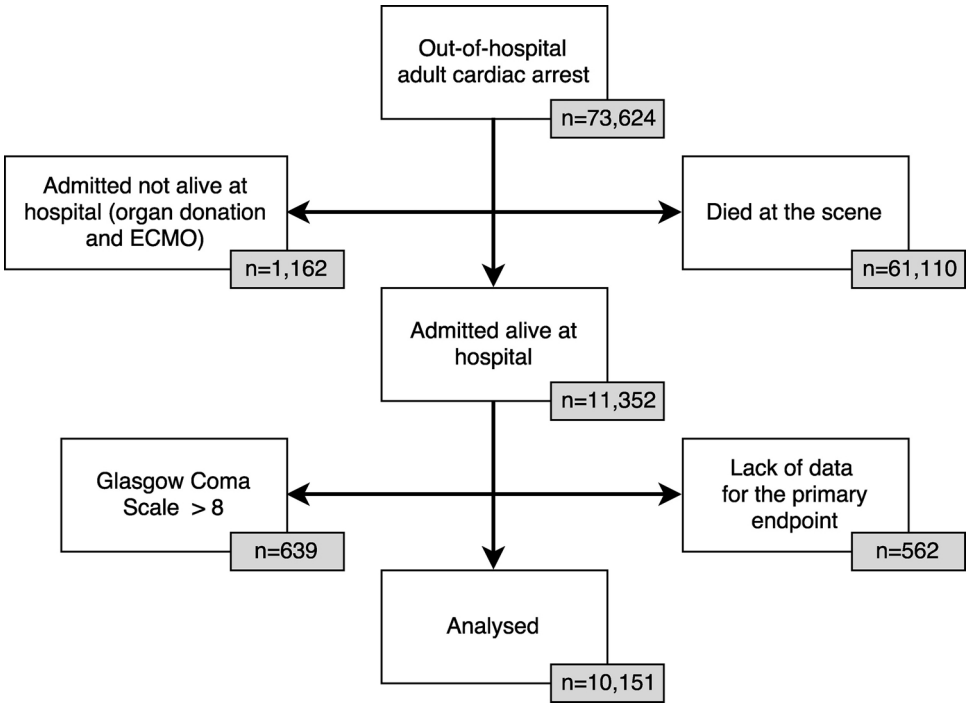

Fig. 1. Study flow chart.
ECMO, extracorporeal membrane oxygenation.

Methods

Study design and setting

We performed a retrospective cohort study based on data extracted from the RéAC. RéAC is the French national CA registry created in June 2011. RéAC is a prospective cohort and includes OHCA patients of any age irrespective of the aetiology and, when a mobile medical team (MMT) was involved, irrespective of resuscitation attempt. This database collects patient characteristics, cardiopulmonary resuscitation data, hospital admission parameters and the vital and neurological status on day 30. The RéAC form met the requirements of French emergency medical services (EMS) organizations and was structured according to the Utstein universal style [15]. All participating Mobile Emergency Response System (MERS) used this form during the intervention. The data were reported in the RéAC secured database (www.registreac.org) [16]. Data completeness is checked regularly. The local investigators were responsible for data entry, verification, and updating.

Basic life support (BLS) was initiated on scene either by witnesses or by fire department ambulance personnel. BLS includes external cardiac massage, defibrillation if necessary, and oxygen mask ventilation. Advanced life support (ALS) was performed by the MMT upon arrival at the scene of the cardiac arrest.

In this study, we selected from the RéAC cohort every cardiac arrest occurring in adults (≥18 years of age) between July 2011 and July 2017 and treated by a MMT. Each MMT is composed of at least an emergency physician, a nurse and an ambulance driver. The exclusion criteria were the absence of data availability for PLR upon hospital admission, for GCS upon hospital admission and for prognosis on day 30. Subjects who were awake or neurologically intact (i.e. GCS > 8) upon hospital admission were also excluded from this study.

Classification of prognosis

The prognosis was evaluated 30 days after the initial cardiac arrest. The neurological status was evaluated using the Cerebral Performance Category (CPC) [17]. It was collected either by the ward physician if the patient remained hospitalized, on the medical record, or during a follow-up consultation. The prognosis was classified as good for CPC 1 or 2, and poor for CPC 3–5 or in case of death.

Statistical analyses

Continuous variables are presented with their median and first and third quartiles (Q1–Q3). Categorical variables are summarized with the number of patients and the percentage with its 95% confidence interval. Chi-squared tests and U-Mann-Whitney tests were used to compare groups when appropriate. As recommended by Pepe et al. [18], multivariate log binomial models were constructed to estimate the effect of different factors on the true positive fraction (sensitivity) and the false positive fraction (1-specificity). The advantage of log binomial models over classical binomial models (logistic regressions) is that they allow for a direct estimation of relative true and false positive fractions, rather than odds ratios. All analyses were performed using R version 3.2.5 and the logbin package for logbinomial models.

Ethical approval

This study was approved by the French advisory committee on information processing in health research (CCTIRS) and the French National Data Protection Commission (CNIL, authorization no. 910946). It was approved as a medical assessment registry without the requirement for patient consent [16].

Results

Between July 2011 and July 2017, 73624 adult cardiac arrests were included in the RéAC database. Most patients, i.e. 61110 (83.0%; 95%CI, 82.7–83.3) died at the scene, 1162 (1.6%; 95%CI, 1.5–1.7) were admitted not alive at hospital for organ donation or extracorporeal membrane oxygenation (ECMO) and 11352 (15.4%; 95%CI, 15.2–15.7) were admitted alive to the hospital. The 30-day status was not available for 300 patients, GCS was not available for 78 subjects and PLR status