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Combination of hemoglobin and low-flow duration can predict neurological outcome in the initial phase of out-of-hospital cardiac arrest

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ABSTRACT

Purpose: To predict neurological outcome following out-of-hospital cardiac arrest (OHCA) using a combination of hemoglobin (Hb) and low-flow duration (LFD).
Materials and methods: We retrospectively examined 131 patients (75 ± 13 years, 64 men) with return of spontaneous circulation (ROSC) following non-traumatic OHCA. The LFD was the duration from the start of cardiopulmonary resuscitation to ROSC. To obtain the Hb/LFD value, we divided the Hb level by the LFD. Multivariate logistic regression analyses were performed to predict full neurological recovery (FNR), defined as Cerebral Performance Category scale scores of 1 or 2 at discharge.
Results: Nineteen patients (15%) achieved FNR. Patients with FNR had high Hb levels (14.9 ± 2.1 vs. 11.3 ± 2.7 g/dl, p = 0.001) and short LFDs (10 [5, 18] vs. 35 [28, 43] min, p = 0.001). Multivariate analyses identified the initial ventricular fibrillation rhythm and Hb/LFD as significant predictors for FNR (odds ratio: 24.9, 3.58; p = 0.001, 0.02, respectively). Receiver operating characteristic (ROC) curve analyses indicated that a high Hb/LFD predicted FNR (cut-off value: 0.50, sensitivity: 94.7%, specificity: 84.5%, area under the curve: 0.933).
Conclusions: Patients with FNR following OHCA had high Hb levels and short LFDs; the Hb/LFD value significantly predicted FNR.

1. Introduction

Only 22–51% of patients who experience out-of-hospital cardiac arrest (OHCA) have a return of spontaneous circulation (ROSC), and even fewer achieve preferable neurological outcomes [1-3]. As it is unclear whether patients with OHCA can achieve neurological recovery in the initial phase, the current guidelines are against "withdrawing life-sustaining therapy because of perceived poor neurological prognosis" before 72 h [4]. However, the early withdrawal of life-sustaining therapy because of perceived poor neurological prognosis still negatively affects patients with OHCA [5]. Therefore, physicians need a method capable of accurately predicting the neurological recovery of these critical patients in the early stages, in order to determine the optimal course of care and to provide families with reasonable expectations of outcome [6].

The clinical circumstances of OHCA, including whether the event was witnessed and cardiopulmonary resuscitation (CPR) was started by bystander(s), are helpful in predicting prognosis [7]. These variables may reflect "the burden of cerebral hypoxia accompanying hypoperfusion before ROSC following OHCA," which may result in irreversible brain damage. The hypoperfusion duration (HD) may be a major determinant of the burden; however, 26–58% of OHCA events are not witnessed, making it difficult to obtain an accurate measurement of the HD [8]. Instead, the low-flow duration (LFD), defined as the duration from the initiation of CPR to ROSC, is reportedly a useful marker for predicting full neurological recovery (FNR) [9, 10].

On the other hand, the burden of cerebral hypoxia may be affected by the hemoglobin (Hb) level, which is known to be an essential determinant of oxygen delivery. In fact, the Hb level is reportedly associated with neurological outcome in patients following OHCA [11-14], and is indicative of irreversible cell death, an imbalance in the cerebral metabolic demand, and decreased cerebral oxygen delivery. It was also reported that low Hb levels are associated with lower cerebral saturations after cardiac arrest [15]. Considering the association

Abbreviations: CI, confidence interval; CPR, cardiopulmonary resuscitation; FNR, full neurological recovery; Hb, hemoglobin; HD, hypoperfusion duration; LFD, low-flow duration; NFD, no-flow duration; OD, odds ratio; OHCA, out-of-hospital cardiac arrest; ROC, receiver operating characteristic; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

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between Hb and the hypoperfusion state, higher Hb levels may lead to a longer tolerance while lower Hb levels may lead to a shorter tolerance for hypoperfusion following OHCA. However, whether the Hb level and HD can be used together to predict FNR in patients following OHCA remains unclear.

Therefore, the aim of this study was to investigate the utility of the Hb level and LFD for predicting neurological outcome in patients in the initial phase of ROSC following OHCA. Moreover, we examined the predictive ability of the Hb/LFD value (calculated by dividing the Hb level by the LFD). We hypothesized that the combination of the Hb level and LFD would predict FNR following OHCA.

2. Material and methods

2.1. Study population

We enrolled 664 consecutive OHCA patients who were transferred to Yokohama Minami Kyosai Hospital between February 2013 and August 2017. One hundred and ninety-five patients achieved ROSC either before or after transfer. Sixty-four patients were excluded for the following reasons: age <18 years, traumatic arrest, mechanical occlusion of the airway (including suffocation), aortic disease (such as aortic dissection and rupture of an aortic aneurysm), intracranial bleeding, hemorrhagic shock, transferred to another hospital immediately after ROSC, and/or insufficient data. Ultimately, we examined the data from 131 patients (Fig. 1).

2.2. Data collection, study definition, and endpoints

Prehospital data, including witnessed cardiac arrest, bystander CPR, and initial ventricular fibrillation (VF) rhythm, were systematically collected at admission according to the Utstein guidelines [16]. The no-flow duration (NFD) and LFD were defined as the duration from cardiac arrest to the start of CPR and the duration from the start of CPR to ROSC, respectively. Blood gas analyses were performed upon hospital arrival. We defined FNR as a Cerebral Performance Category scale score of 1 or 2 at hospital discharge.

2.3. Post-cardiac arrest care

All patients who achieved stable ROSC were admitted to the cardiac intensive care unit. Targeted temperature management was considered if the patient did not have a contraindication such as infection or bleeding. Targeted temperature management was initiated at 34 °C for 24 h using a combination of ice-packs, cooled fluids, and active surface cooling blankets, followed by rewarming to 36 °C for 24 h. All patients had central venous and arterial catheters inserted. The target mean arterial pressure was ≥80 mm Hg. Shivering was treated with intravenous sedation and neuromuscular paralysis.

2.4. Statistical analysis

Parametric continuous variables are presented as the mean ± the standard deviation. Non-parametric variables are presented as the median and interquartile range. Parametric variables were analyzed by two-tailed *t*-tests, while non-parametric variables were analyzed using Mann-Whitney *U* tests.

We explored the overall population to identify variables correlated with favorable neurological outcomes. Univariate analyses were performed on all variables of interest (age, sex [male], initial VF rhythm, witness, bystander, creatinine, glucose, lactate, hypothermia, Hb level, LFD, and Hb/LFD) to detect predictors for FNR following OHCA. Multivariate logistic regression with stepwise backward elimination was used to adjust for covariates that were found to be significantly related ($p < 0.05$) to a good neurological outcome in the univariate analyses. We excluded the Hb level and LFD because these variables were strongly correlated with the Hb/LFD value. Receiver-operating characteristic (ROC) curve analyses were also performed to examine the most accurate cut-off value for predicting FNR. Statistical significance was set at $p < 0.05$.

3. Results

The baseline characteristics of the 131 patients (mean age: 75 ± 13 years, 64 men) are summarized in Table 1. Nineteen patients (15%) achieved FNR after ROSC. Several clinical characteristics were significantly different between patients with and without FNR, including age (59 ± 12 years vs. 77 ± 11 years, $p = 0.001$), initial VF rhythm (16 [84%] vs. 17 [15%], $p = 0.001$), and bystander CPR (14 [74%] vs. 48 [43%], $p = 0.006$). Patients with FNR had significantly shorter LFDs than did patients without FNR (10 [5, 18] min vs. 35 [28, 43] min, $p = 0.001$). Blood gas analyses revealed that patients with vs. without FNR had significantly higher Hb levels (14.9 ± 2.1 g/dl vs. 11.3 ± 2.7 g/dl, $p = 0.001$) and lower lactate levels (8.4 ± 3.2 mmol/l vs. 12.9 ± 4.2 mmol/l, $p = 0.001$). Accordingly, the Hb/LFD value was significantly higher in patients with FNR than without FNR (1.60 vs. 0.34, $p = 0.001$). Hypothermia was performed significantly more frequently in patients with vs. without FNR (9 [47%] vs. 18 [16%], $p = 0.004$).

Univariate logistic regression analyses identified the Hb level, LFD, and Hb/LFD value as predictors for FNR (Hb level: odds ratio [OR]:

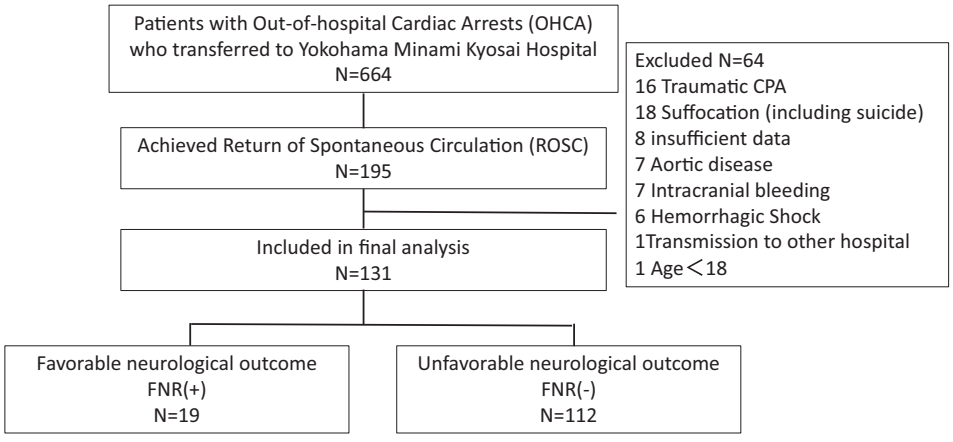

Fig. 1. Study flow diagram. Among the 664 consecutive patients with out-of-hospital cardiac arrest who were transferred to Yokohama Minami Kyosai Hospital, 195 patients achieved return of spontaneous circulation (ROSC). Sixty-four patients were excluded for the following reasons: age < 18 years, traumatic arrest, mechanical occlusion of the airway (including suffocation), aortic disease (such as aortic dissection and rupture of an aortic aneurysm), intracranial bleeding, hemorrhagic shock, transferred to another hospital immediately after ROSC, and/or insufficient data. Ultimately, we examined the data form 131 patients in the present study.