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The association between hemoglobin concentration and neurologic outcome after cardiac arrest $\stackrel{\bigstar}{\asymp}$



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ABSTRACT

Purpose: The purpose of the study is to determine the association between hemoglobin concentration (Hgb) and neurologic outcome in postarrest patients.

Methods: We conducted a retrospective cohort study using the Penn Alliance for Therapeutic Hypothermia (PATH) cardiac arrest registry. Inclusion criteria were resuscitated cardiac arrest (inhospital or out of hospital) and an Hgb value recorded within 24 hours of return of spontaneous circulation. The primary outcome was favorable neurologic status at hospital discharge. Survival to hospital discharge was a secondary outcome.

Results: There were 598 eligible patients from 21 hospitals. Patients with favorable neurologic outcome had significantly higher median Hgb in the first 2 hours (12.7 vs 10.5 g/dL; P < .001) and 6 hours (12.6 vs 10.6 g/dL; P < .001) postarrest. Controlling for age, pulseless rhythm, etiology, location of arrest, receipt of targeted temperature management, hematologic or metastatic malignancy, or preexisting renal insufficiency, there was a significant relationship between Hgb and neurologic outcome within the first 6 hours after arrest (odds ratio, 1.23; 95% confidence interval, 1.09-1.38) and survival to hospital discharge (odds ratio, 1.20; 95% confidence interval, 1.08-1.34).

Conclusion: Higher Hgb after cardiac arrest is associated with favorable neurologic outcome, particularly within the first 6 hours. It is unclear if this effect is due to impaired oxygen delivery or if Hgb is a marker for more severe illness. © 2016 Elsevier Inc. All rights reserved.

1. Introduction

An estimated 600 000 patients have cardiac arrest in the United States each year [1]. Many patients who survive the initial event have the postcardiac arrest syndrome (PCAS), a condition characterized by ischemia-reperfusion injury leading to oxidative stress, neurologic injury, myocardial dysfunction, and a systemic inflammatory response [2].

E-mail address: nickjjohnson@gmail.com (N.J. Johnson).*URL*: http://www.twitter.com/@NickJohnsonMD (N.J. Johnson). Inhospital mortality for resuscitated patients remains high, with estimates ranging from 63% to 72% [2-4].

Targeted temperature management (TTM) has been shown in randomized, prospective clinical trials to improve outcomes for patients with postarrest anoxic encephalopathy, although the optimal target temperature remains controversial [5-7]. In addition to TTM, researchers have suggested that optimal PCAS care is a comprehensive bundle that includes the following: early percutaneous coronary interventions, hemodynamic optimization (goal-directed resuscitation), low tidal volume mechanical ventilation, electrolyte management including glucose control, comprehensive neuromonitoring, and objective criteria for prognostication and withdrawal of life-sustaining therapy [8-11].

An essential component of PCAS care is optimizing oxygen delivery to the brain and other injured organs. Oxygen delivery is dependent both on cardiac output and arterial oxygen content, which is heavily influenced by the hemoglobin concentration (Hgb). Improving oxygen delivery to tissues by increasing the Hgb has been studied in several populations of critically ill patients, with the most robust trials showing

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that a liberal transfusion strategy is no better than a conservative one [12-18]. Patients with active myocardial ischemia and recent cardiac arrest were excluded from most of these studies, and data regarding patients undergoing cardiovascular surgery suggest that some subgroups might benefit from higher Hgb [12]. Limited data exist regarding the association between Hgb and outcome in resuscitated postarrest patients or whether increasing the Hgb via blood transfusion is associated with improvement in outcome [19-21].

The aim of this study is to investigate the relationship between Hgb and neurologic outcome after cardiac arrest. We hypothesize that that higher Hgb during the first 24 hours postarrest is associated with favorable neurologic outcome and improved survival at hospital discharge.

2. Methods

2.1. Setting

We performed a retrospective, observational cohort study of PCAS patients from 21 member institutions of the Penn Alliance for Therapeutic Hypothermia (PATH) registry. The study was approved by the University of Pennsylvania Institutional Review Board.

2.2. Patients

The cohort included successfully resuscitated adult patients who experienced a nontraumatic cardiac arrest with subsequent cardiopulmonary resuscitation, achieved return of spontaneous circulation (ROSC), and had at least 1 recorded Hgb value within 24 hours postarrest. Patients were excluded if they had an active "do not resuscitate" or "do not intubate" order. Patients with hemorrhage as the suspected etiology for their cardiac arrest were excluded from the analysis.

2.3. Outcomes

The primary outcome was neurologic status at hospital discharge, measured as a Cerebral Performance Category (CPC) score dichotomized into "favorable" (CPC 1-2) and "unfavorable" (CPC 3–5). The independent variables were Hgb (main exposure), sex, race, age, location of cardiac arrest (inhospital or out of hospital), whether the cardiac arrest event was witnessed, the first detected pulseless rhythm, whether the event was of cardiac etiology, and whether the patient received TTM, preexisting hematologic or metastatic malignancy, or preexisting renal insufficiency.

2.4. Data collection

The PATH is a multicenter, Web-based national cardiac arrest registry hosted by the University of Pennsylvania [22]. In addition to demographic data, cardiac arrest characteristics, and outcomes, Hgb was abstracted for the following periods: the first 2 hours, the first 6 hours, between 6 and 12 hours, and between 12 and 24 hours postarrest. If multiple Hgb values were available for a given period, the first value recorded was analyzed.

2.5. Statistical analysis

Baseline characteristics were compared using 2-tailed χ^2 tests for categorical variables and *t* tests for continuous variables. The Wilcoxon rank sum test was used to compare the median Hgb during each of the 4 periods: the first 2 hours, the first 6 hours, between 6 and 12 hours, and between 12 and 24 hours postarrest. Hemoglobin concentration was investigated as a continuous predictor of neurologic outcome and then as a dichotomized predictor, first with a cutoff of 7 g/dL and again with a cutoff of 10 g/dL. These cutoffs were determined a priori and loosely based on prior transfusion trials in critically ill populations [12,13,15].

Multivariate logistic regression was used to test for the association between Hgb neurologic outcome and hospital mortality at each of the 4 time points. The analyses were adjusted for the following covariates: age, initial cardiac rhythm, cardiac etiology of arrest, location of arrest (inhospital or out of hospital), receipt of TTM, hematologic or metastatic malignancy, or preexisting renal insufficiency. All analyses were conducted using STATA 12.0 (College Station, TX).

3. Results

3.1. Patient and cardiac arrest characteristics

There were 598 eligible patients. Mean age was 61 ± 17 years, 55% were white, 63% had an out-of-hospital arrest, 34% had a shockable rhythm, and 54% received TTM (Table 1). Patients who had a favorable neurologic outcome were more likely to be younger and male. They were also more likely to have the following: a witnessed cardiac arrest event, a cardiac etiology for their arrest, and an initial shockable rhythm.

A total of 476 patients had preexisting medical comorbidities entered into the PATH database (Table 2). Of these, coronary artery disease, congestive heart failure, and diabetes mellitus were most common. Only 6 patients had hemorrhage as a possible arrest etiology (3 gastrointestinal bleeding, 1 postoperative hemorrhage, 1 tracheal bleeding, and 1 not specified). These patients were excluded from the analyses below.

3.2. Neurologic outcome

Patients with favorable neurologic outcome had significantly higher median Hgb in the first 2 hours (12.7 vs 10.5 g/dL; P < .001) and 6 hours (12.6 vs 10.6 g/dL; P < .001) postarrest (Table 3). After adjusting for age, shockable rhythm, cardiac etiology, arrest location (inhospital vs out of hospital), receipt of TTM, malignancy, and preexisting renal insufficiency, there was a significant relationship between higher Hgb within the first 6 hours after arrest and favorable neurologic outcome (odds ratio [OR], 1.23; 95% confidence interval [CI], 1.09–1.38) (Table 4). Each 1 g/dL increase in Hgb within the first 6 hours after arrest was associated with a 25% increase in the odds of having a favorable neurologic outcome at hospital discharge. There was no significant association between median Hgb 6 to 12 hours or 12 to 24 hours postarrest and neurologic outcome at hospital discharge.

Table 1

Patient characteristics according to neurologic outcome

Characteristic, n (%)	All patients	CPC 1-2	CPC 3-5	Р
Sex				
Male	342 (57.7)	138 (69.0)	202 (52.1)	<.001
Female	251 (42.3)	62 (31.0)	186 (47.9)	
Race				
White	314 (55.2)	114 (59.4)	198 (53.2)	.318
Black	221 (38.8)	69 (35.9)	149 (40.1)	
Other	34 (6.0)	9 (4.7)	25 (6.7)	
Age, mean \pm SD	61 ± 17	57 ± 18	63 ± 17	<.001
Location, n (%)				
Inhospital	221 (37.1)	78 (38.8)	142 (36.5)	.584
Out of hospital	374 (62.9)	123 (61.2)	247 (63.5)	
Witnessed				
Yes	463 (79.7)	175 (87.9)	283 (75.1)	<.001
No	118 (20.3)	24 (12.1)	94 (24.9)	
Rhythm				
Shockable	189 (34.4)	101 (55.3)	88 (24.0)	<.001
Nonshockable	361 (65.6)	81 (44.7)	278 (76.0)	
Cardiac etiology				
Yes	398 (68.6)	150 (76.1)	245 (64.8)	.006
No	182 (31.4)	47 (23.9)	133 (35.2)	
TTM				
Yes	318 (53.5)	105 (52.5)	211 (54.2)	.688
No	276 (46.5)	95 (47.5)	178 (45.8)	
Transfusion ^a				
Yes	117 (32.7)	29 (23.4)	86 (37.6)	.007
No	241 (67.3)	95 (76.6)	143 (62.4)	

 a Transfusion information was obtained only for a subpopulation of patients (n = 361).

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