Acute and Critical Care

Acute and Critical Care 2026 August 41(3):588-597
https://doi.org/10.4266/acc.005075

| pISSN 2586-6052 | eISSN 2586-6060

Prognostic value of initial hemoglobin levels for neurological outcomes in patients with out-of-hospital cardiac arrest in South Korea

Jihun Keum[1], Kyung Hun Yoo[1,2], Yongil Cho[1,2,3], Tae Ho Lim[1,2], Hyunggoo Kang[1,2], Jaehoon Oh[1,2], Byuk Sung Ko[1,2], Juncheol Lee[1,2]

[1]Department of Emergency Medicine, Hanyang University Hospital, Seoul, Korea
[2]Department of Emergency Medicine, Hanyang University College of Medicine, Seoul, Korea
[3]Hanyang Institute of Bioscience and Biotechnology, Hanyang University, Seoul, Korea

Background: Previous studies suggest that lower hemoglobin (Hb) levels are associated with adverse outcomes after out-of-hospital cardiac arrest (OHCA). However, most of these were limited by small sample sizes and single-center designs. We aimed to evaluate the association between initial Hb levels and clinical outcomes after OHCA using a large multicenter registry.

Methods: This retrospective observational study analyzed prospectively collected multicenter registry data. Hb levels measured at emergency department arrival were analyzed as continuous variables with restricted cubic spline (RCS) models, which flexibly characterize dose–response relationships with unfavorable neurological outcomes and in-hospital mortality. Generalized estimating equations with a logit link were used to account for within-hospital clustering and to adjust for clinically relevant covariates.

Results: Lower Hb levels were independently associated with higher adjusted odds of unfavorable neurological outcomes and in-hospital mortality. RCS analyses showed a statistically significant overall association between Hb levels and both outcomes after multivariable adjustment (overall P<0.001). The adjusted odds of adverse outcomes increased progressively with decreasing Hb levels. Cluster-adjusted analyses using generalized estimating equations yielded consistent results.

Conclusions: Initial Hb levels were independently associated with neurological outcomes and in-hospital mortality after OHCA. Modeling Hb as a continuous variable showed a graded association across the Hb spectrum. These findings highlight the prognostic relevance of baseline Hb levels.

Key Words: anemia; early diagnosis; hemoglobins; mortality; out-of-hospital cardiac arrest

Original Article

Received: October 21, 2025
Revised: March 2, 2026
Accepted: March 2, 2026

Corresponding author
Kyung Hun Yoo
Department of Emergency Medicine, Hanyang University College of Medicine, 222-1 Wangsimni-ro, Seongdong-gu, Seoul 04763, Korea
Tel: +82-2-2290-9296
Fax: +82-2-2290-9280
Email: ewwkay@hanyang.ac.kr

© 2026 The Korean Society of Critical Care Medicine

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/li-censes/by-nc/4.0/) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Patients resuscitated from out-of-hospital cardiac arrest (OHCA) have a high mortality rate

at hospital discharge and often experience long-term neurological disabilities [1]. Many survivors develop permanent neurological impairments, caused not only by cerebral anoxia resulting from the interruption of brain perfusion at the time of arrest but also by ischemic brain injury that occurs during the post-cardiac arrest phase [2,3]. The International Resuscitation Committee recommends comprehensive therapeutic strategies to improve OHCA outcomes [4-6]. The fundamental goal of post-cardiac arrest management is to maintain an optimal balance between oxygen delivery and consumption. Achieving this balance facilitates neurologically favorable survival by alleviating the impact of ischemia and hypoxia on the brain tissue after cardiac arrest. During the resuscitation phase, the primary focus is on strategies that enhance perfusion to the heart and the brain [4,6].

Witnessed cardiac arrest or bystander cardiopulmonary resuscitation (CPR) are well-established prognostic variables [4,6]. These factors reflect the burden of cerebral hypoxia associated with hypoperfusion. Hemoglobin (Hb) plays an essential role in the delivery of oxygen to tissues [7]. Therefore, the burden of cerebral hypoxia may be influenced by Hb levels. Hb levels may also affect cerebral blood flow after achieving a return of spontaneous circulation. The cerebrovascular system responds to hypoxia by increasing nitric oxide (NO) production and stimulating sympathetic receptors to facilitate adequate vasodilation and maintain cerebral blood flow [8]. However, the response is eventually limited in the context of severe anemia and cannot fully compensate for the decrease in arterial oxygen content caused by low Hb levels [9].

Previous studies have suggested that low Hb levels may be detrimental to patients with OHCA. However, these studies were conducted at single centers and had relatively small sample sizes [10-15]. The optimal neuroprotective Hb level after cardiac arrest has not yet been determined, and the specific threshold at which outcomes begin to worsen remains unclear. Moreover, Hb has rarely been studied as a prognostic indicator in OHCA patients. Therefore, this study aimed to investigate the association between Hb levels and clinical outcomes using multicenter data. We aimed to evaluate the prognostic value of Hb in predicting neurological outcomes and in-hospital mortality in OHCA patients.

KEY MESSAGES

- Lower hemoglobin (Hb) levels upon arrival at the emergency department were independently associated with adverse neurological outcomes and increased in-hospital mortality in patients experiencing out-of-hospital cardiac arrest.
- There was a graded link across the Hb spectrum, with higher adjusted odds of adverse outcomes at lower Hb levels.
- Hb is a simple and accessible biomarker that offers significant prognostic insights into early physiological status following cardiac arrest.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of the Hanyang University Hospital (No. HYUH 2015-10-021-039). The requirement for informed consent was waived owing to the retrospective nature of the study. The KoCARC registry is registered at ClinicalTrials.gov (protocol: NCT03222999). This study was conducted in accordance with the principles of the Declaration of Helsinki.

Data Source and Data Collection

This study used data from the Korean Cardiac Arrest Research Consortium (KoCARC), a prospective, collaborative, multicenter data collection system. Patients with OHCA from 62 participating hospitals in South Korea, registered with KoCARC between October 2015 and December 2023, were included in the study. The KoCARC registry contains data of patients with cardiac arrest, including age, sex, medical history, the presence of trauma, initial cardiac rhythm, and prognosis. Patients with nontraumatic OHCA who were consecutively transferred to participating emergency departments (EDs) following resuscitation were registered in the KoCARC registry. Patients with terminal illnesses recorded in the medical records, who received hospice care, were pregnant, and with "do not resuscitate" orders were excluded from registration. Additionally, patients with OHCA resulting from noncardiac causes, including trauma, drowning, poisoning, burns, asphyxia, or hanging, were excluded. Data were collected using standardized registry forms and entered into a web-based electronic database registry in accordance with the Utstein style, using emergency

medical services records and hospital medical records [16].

Study Design and Setting

Exclusion criteria encompassed patients under the age of 20 years, those transferred from other facilities, and those with documented bleeding. In this context, "documented bleeding" referred specifically to evidence of bleeding at the time of first medical contact. The study focused on patients who survived and were admitted directly from the ED. Patients with missing data on clinical outcomes or without laboratory blood tests were also excluded. We evaluated the impact of initial Hb levels measured at ED arrival on outcomes in patients with OHCA.

Outcomes

The primary outcomes were neurological status and mortality. Neurological status was assessed using the Cerebral Performance Category (CPC) score and categorized as favorable (CPC 1–2) or unfavorable (CPC 3–5).

Statistical Analysis

Baseline characteristics were summarized according to neurological outcomes and in-hospital mortality. Continuous variables were expressed as means with standard deviations or medians with interquartile ranges. The normality of continuous variables was assessed using the Shapiro-Wilk test. Depending on data distribution, continuous variables were compared using the Student t-test or the Mann-Whitney U-test, and categorical variables were compared using Fisher's exact test.

Hb was primarily analyzed as a continuous variable using restricted cubic spline (RCS) modeling to characterize its association with clinical outcomes flexibly. To facilitate clinical interpretation, 14.0 g/dl was specified as the reference value for spline-based analyses. The value of 14.0 g/dl was selected because it corresponds to a clinically typical mid-normal Hb level and was close to the median Hb concentration of the study population. The overall association between Hb levels and outcomes, as well as potential non-linearity, was evaluated using Wald statistics derived from the spline terms.

To account for within-hospital clustering of patients, the association between initial Hb level and clinical outcomes was further evaluated using generalized estimating equations (GEE) with a logit link function and an exchangeable working correlation structure. Results of univariate analyses were expressed as odds ratios (ORs) with 95% CIs. Multivariable GEE models were constructed to adjust for clinically relevant covariates, yielding adjusted ORs (aORs) with 95% CIs.

Adjusted covariates included age, sex, witnessed arrest, bystander CPR, shockable rhythm, CPR duration, total epinephrine dose, and comorbidities (diabetes mellitus, heart disease, lung disease, cerebrovascular disease, cancer, and renal failure). In addition, biomarkers reflecting severity and commonly incorporated into established scoring systems such as Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) were included (platelet count, creatinine, potassium, total bilirubin, base excess, arterial pH, and serum lactate).

Post-resuscitation treatments, including percutaneous coronary intervention (PCI) and targeted temperature management (TTM), were not included in the primary multivariable models because they were considered potential mediators on the causal pathway between initial Hb levels and clinical outcomes. The assumed causal structure underlying this analytical approach was illustrated using a directed acyclic graph (Supplementary Figure 1). Sensitivity analyses were conducted to evaluate the robustness of the spline-based associations by also adjusting for PCI and TTM.

All tests were two-tailed, and a P-value <0.05 was considered statistically significant. All statistical analyses were conducted using the R software, version 4.3.3 (R: A Language and Environment for Statistical Computing, R Core Team, R Foundation for Statistical Computing; http://www.R-project.org/).

RESULTS

Characteristics of the Study Population

In total, 4,156 patients were included in the final study population (Figure 1). Of these patients, 2,858 (68.8%) experienced unfavorable neurological outcomes, whereas 1,298 (31.2%) had favorable neurological outcomes. Baseline characteristics stratified by neurological outcome are summarized in Table 1. Patients with unfavorable neurological outcomes had a mean age of 64.8 years, and 70.0% were male. The mean Hb level in this group was 11.8 g/dl. Cardiac arrest was witnessed in 81.5% of patients, and 47.4% received bystander CPR. Shockable

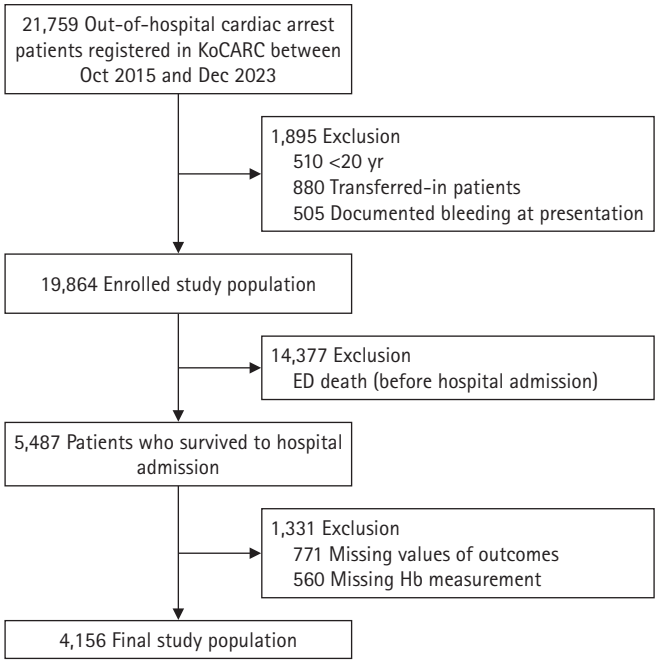

Figure 1. Flowchart of the study population selection. KoCARC: Korean Cardiac Arrest Research Consortium; ED: emergency department; Hb: hemoglobin.

rhythm was present in 29.3%. Prolonged CPR duration (>20 minutes) and higher total epinephrine doses were more frequently observed in this group. Laboratory biomarkers reflecting shock severity differed significantly between patients with unfavorable and favorable neurological outcomes. In patients with favorable neurological outcomes, the mean age was 56.9 years, and 81.3% were male. The mean Hb level was 14.0 g/dl. Witnessed arrest and bystander CPR occurred in 90.7% and 61.7% of patients, respectively, and shockable rhythm was observed in 77.0%. Baseline characteristics stratified by in-hospital mortality are presented in Supplementary Table 1.

Table 1. Baseline characteristics of the study population stratified by neurological outcomes

Variable	Favorable neurological outcomes (n=1,298)	Unfavorable neurological outcomes (n=2,858)
Hemoglobin (g/dl)	14.0±2.2	11.8±3.0
Age (yr)	56.9±13.4	64.8±14.8
Sex		
Male	1,055 (81.3)	2,001 (70.0)
Female	243 (18.7)	857 (30.0)
Witnessed arrest	1,177 (90.7)	2,328 (81.5)
Bystander CPR	801 (61.7)	1,356 (47.4)
Shockable rhythm (any)	999 (77.0)	838 (29.3)
CPR duration (>20 min)	77 (5.9)	674 (23.6)
Epinephrine (total)	2.7±4.1	4.9±5.1
Comorbidity		
Diabetes mellitus	284 (21.9)	993 (34.7)
Heart disease	325 (25.0)	555 (19.4)
Lung disease	29 (2.2)	164 (5.7)
Cerebrovascular disease	52 (4.0)	171 (6.0)
Cancer	46 (3.5)	209 (7.3)
Renal failure	39 (3.0)	233 (8.2)
Biomarkers		
Platelet count ($\times10^3$/μl)	226 (181 to 270)	180 (133 to 233)
Creatinine (mg/dl)	1.2 (1.0 to 1.4)	1.3 (1.0 to 2.0)
Potassium (mEq/L)	3.7 (3.4 to 4.2)	4.6 (3.8 to 5.8)
Total bilirubin (mg/dl)	0.5 (0.4 to 0.7)	0.4 (0.3 to 0.7)
Base excess (mEq/L)	−10.0 (−14.4 to −5.8)	−14.1 (−19.4 to −8.4)
pH	7.2 (7.1 to 7.3)	7.0 (6.8 to 7.1)
Lactate (mmol/L)	8.1 (5.7 to 11.3)	11.3 (8.4 to 14.5)
Further treatment		
PCI	619 (47.7)	589 (20.6)
TTM	422 (32.5)	901 (31.5)

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
CPR: cardiopulmonary resuscitation; PCI: percutaneous coronary intervention; TTM: targeted temperature management.

Neurological Outcomes

Figure 2A presents the association between the initial Hb level and an unfavorable neurological outcome modeled as a continuous variable using RCS. After multivariable adjustment, Hb levels showed a statistically significant overall association with an unfavorable neurological outcome (overall P<0.001). The non-linear component of the spline term was not statistically significant (P=0.081). Across the evaluated Hb range, lower Hb levels were associated with a higher aOR for unfavorable neurological outcomes. The aOR decreased progressively with increasing Hb concentration.

In GEE analyses accounting for hospital-level clustering, each 1 g/dl increase in Hb level was associated with lower odds of unfavorable neurological outcomes in both crude and adjusted models (Table 2). In the adjusted GEE model, the aOR per 1 g/dl increase in Hb was 0.84 (95% CI, 0.80–0.89; P<0.001), with an estimated exchangeable working correlation (α) of 0.023.

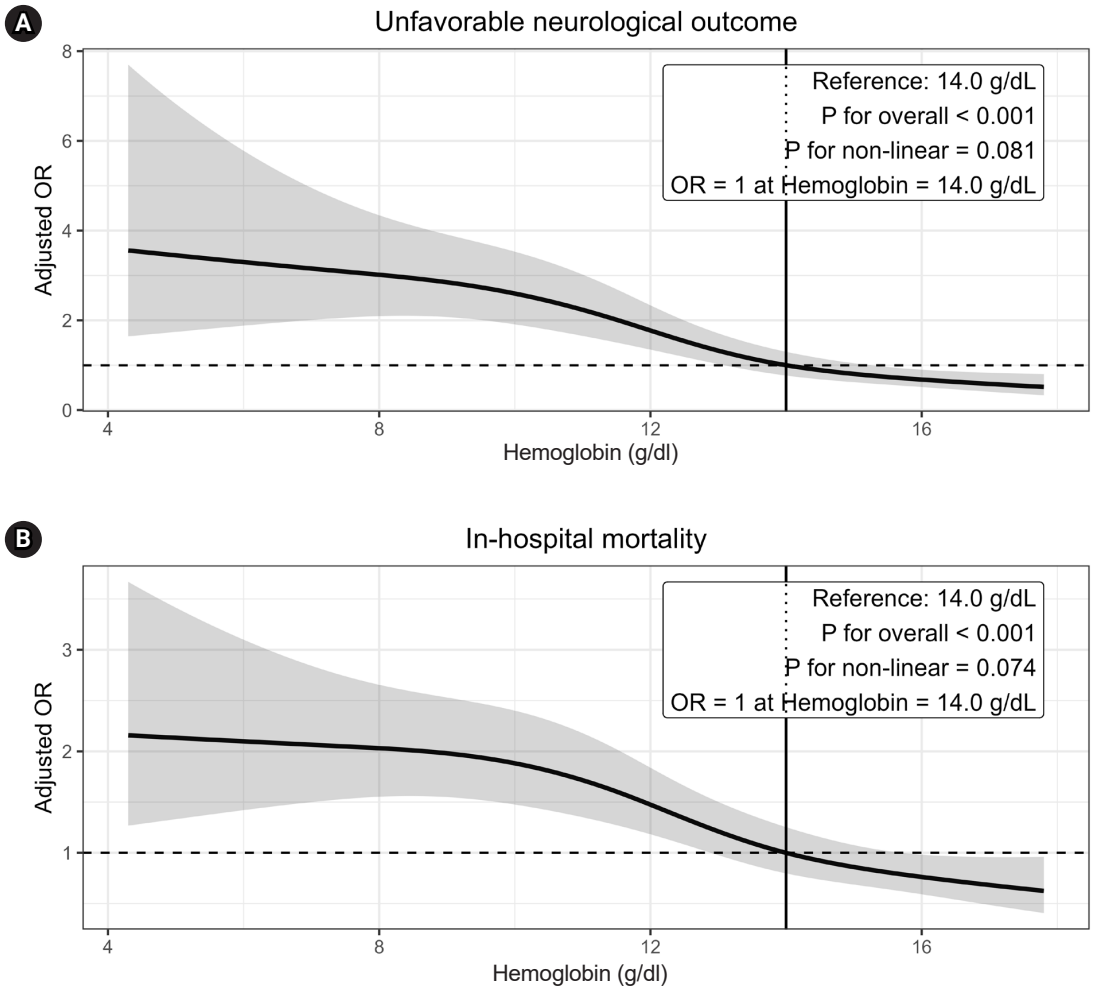

Figure 2. Restricted cubic spline analysis of hemoglobin and clinical outcomes after out-of-hospital cardiac arrest. Restricted cubic spline curves illustrate the adjusted association between hemoglobin level and (A) unfavorable neurological outcome and (B) in-hospital mortality. Solid lines represent adjusted odds ratios (ORs), and shaded areas indicate 95% CIs. Models were adjusted for age, sex, witnessed arrest, bystander cardiopulmonary resuscitation, shockable rhythm, cardiopulmonary resuscitation duration, total epinephrine dose, platelet count, creatinine, potassium, bilirubin, base excess, pH, lactate, and comorbidities (diabetes mellitus, heart disease, lung disease, cerebrovascular disease, cancer, and renal failure). Hemoglobin level was modeled as a continuous variable using restricted cubic splines, with 14.0 g/dl set as the reference value; therefore, all odds ratios shown are expressed relative to a hemoglobin concentration of 14.0 g/dl.

In-Hospital Mortality

The RCS analysis for in-hospital mortality is shown in Figure 2B. The Hb level showed a significant overall association with in-hospital mortality following multivariable adjustment (overall P<0.001). The non-linear component was not statistically significant (P=0.074). Lower Hb levels were associated with a higher aOR of in-hospital mortality across the analyzed range. The aOR declined with increasing Hb concentration. Consistent with spline analyses, GEE models accounting for hospital-level clustering showed an inverse association between Hb level and in-hospital mortality (Table 2). In the adjusted GEE model, each 1 g/dl increase in Hb level was associated with a reduced odds of in-hospital mortality (aOR, 0.90; 95% CI, 0.88–0.92; P<0.001), with an estimated working correlation (α) of 0.019.

Sensitivity Analysis, Including Post-resuscitation Treatments

Sensitivity analysis incorporating post-resuscitation treatments, including PCI and TTM, yielded spline curves that were qualitatively similar to those of the primary models (Supplementary Figure 2). The overall shape and direction of the as-

Table 2. Associations between hemoglobin level and clinical outcomes using generalized estimating equations accounting for hospital-level clustering

	Crude	P-value	Adjusted	P-value	α
Unfavorable neurological outcome					
Hemoglobin (per 1 g/dl)	0.72 (0.68–0.75)	<0.001	0.84 (0.80–0.89)	<0.001	0.023
In-hospital mortality					
Hemoglobin (per 1 g/dl)	0.78 (0.76–0.80)	<0.001	0.90 (0.88–0.92)	<0.001	0.019

Values are presented as odds ratio (95% CI). Crude models included hemoglobin only and accounted for hospital-level clustering using generalized estimating equations. The adjusted models included age, sex, witnessed arrest, bystander cardiopulmonary resuscitation, shockable rhythm, cardiopulmonary resuscitation duration, total epinephrine dose, platelet count, creatinine, potassium, bilirubin, base excess, pH, lactate, and comorbidities (diabetes mellitus, heart disease, lung disease, cerebrovascular disease, cancer, and renal failure). α: exchangeable working correlation.

sociation between Hb levels and both neurological outcomes and in-hospital mortality remained consistent after additional adjustments for these variables.

DISCUSSION

This study showed that initial Hb levels in patients with OHCA were independently associated with both neurological outcomes and in-hospital mortality. When modeled as a continuous variable using RCS, lower Hb levels were consistently linked to a higher aOR for unfavorable neurological outcomes and in-hospital mortality, even after accounting for hospital-level clustering and multiple clinically relevant covariates. This analysis characterized the dose–response relationship across the complete range of observed Hb values. The spline-based analyses revealed an increase in risk as Hb levels decreased.

The findings of this study align with those of previous studies, which reported an association between low Hb levels and poor outcomes [17]. The Survey of Survivors after Cardiac Arrest in the Kanto area (SOS-KANTO) study group analyzed 137 patients with witnessed OHCA and reported that the Hb level at the time of hospital arrival was an independent predictor of neurological outcomes [12]. Several studies have shown similar results. However, the optimal Hb cutoff level for predicting the neurological outcomes of OHCA survivors remains unclear [10,12-15]. Albaeni et al. examined 146 patients with OHCA and found that an Hb level <10 g/dl was associated with poor neurological outcomes [10]. In a study of 82 patients with OHCA, Ameloot et al. [11] reported that a mean Hb level <12.3 g/dl was independently associated with worse neurological outcomes. In a recent retrospective study of 131 participants conducted at a single center in Japan, the optimal Hb cutoff value for predicting favorable neurological outcomes was 14.4 g/dl [13]. Previous studies have limitations in generalizing results due to the small sample sizes and single-center settings. In the present study, we used multicenter data and included a relatively large number of participants, enhancing the generalizability of the findings. Although no optimal Hb cutoff was identified, the spline-based analyses showed that key features of the risk curve occurred within a similar Hb range to that described in previous studies. These findings highlight consistency in the overall exposure–outcome relationship while underscoring the need for future research to establish clinically actionable thresholds.

Oxygen delivery to the brain is directly related to both cerebral blood flow and arterial oxygen content, with the latter being directly proportional to Hb levels and arterial oxygen saturation [9]. Reduced Hb levels induce the upregulation of NO production by perivascular neurons and endothelial cells, leading to cerebral vasodilation [18]. Additionally, cerebral hypoxia upregulates the production of other biochemical mediators, such as the hypoxia-inducible factor, in response to anemia [19]. This cascade of events leads to increased cerebral blood flow, which helps maintain consistent cerebral oxygen delivery. Consequently, a significant reduction in Hb levels may lead to tissue hypoxia if the compensatory mechanisms aimed at maintaining constant tissue oxygenation fail or become overwhelmed [20]. A progressive reduction in Hb levels in a healthy brain can be compensated by an increase in cerebral blood flow through cerebral vasodilation until a critical Hb level of approximately 5–6 g/dl is reached [9]. However, the results of this study suggest that data from healthy individuals may not directly apply to patients with brain injury, as the latter may require a higher Hb threshold.

Brain lesions observed after cardiac arrest may be highly heterogeneous. For instance, in anemia, certain regions may experience insufficient oxygen supply to meet the demand, leading to a condition known as ischemic penumbra [9]. This area, sustained by residual small blood vessels, undergoes functional rather than structural cell damage [21]. Brain injury

can be mitigated by rescuing the ischemic penumbra through restoring blood flow as early as feasible [22]. However, at similar Hb levels, the cerebral blood flow is reportedly lower in the injured brain than in the healthy brain [9]. Moreover, previous studies have demonstrated that the cerebral metabolic rate and oxygen delivery in the penumbra gradually decline as the Hb concentration decreases [23]. In this study, we showed that lower Hb levels were associated with a progressively higher aOR for unfavorable neurological outcomes and mortality.

A restrictive red blood cell (RBC) transfusion threshold of Hb 7 g/dl is recommended for critically ill patients, but there is limited evidence regarding transfusion thresholds for OHCA patients [24,25]. Several studies have indicated that patients may require a higher Hb threshold for RBC transfusion after cardiac arrest. Patients often experience hemodynamic instability, including myocardial dysfunction, after OHCA. This can significantly impair the compensatory increase in the cardiac output required to maintain adequate cerebral oxygen delivery during anemia [26]. Moreover, cerebral autoregulation is disrupted in approximately 30%–50% of patients after cardiac arrest [27]. Consequently, arterial hypotension after cardiac arrest may result in cerebral hypoperfusion, limiting the ability of cerebral blood vessels to vasodilate in response to anemia compared with healthy individuals [9,27]. The KoCARC registry data used in our study did not include information on RBC transfusion, and we were unable to verify this directly. Therefore, important questions regarding optimal Hb thresholds for RBC transfusion remain unanswered. Currently, prospective studies specifically designed to address this issue are lacking.

This study should be interpreted with the following limitations. First, this study focused on a cohort of patients who survived ED resuscitation and were subsequently admitted to the hospital, which introduces survivorship bias and potential collider stratification into our results. Patients who died in the ED before being admitted were very different from those who survived to admission (Supplementary Table 2). This result shows that the admission cohort is a clinically distinct subgroup. Consequently, the identified relationships should be regarded as prognostic associations among patients attaining clinically significant return of spontaneous circulation and survival to admission, rather than causal factors relevant to all OHCA patients. Second, although we adjusted for multiple resuscitation-phase variables and biomarkers of shock severity, unmeasured confounding related to early fluid administration could not be fully addressed due to registry limitations. Third, this study lacks detailed data on RBC transfusion, including transfusion status, timing, volume, and transfusion thresholds. Patients presenting with lower initial Hb levels are probably more prone to receive transfusions during their hospital course, and such post-resuscitation interventions may have modified subsequent neurological outcomes and survival. However, transfusion is anticipated to mitigate rather than amplify the association between low initial Hb levels and adverse outcomes, as it may partially restore oxygen-carrying capacity in anemic individuals. Therefore, the absence of transfusion data may have biased the observed associations toward the null. Importantly, this study was designed to evaluate the prognostic relevance of Hb levels measured at ED arrival, reflecting the initial physiological status before post-resuscitation therapeutic interventions, rather than to assess the causal effects of transfusion strategies. Accordingly, our findings should not be interpreted as evidence to support any specific transfusion threshold or treatment strategy. Future prospective studies incorporating detailed transfusion-related variables will be required to clarify how baseline Hb levels interact with transfusion practices to influence neurological outcomes and survival after OHCA. Fourth, Hb levels were measured only once upon arrival at the ED. Consequently, we were unable to evaluate dynamic changes in Hb levels over time or their temporal relationship with the clinical course. Longitudinal Hb trajectories may provide additional prognostic information beyond a single baseline measurement, but such analyses were not feasible due to limitations of the registry data. Also, incomplete information on sampling timing and resuscitation fluids could bias the observed Hb–outcome relationship and may influence both the magnitude and the shape of the association. Finally, detailed information on the specific etiology of low Hb levels was not available. Although patients with documented evidence of bleeding were excluded and we adjusted for several comorbidities commonly associated with chronic anemia, including cancer and renal disease, unmeasured or undocumented hemorrhage may still have occurred. In such cases, hypovolemia rather than anemia per se may have contributed to adverse outcomes, and this residual confounding should be considered when interpreting the results.

In conclusion, Hb levels obtained at ED arrival were inde-

pendently associated with neurological outcomes and in-hospital mortality in patients with OHCA. RCS analyses showed that lower Hb levels were associated with progressively higher adjusted odds of unfavorable neurological outcomes and mortality, without evidence of a clear non-linear threshold effect. The lowest estimated risks were observed at Hb levels around the mid-normal range. These findings suggest that Hb level is a clinically relevant prognostic marker in OHCA patients and should be considered in the early risk stratification and post-resuscitation management of this population.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

FUNDING

This research was supported by a grant under the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) (RS-2022-KH129835 to Yongil Cho), a National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (RS-2023-00280373 to Yongil Cho), and the research fund of Hanyang University (HY-202500000001277 to Kyung Hun Yoo).

ACKNOWLEDGMENTS

We would like to acknowledge and thank investigators from all participating hospitals of the Korean Cardiac Arrest Resuscitation Consortium: Sang Kuk Han, Phil Cho Choi (Kangbuk Samsung Medical Center), Young Hwan Lee, Sang O Park (Konkuk University Medical Center), Jong Seok Lee, Ki Young Jeong (Kyung Hee University Hospital), Sung Hyuk Choi, Young Hoon Yoon (Korea University Guro Hospital), Su Jin Kim, Kap Su Han (Korea University Anam Hospital), Min Seob Sim, Gun Tak Lee (Samsung Medical Center), Youn Jung Kim (Asan Medical Center), Jong Whan Shin, Hui Jai Lee (SMG-SNU Boramae Medical Center), Keun Hong Park, Hahn Bom Kim (Seoul Medical Center), Yoo Seok Park, Arom Choi (Yonsei University Severance Hospital), Tae Young Kong, Hyuna Hwang (Yonsei University Gangnam Severance Hospital), Youngsuk Cho (Hallym University Kangdong Sacred Heart Hospital), Gu Hyun Kang, Yong Soo Jang (Hallym University Kangnam Sacred Heart Hospital), Sung Wook Park, Wook Tae Yang (Pusan National University Hospital), Hyun Wook Ryu, Jae Yun Ahn (Kyungpook National University Hospital), Hyuk Jun Yang, Jae-hyug Woo (Gachon University Gil Medical Center), Sung Hyun Yun, Chong Sun Kim (Catholic Kwandong University International St. Mary's Hospital), Sun Pyo Kim (Chosun University Hospital), Jin Woong Lee, Wonjoon Jeong (Chungnam National University Hospital), Sung Soo Park, Jae Kwang Lee (Konyang University Hospital), Ryeok Ahn, Wook Jin Choi (Ulsan University Hospital), Bang Shill Rhee (Ajou University Hospital), You Hwan Jo, Sung Min Park (Seoul National University Bundang Hospital), In Byung Kim, Ki Ok Ahn (Myongji Hospital), Se Joong Ahn (Korea University Ansan Hospital), Seung Cheol Lee, Sang Hun Lee, Kyeong Min Lee (Dongguk University Ilsan Hospital), Young Sik Kim (Bundang Jesaeng Hospital), Jin Sik Park, Myung Hee Park (Sejong Hospital), Dai Han Wi (Wonkwang University Sanbon Hospital), Jin Kun Bae, Yong Hee Lee (Cha University Bundang Medical Center), Sang Ook Ha, Won Seok Yang (Hallym University Pyeongchon Sacred Heart Hospital), Ju Ok Park, Hang A Park (Hallym University Dongtan Sacred Heart Hospital), Kyoung Chul Cha, Woo Jin Jung (Wonju Severance Christian Hospital), Taek Geun Ohk, Myoung Cheol Shin (Kangwon National University Hospital), An Mu Eob, Kyung Sook Park (Hallym University Chuncheon Sacred Heart Hospital), Sang Chul Kim, Gwan Jin Park (Chungbuk National University Hospital), Han Joo Choi, Yong Oh Kim (Dankook University Hospital), Tae Oh Jung, Jae Chol Yoon (Jeonbuk National University Hospital), Young Tae Park, Ju Taek Lee (Dongguk University Gyeongju Hospital), Jin Hee Jeong, Sang Bong Lee (Gyeongsang National University Hospital), Won Kim, Yi Sang Moon (Cheju Halla General Hospital), Sung Wook Song, Seo Young Ko (Jeju National University Hospital), Joon-myoung Kwon, Eui Hyuk Kang (Mediplex Sejong Hospital), Sang Chan Jin, Tae-kwon Kim (Keimyung University Dongsan Medical Center), Chang Sun Kim, Hyun Goo Shin (Hanyang University Guri Hospital), Dong Sun Choi (Uijeongbu Eulji Medical Center, Eulji University), Chul Min Ha (Hanil General Hospital), Jai Woog Ko, and Yun Jeong Hwang (Yongin Severance Christian Hospital).

We also acknowledge and thank the Steering Committee: Sung Phil Chung (Chair, Yonsei University Gangnam Severance Hospital), Kyung Jun Song (Chair of the Steering Com-

mittee, SMG-SNU Boramae Medical Center), Sang Hoon Na (Advisory Committee, Seoul National University Hospital), Gyu Chong Cho (Data Safety and Management Board, Hallym University Kangdong Sacred Heart Hospital), Seung Sik Hwang (Security and Monitoring Board, Seoul National University), Sung Oh Hwang (Past Chair, Wonju Severance Christian Hospital), Sang Do Shin (Past executives of the Steering Committee, Seoul National University Hospital), Hyuk Jun Yang (Past executives of Advisory Committee, Gachon University Gil Hospital), Jeong Ho Park (Secretariat, Seoul National University Hospital), Jong Hak Park (Community and Prehospital Committee, Korea University Ansan Hospital), Jin Hee Jung (Pediatric Resuscitation Committee, SMG-SNU Boramae Medical Center), Kyoung Chul Cha (Prospective Research Committee, Wonju Severance Christian Hospital), and Ji Hoon Kim (Data Science Committee, Yonsei University Severance Hospital). Additionally, we acknowledge members of the Secretariat: Yeongho Choi (Seoul National University Bundang Hospital), Seulki Choi (Seoul National University Hospital), Se Jin Lee (Seoul National University Hospital), and Hye Jee Joo (Seoul National University Hospital).

Finally, we thank the National Fire Agency for providing prehospital EMS data and the Korean Association of Cardiopulmonary Resuscitation for support.

ORCID

Jihun Keum	https://orcid.org/0009-0006-9703-1429
Kyung Hun Yoo	https://orcid.org/0000-0003-2250-5280
Yongil Cho	https://orcid.org/0000-0001-5027-6345
Tae Ho Lim	https://orcid.org/0000-0003-1045-413X
Hyunggoo Kang	https://orcid.org/0000-0002-9522-2532
Jaehoon Oh	https://orcid.org/0000-0001-8055-1467
Byuk Sung Ko	https://orcid.org/0000-0002-4212-2255
Juncheol Lee	https://orcid.org/0000-0003-3058-4759

AUTHOR CONTRIBUTIONS

Conceptualization: KHY, YC. Methodology: KHY, YC. Formal analysis: KHY, YC. Data curation: JK. Funding acquisition: KHY, YC. Writing - original draft: JK, KHY. Writing - review & editing: KHY, YC, THL, HK, JO, BSK, JL. All authors read and agreed to the published version of the manuscript.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4266/acc.005075.

REFERENCES

1. Henson T, Rawanduzy C, Salazar M, Sebastian A, Weber H, Al-Mufti F, et al. Outcome and prognostication after cardiac arrest. Ann N Y Acad Sci 2022;1508:23-34.
2. Sekhon MS, Ainslie PN, Griesdale DE. Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model. Crit Care 2017;21:90.
3. Jeong D, Shin SD, Shin TG, Lee GT, Park JE, Hwang SY, et al. Initial arterial pH predicts survival of out-of-hospital cardiac arrest in South Korea. Acute Crit Care 2025;40:444-51.
4. Oh J, Cha KC, Lee JH, Park S, Kim DH, Lee BK, et al. Erratum to "2020 Korean Guidelines for Cardiopulmonary Resuscitation. Part 4. Adult advanced life support". Clin Exp Emerg Med 2022;9:162-3.
5. Nolan JP, Sandroni C, Böttiger BW, Cariou A, Cronberg T, Friberg H, et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. Intensive Care Med 2021;47:369-421.
6. Panchal AR, Bartos JA, Cabañas JG, Donnino MW, Drennan IR, Hirsch KG, et al. Part 3: adult basic and advanced life support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2020;142:S366-468.
7. Ciaccio C, Coletta A, Coletta M. Role of hemoglobin structural-functional relationships in oxygen transport. Mol Aspects Med 2022;84:101022.
8. Hoiland RL, MacLeod DB, Stacey BS, Caldwell HG, Howe CA, Nowak-Flück D, et al. Hemoglobin and cerebral hypoxic vasodilation in humans: evidence for nitric oxide-dependent and S-nitrosothiol mediated signal transduction. J Cereb Blood Flow Metab 2023;43:1519-31.
9. Lelubre C, Bouzat P, Crippa IA, Taccone FS. Anemia management after acute brain injury. Crit Care 2016;20:152.
10. Albaeni A, Eid SM, Akinyele B, Kurup LN, Vaidya D, Chandra-Strobos N, et al. The association between post resuscitation hemoglobin level and survival with good neurological outcome following out of hospital cardiac arrest. Resuscitation 2016;99:7-

12.
11. Ameloot K, Genbrugge C, Meex I, Janssens S, Boer W, Mullens W, et al. Low hemoglobin levels are associated with lower cerebral saturations and poor outcome after cardiac arrest. Resuscitation 2015;96:280-6.
12. SOS-KANTO study group. Relationship between the hemoglobin level at hospital arrival and post-cardiac arrest neurologic outcome. Am J Emerg Med 2012;30:770-4.
13. Iiya M, Shimizu M, Takahashi K, Fujii H, Suzuki M, Yamawake N, et al. Combination of hemoglobin and low-flow duration can predict neurological outcome in the initial phase of out-of-hospital cardiac arrest. J Crit Care 2018;47:269-73.
14. Wormsbecker A, Sekhon MS, Griesdale DE, Wiskar K, Rush B. The association between anemia and neurological outcome in hypoxic ischemic brain injury after cardiac arrest. Resuscitation 2017;112:11-6.
15. Zama Cavicchi F, Iesu E, Franchi F, Nobile L, Annoni F, Vincent JL, et al. Low hemoglobin and venous saturation levels are associated with poor neurological outcomes after cardiac arrest. Resuscitation 2020;153:202-8.
16. Kim JY, Hwang SO, Shin SD, Yang HJ, Chung SP, Lee SW, et al. Korean Cardiac Arrest Research Consortium (KoCARC): rationale, development, and implementation. Clin Exp Emerg Med 2018;5:165-76.
17. Hou H, Pang L, Zhao L, Liu Z, Xing JH. Hemoglobin as a prognostic marker for neurological outcomes in post-cardiac arrest patients: a meta-analysis. Sci Rep 2023;13:18531.
18. McLaren AT, Mazer CD, Zhang H, Liu E, Mok L, Hare GM, et al. A potential role for inducible nitric oxide synthase in the cerebral response to acute hemodilution. Can J Anaesth 2009;56:502-9.
19. Ham PB, Raju R. Mitochondrial function in hypoxic ischemic injury and influence of aging. Prog Neurobiol 2017;157:92-116.
20. Hare GM, Tsui AK, McLaren AT, Ragoonanan TE, Yu J, Mazer CD, et al. Anemia and cerebral outcomes: many questions, fewer answers. Anesth Analg 2008;107:1356-70.
21. Hou Z, Brenner JS. Developing targeted antioxidant nanomedicines for ischemic penumbra: novel strategies in treating brain ischemia-reperfusion injury. Redox Biol 2024;73:103185.
22. Baron JC. Protecting the ischaemic penumbra as an adjunct to thrombectomy for acute stroke. Nat Rev Neurol 2018;14:325-37.
23. Todd MM, Wu B, Maktabi M, Hindman BJ, Warner DS. Cerebral blood flow and oxygen delivery during hypoxemia and hemodilution: role of arterial oxygen content. Am J Physiol 1994;267:H2025-31.
24. Vlaar AP, Oczkowski S, de Bruin S, Wijnberge M, Antonelli M, Aubron C, et al. Transfusion strategies in non-bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine. Intensive Care Med 2020;46:673-96.
25. Kim TS, Cho Y, Choi HJ, Park J, Kim W, Ahn C, et al. Red blood cell transfusion for critically ill patients admitted through the emergency department in South Korea. Acute Crit Care 2024;39:517-25.
26. Grand J, Kjaergaard J, Bro-Jeppesen J, Wanscher M, Nielsen N, Lindholm MG, et al. Cardiac output, heart rate and stroke volume during targeted temperature management after out-of-hospital cardiac arrest: association with mortality and cause of death. Resuscitation 2019;142:136-43.
27. Sandroni C, Cronberg T, Sekhon M. Brain injury after cardiac arrest: pathophysiology, treatment, and prognosis. Intensive Care Med 2021;47:1393-414.