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Association between early red blood cell transfusion after return of spontaneous circulation and clinical outcomes in cardiac arrest patients

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Red blood cell (RBC) transfusion is frequently administered to patients after cardiac arrest; however, its association with patient outcomes has not been well established. This study investigated the association between early RBC transfusion after the return of spontaneous circulation (ROSC) and patient outcomes in adults with cardiac arrest. We analyzed data from 586 adult patients who achieved ROSC at two university-affiliated hospitals in Korea between August 2014 and December 2023. Early transfusion was defined as RBC transfusion administered within 24 h after ROSC. Overlap propensity score weighting was used to adjust for confounding, and weighted analysis was performed to assess associations between early transfusion and patient outcomes. Within 24 h after ROSC, 79 patients (13.5%) received RBC transfusions. Early RBC transfusion was not significantly associated with 30-day mortality (adjusted hazard ratio [aHR] 0.97, 95% confidence interval [CI] 0.65–1.47), 90-day mortality (aHR 0.95, 95% CI 0.64–1.42), in-hospital mortality (adjusted odds ratio [aOR] 0.99, 95% CI 0.91–1.07), or neurologic outcome (aOR 0.97, 95% CI 0.92–1.03). Consistent findings were observed when early transfusion was defined as occurring within 48 or 72 h after ROSC. The number of RBC units transfused was also not associated with patient outcomes. Early RBC transfusion after ROSC was not associated with survival or neurologic outcomes in patients with cardiac arrest.

Keywords Cardiac arrest, Return of spontaneous circulation, RBC transfusion, Survival, Neurologic outcome

Cardiac arrest is a critical medical emergency associated with high morbidity and mortality[1–4]. Despite advances in resuscitation and post-arrest care, clinical outcomes remain poor[5,6]. Identifying prognostic factors and optimizing therapeutic strategies during the post-resuscitation period are therefore essential to improving patient outcomes. Previous studies have evaluated various interventions administered during and after cardiac arrest, highlighting their potential influence on recovery[7]. Consequently, numerous strategies have been implemented, contributing to advances in resuscitation and post-arrest care[8–13].

Red blood cell (RBC) transfusion is a common intervention in patients after cardiac arrest, particularly during the acute post-resuscitation phase[14–16]. While transfusion can be lifesaving, it is associated with potential adverse reactions[17]. Moreover, accumulating evidence suggests that transfusion may be associated with worse clinical outcomes[18–20], leading to the adoption of more restrictive transfusion strategies in many clinical settings[21].

However, the role of transfusion in patients who have achieved return of spontaneous circulation (ROSC) after cardiac arrest remains poorly defined. In particular, data evaluating the association between transfusion administered during the early post–resuscitation period and subsequent clinical outcomes are limited. Clarifying the clinical associations of transfusion during this phase may help address this uncertainty.

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In this study, we investigated the association between early RBC transfusion after ROSC and clinical outcomes in patients with cardiac arrest.

Methods

Study design and participants

This retrospective observational study was conducted at two university-affiliated hospitals (Severance hospital and Gangnam Severance hospital) in Seoul, Korea. We reviewed the medical records of patients who underwent resuscitation in the emergency departments after cardiac arrest between August 2014 and December 2023. Patients who achieved ROSC and survived for at least 24 h were eligible for inclusion.

Collected data included age, sex, diagnosis, resuscitation characteristics, cause of arrest, presence of bleeding, comorbidities, cerebral performance category (CPC) at discharge, transfusion details, and initial laboratory values (hemoglobin level and arterial pH) obtained after ROSC. Bleeding was defined as overt non-traumatic bleeding documented in the medical record, including gastrointestinal, airway, or other internal bleeding.

Patients were excluded if they were younger than 18 years, experienced cardiac arrest due to trauma, underwent surgery within 24 h of ROSC, or had incomplete data on variables included in the primary analysis. In addition, patients with a history of RBC transfusion within 1 year prior to ROSC were excluded to minimize potential residual effects of prior transfusion.

This study was reviewed and approved by the Institutional Review Board of the Yonsei University Health System (4-2024-0333) and was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived owing to the retrospective nature of the study and the use of de-identified data.

Outcomes

The primary outcomes were 30- and 90-day mortality, in-hospital mortality, and favorable neurologic outcome. A favorable neurologic outcome was defined as a CPC score of 1 or 2 at hospital discharge.

Criteria for red blood cell transfusion

In both participating institutions, restrictive transfusion thresholds were generally followed in accordance with current guidelines, with minor institutional modifications. A hemoglobin level of 7–8 g/dL was used as the standard transfusion threshold. For patients with underlying cardiovascular or cerebrovascular disease, a higher threshold of 10 g/dL was applied. In cases of major bleeding or when urgent transfusion was deemed necessary at the discretion of the attending physician, RBC transfusion was administered regardless of the hemoglobin level.

Statistical analysis

Categorical variables are presented as counts and percentages, and continuous variables are presented as means and standard deviations. Continuous variables were compared between groups using Student's t test or Welch's t test, as appropriate. The association between initial hemoglobin level after ROSC and clinical outcomes was assessed using unweighted Cox proportional hazards models and logistic regression analyses.

To address confounding inherent to this non-randomized retrospective cohort, overlap propensity score weighting was applied. Propensity scores for receiving RBC transfusion within 24 h after ROSC were estimated using multivariable logistic regression, incorporating the following variables: age, sex, location of arrest (in-hospital or out-of-hospital), initial cardiac rhythm (shockable or non-shockable), duration of cardiopulmonary resuscitation (CPR, minutes), use of therapeutic hypothermia, presence of bleeding, study site, history of hypertension, history of congestive heart failure, history of coronary heart disease, history of chronic kidney disease, history of malignancies, cardiac cause of arrest, hemoglobin level and arterial pH. CPR durations exceeding 40 min were truncated at 40 min.

Covariate balance before and after weighting was assessed using standardized mean differences, with values < 0.1 indicating adequate balance. After weighting, Cox proportional hazards models were used to estimate the adjusted hazard ratios (aHRs) and corresponding 95% confidence intervals (CIs) for 30- and 90-day mortality. Weighted logistic regression models were used to estimate adjusted odds ratios (aORs) and corresponding 95% CIs for in-hospital mortality and favorable neurologic outcome.

All statistical analyses were performed using R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria). A p-value of < 0.05 was considered statistically significant.

Sensitivity analyses

Sensitivity analyses were conducted to evaluate the robustness and reliability of the primary findings. Four additional analyses were performed. In analysis 1, the association between RBC transfusion within 48 h after ROSC and patient outcomes was assessed. In analysis 2, the association between RBC transfusion within 72 h after ROSC and patient outcomes was assessed. In analysis 3, the lowest hemoglobin level within 24 h after ROSC was used for propensity score calculation instead of the initial hemoglobin level after ROSC. In analysis 4, propensity score matching was performed using a 1:2 matching ratio with a caliper width of 0.2. Variables that remained imbalanced after matching (standardized mean differences ≥ 0.1) were additionally adjusted for in the final models.

Results

Patient characteristics

During the study period, 863 patients who achieved ROSC in the emergency department after arrest and survived at least 24 h were identified. Of these, 277 patients who did not meet the criteria for inclusion were

Characteristics	Before weighting			After weighting		
	No transfusion (n = 507)	RBC transfusion (n = 79)	SMD	No transfusion (n = 157.4)	RBC transfusion (n = 59.5)	SMD
Age, y	65.1 (15.6)	65.9 (15.5)	0.055	66.4 (15.4)	66.4 (14.5)	< 0.001
Female sex %	34.7	39.2	0.045	36.9	36.9	< 0.001
In-hospital arrest %	38.9	41.8	0.029	34.1	34.1	< 0.001
Initial rhythm, shockable %	22.9	11.4	0.115	14.3	14.3	< 0.001
Duration of CPR, min	9.0 (9.1)	11.7 (9.4)	0.281	10.7 (10.3)	10.7 (9.0)	< 0.001
Targeted temperature management %	39.1	39.2	0.002	44.1	44.1	< 0.001
Cause of arrest, cardiac %	35.3	29.1	0.062	33.6	33.6	< 0.001
Presence of bleeding, %	9.1	19.0	0.099	9.8	9.8	< 0.001
Study site 2, %	30.6	37.8	0.074	39.7	39.7	< 0.001
Hypertension	49.5	45.6	0.039	42.7	42.7	< 0.001
Congestive heart failure	7.9	11.4	0.035	9.7	9.7	< 0.001
Coronary heart disease	13.2	15.2	0.020	14.7	14.7	< 0.001
Chronic kidney disease	16.2	27.9	0.117	30.2	30.2	< 0.001
Malignancies	16.4	25.3	0.090	22.1	22.1	< 0.001
Hemoglobin, g/dL	12.3 (2.4)	8.5 (3.0)	1.631	9.9 (2.0)	9.9 (2.6)	< 0.001
< 7 g/dL %	0.3	30.4	0.299	2.8	11.1	0.084
Arterial pH	7.10 (0.20)	7.06 (0.20)	0.211	7.07 (0.19)	7.07 (0.21)	< 0.001

Table 1. Baseline patient characteristics before and after propensity score overlap weighting. RBC, red blood cell; SMD, standardized mean difference; CPR, cardiopulmonary resuscitation.

	Unadjusted		Adjusted	
	HR/OR (95% CI)	*P*	HR/OR (95% CI)	*P*
30-day mortality	1.44 (1.04–2.01)	0.030	0.97 (0.65–1.47)	0.898
90-day mortality	1.44 (1.05–1.98)	0.023	0.95 (0.64–1.42)	0.813
In-hospital mortality	1.15 (1.03–1.30)	0.018	0.99 (0.91–1.07)	0.720
Favorable neurologic outcome	0.88 (0.79–0.97)	0.012	0.97 (0.92–1.03)	0.351

Table 2. The association of RBC transfusion within 24 h after ROSC with patient outcomes. HR, hazard ratio; OR, odds ratio; CI, confidence interval.

excluded: age younger than 18 years (n = 51), traumatic cardiac arrest (n = 91), surgery within 24 h after ROSC (n = 16), a history of RBC transfusion within 1 year (n = 96), and missing data (n = 23). Ultimately, 586 patients were included in the final analysis.

Baseline characteristics stratified by RBC transfusion within 24 h after ROSC are summarized in Table 1. Among the included patients, 79 (13.5%) received an RBC transfusion within 24 h after ROSC. The median time to initial RBC transfusion was 7.0 h (interquartile range 1.6–15.7 h). Before weighting, several baseline characteristics differed between the non-transfusion group and the transfusion group. Compared with the transfusion group, patients in the non-transfusion group had a higher proportion of initial shockable rhythm (22.9% vs 11.4%), a shorter duration of CPR (9.0 ± 9.1 min vs 11.7 ± 9.4 min), and a lower prevalence of chronic kidney disease (16.2% vs 27.9%). In addition, the non-transfusion group had higher initial hemoglobin levels after ROSC (12.3 ± 2.4 g/dL vs 8.5 ± 3.0 g/dL) and higher arterial pH values (7.10 ± 0.20 vs 7.06 ± 0.20). After overlap propensity score weighting, all baseline variables were well-balanced between the non-transfusion and the transfusion group, with standardized mean differences < 0.1.

Transfusion and patient outcome

Previous studies have shown that hemoglobin levels are associated with outcomes after ROSC[22–25]. To examine whether hemoglobin levels were associated with patient outcomes in our patient cohort, we performed analyses and found that higher hemoglobin levels were significantly associated with lower in-hospital mortality and higher odds of favorable neurologic outcome (Supplementary Table 1). Although statistical significance was not observed, 30- and 90-day mortality showed similar trends.

The association between RBC transfusion within 24 h after ROSC and patient outcomes was analyzed, and the results are summarized in Table 2. In the unadjusted analyses, RBC transfusion was associated with higher 30- and 90-day mortality, higher in-hospital mortality, and lower odds of favorable neurologic outcomes. However, after adjustment using overlap propensity score weighting, RBC transfusion was not significantly associated with mortality (30-day mortality; aHR 0.97, 95% CI 0.65–1.47, 90-day mortality; aHR 0.95, 95% CI 0.64–1.42, In-hospital mortality; aOR 0.99, 95% CI 0.91–1.07) and favorable neurologic outcome (aOR 0.97,

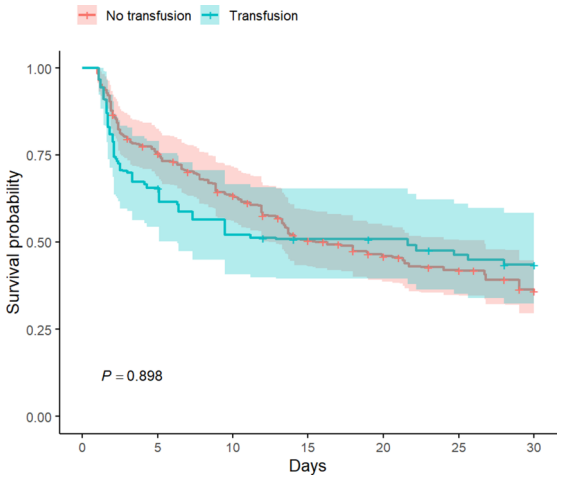

Fig. 1. Weighted Kaplan–Meier curve for 30-day mortality. The *P* value was derived from a weighted Cox proportional hazards model. Shaded areas indicate 95% confidence intervals.

	Analysis 1		Analysis 2		Analysis 3		Analysis 4	
	aHR/aOR (95% CI)	*P*	aHR/aOR (95% CI)	*P*	aHR/aOR (95% CI)	*P*	aHR/aOR (95% CI)	*P*
30-day mortality	0.79 (0.51–1.23)	0.301	0.66 (0.42–1.05)	0.079	0.88 (0.57–1.36)	0.579	1.00 (0.62–1.62)	0.997
90-day mortality	0.77 (0.51–1.18)	0.230	0.69 (0.45–1.04)	0.073	0.91 (0.60–1.37)	0.639	0.98 (0.61–1.56)	0.930
In-hospital mortality	0.91 (0.84–1.00)	0.048	0.93 (0.86–1.02)	0.124	0.98 (0.90–1.06)	0.532	1.04 (0.88–1.23)	0.651
Favorable neurologic outcome	1.05 (0.98–1.12)	0.138	1.04 (0.97–1.12)	0.265	0.97 (0.92–1.03)	0.338	0.97 (0.87–1.09)	0.635

Table 3. Sensitivity analyses. aHR, adjusted hazard ratio; aOR, adjusted odds ratio; CI, confidence interval.

95% CI 0.92–1.03). Similarly, the number of RBC units transfused within 24 h after ROSC was not significantly associated with patient outcomes (Supplementary Table 2). Weighted Kaplan–Meier curves also demonstrated no significant difference in 30-day mortality between the non-transfusion and the transfusion groups (Fig. 1).

There was no significant difference in length of stay according to RBC transfusion status within 24 h after ROSC. The number of RBC units transfused during the period beyond 24 h up to 30 days after ROSC was significantly greater in the transfusion group (Supplementary Table 3).

Sensitivity analyses

Sensitivity analyses were conducted to assess the robustness of the primary findings (Table 3). Overall, the associations between transfusion and patient outcomes remained largely consistent across analyses. When early transfusion was defined as occurring within 48 h after ROSC, a marginal association with in-hospital mortality was observed (adjusted odds ratio 0.91, 95% confidence interval 0.84–1.00; p = 0.048), whereas other outcomes remained non-significant. The findings based on transfusion within 72 h after ROSC were consistent with the primary analysis.

Discussion

This study investigated the association between early RBC transfusion after ROSC and clinical outcomes in patients with cardiac arrest. We found that early RBC transfusion was not associated with mortality or neurologic outcomes.

Previous studies have reported an association between hemoglobin levels and neurologic outcomes in patients who achieved ROSC after cardiac arrest, showing that higher hemoglobin levels were associated with more favorable neurologic outcomes[14,22–24]. Consistent with these findings, higher hemoglobin levels were also associated with favorable neurologic outcomes in our cohort. However, our results indicate that this association does not translate into improved neurologic outcomes with early RBC transfusion after ROSC. Although several studies have examined the relationship between hemoglobin levels and neurologic outcomes after cardiac arrest[22–24], few have specifically evaluated the association between RBC transfusion and neurologic outcomes in this population. In the present study, early RBC transfusion was not associated with neurologic outcomes, suggesting that while baseline hemoglobin levels may be associated with neurologic recovery, rapid correction of hemoglobin levels through early transfusion after ROSC may not provide additional benefit.

The relationship between hemoglobin levels and patient survival after cardiac arrest remains inconclusive. One study reported that low pre-arrest hemoglobin levels (< 10 g/dL) were not associated with survival to hospital discharge or ROSC[25]. Another study examining anemia burden after out-of-hospital cardiac arrest found that initial hemoglobin levels were not associated with survival, whereas cumulative anemia burden within 72 h after arrest was associated with 30-day mortality[26]. Notably, these studies did not directly address the association between RBC transfusion and survival. A recent study investigated the association of RBC transfusion with clinical outcomes, but the analysis was limited to those with traumatic out-of-hospital cardiac arrest[27].

In our patient cohort, higher hemoglobin levels were associated with a lower risk of mortality. However, the present study also found that early RBC transfusion after ROSC was not associated with a lower risk of mortality. Although the association between RBC transfusion and survival after cardiac arrest has not been well established, several studies in critically ill patients have suggested that transfusion may be associated with adverse survival-related outcomes[18,28,29]. While patients with cardiac arrest are also considered critically ill, their physiological responses to RBC transfusion may differ from those of other critically ill patients. Taken together, these findings suggest that in patients with cardiac arrest, the adverse effects associated with RBC transfusion observed in other critically ill settings may not be directly applicable. Although the underlying mechanisms remain unclear, RBC transfusion could plausibly influence recovery by supporting oxygen delivery during ischemia and reperfusion following cardiac arrest and CPR.

The present study does not allow determination of a specific hemoglobin threshold for transfusion. Although no studies to date have specifically addressed which transfusion strategy should be adopted in patients after cardiac arrest, several randomized controlled trials evaluating transfusion strategies in neurologically vulnerable populations have recently been reported[30–32]. Findings from a study conducted in patients with acute brain injury have suggested that a liberal transfusion strategy may be associated with more favorable neurological outcomes[30], whereas randomized trials in patients with traumatic brain injury[31] and those with subarachnoid hemorrhage[32] have reported no significant differences in neurological outcomes between liberal and restrictive transfusion strategies. Taken together, the current evidence remains insufficient to determine which transfusion strategy is beneficial even in other neurologically vulnerable populations. Similarly, in patients who achieved ROSC after cardiac arrest, further studies are needed to establish the optimal hemoglobin threshold for guiding RBC transfusion decisions.

This study has several limitations. First, although the analysis included 586 patients—providing sufficient data to examine associations related to transfusion—the relatively small sample size limited certain analyses. To mitigate this limitation, we collected data over an extended period and combined data from two institutions to increase the sample size and reduce potential biases. Nevertheless, larger studies with greater patient numbers are needed to further validate our findings. In addition, subgroup analyses according to the patient characteristics could not be conducted due to limited sample size. Therefore, potentially vulnerable subgroups that may be more strongly affected by transfusion may not have been fully captured in the present study. Second, patients in our patient cohort frequently received transfusions of other blood products, including platelets and fresh frozen plasma, in addition to RBCs. Because of the complexity of transfusion practices, we were unable to account for the independent effects of these other blood products in the present analysis. Third, although we adjusted for several clinically relevant variables using overlap propensity score weighting, the possibility of residual confounding due to unmeasured factors cannot be ruled out. Fourth, patients with a prior history of transfusion were excluded, which may limit the generalizability of our findings to individuals with chronic transfusion requirements or recent transfusion exposure. Fifth, the volume of fluid administered after ROSC was not accounted for. Because large-volume fluid resuscitation is commonly performed in patients after cardiac arrest and may lower hemoglobin levels through hemodilution, it may also influence transfusion decisions. Therefore, the potential impact of hemodilution-related factors on our results cannot be excluded.

Conclusion

Early RBC transfusion was not clearly associated with an increased risk of adverse outcomes among patients who achieved ROSC after cardiac arrest. However, given the observational design and potential for residual confounding, these findings should be interpreted with caution. Our results do not support the routine use of early RBC transfusion after ROSC, and transfusion decisions should remain guided by established clinical indications and individualized clinical judgment.

Data availability

The de-identified patient data is available from the corresponding authors, on reasonable request.

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Author contributions

CHL—Data curation, Investigation, Writing—original draft. JHC—Data curation, Writing—original draft. SSK—Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Visualization, Writing—original draft. JM—Conceptualization, Data curation, Methodology, Resources, Writing—review & editing. SK—Conceptualization, Supervision, Writing—review & editing. IP—Conceptualization, Supervision, Writing—review & editing. HSC—Conceptualization, Supervision, Writing—review & editing.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study was reviewed and approved by the Institutional Review Board of the Yonsei University Health System (4-2024-0333) and was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived owing to the retrospective nature of the study and the use of de-identified data.

Additional information

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