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ORIGINAL ARTICLE
Coronary Revascularization

Perioperative Nadir Hemoglobin Concentration and Outcome in Off-Pump Coronary Artery Bypass Surgery

— A Retrospective Review —

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Background: Emerging evidence advocates the use of restrictive transfusion strategies at hemoglobin (Hb) levels of approximately 7–8 g/dL in cardiac surgeries using cardiopulmonary bypass. Yet, it is unclear whether the same thresholds can be applied to off-pump coronary bypass (OPCAB) that accompanies cardiac displacement and warm regional ischemia-reperfusion injury without the aid of a bypass machine. The aim of this study is to investigate the relationship between perioperative nadir Hb level and outcome following OPCAB.

Methods and Results: Medical records of 1,360 patients were reviewed. Hb levels were serially assessed during and after surgery. The incidence of composite endpoints was 35%, which included myocardial infarction, stroke, acute kidney injury, sternal infection, reoperation, prolonged mechanical ventilation, and in-hospital mortality. The nadir Hb level was significantly lower in the morbidity group than in the non-morbidity group (8.1 [7.4–9.1] vs. 8.8 [7.9–9.8] g/dL, P<0.001). Multivariable logistic regression analysis revealed nadir Hb as an independent risk factor of adverse outcome (odds ratio: 0.878, 95% confidence intervals: 0.776–0.994, P=0.04), whereas preoperative anemia and perioperative transfusion were not. The critical value of Hb for predicting detrimental outcome was 8.05 g/dL.

Conclusions: A significant association is found between perioperative nadir Hb and adverse outcome after OPCAB. Although preoperative anemia was not associated with poor prognosis *per se*, it was the only modifiable risk factor that was closely linked to nadir Hb.

Key Words: Anemia; Blood transfusion; Coronary artery bypass; Off-pump

Based on emerging evidence, recent guidelines advocate the use of restrictive transfusion strategies at hemoglobin (Hb) concentrations of approximately 7 g/dL.[1,2] Yet, there seems to be an uncertainty regarding such a Hb threshold ensuring tissue oxygenation, as it seems to be patient- and surgery-specific.[1,3] This is of particular relevance to patients with coronary artery disease (CAD), who would be even more vulnerable to impeded oxygen-carrying capacity by anemia.[4] Indeed, concerns have been raised about the use of restrictive transfusion strategies resulting in adverse outcomes in patients with cardiovascular disease undergoing non-cardiac surgery.[5] Moreover, transfusion proved to be harmful only at Hb concentrations of >10 g/dL, whereas it seemed to be beneficial in terms of mortality at levels <8 g/dL in CAD patients undergoing percutaneous intervention (PCI).[6]

In contrast, a large randomized controlled trial has recently shown non-inferiority of a restrictive strategy employing a Hb threshold of 7.5 g/dL to a liberal strategy in cardiac surgeries using cardiopulmonary bypass (CPB) consisting of >50% of coronary artery bypass graft (CABG) cases.[7] Notably, in studies involving cardiac surgeries, the lowest Hb concentration mostly appears during CPB by marked hemodilution, which may be beneficial for microcirculation in the presence of hypothermia and non-pulsatile perfusion.[8]

Certainly, these evidences cannot be applied to off-pump CABG (OPCAB) as it faces unique situations compared to on-pump CABG. Despite evading CPB, OPCAB is still associated with significant perioperative blood loss and transfusion requirement.[9] Moreover, it is performed at normothermia, whereas the cardiac output may be marginal

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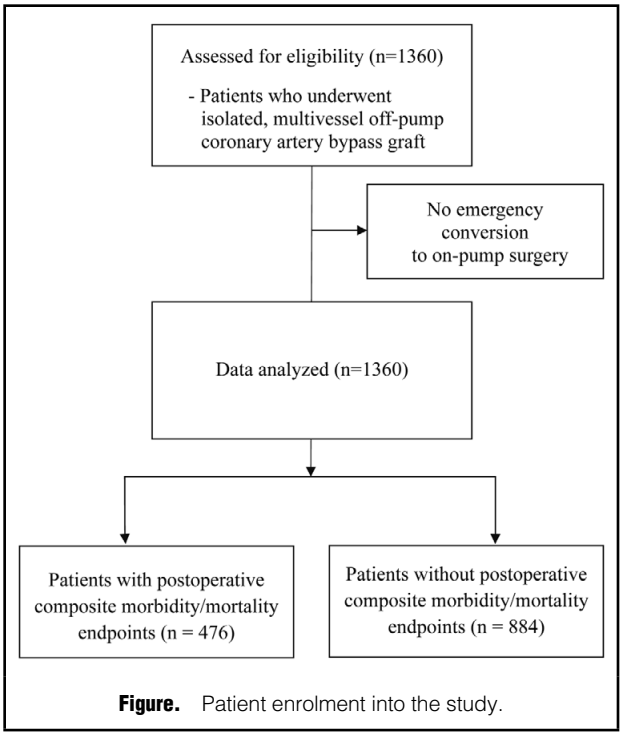

Figure. Patient enrolment into the study.

during mechanical heart displacement, which would seriously compromise tissue oxygenation in the presence of anemia.[10] In that context, a threshold Hb concentration that would be noxious in OPCAB might be different from those of PCI or on-pump CABG; no comprehensive evidence is available to support this.

The primary purpose of this retrospective study was to examine the association between the degree of perioperative anemia represented by the nadir Hb concentration and short-term prognosis in patients who underwent isolated, multivessel OPCAB.

Methods

Patients

This study was a retrospective review from a cohort of patients who underwent isolated, multivessel OPCAB from December 2005 to December 2015. After obtaining approval from the institutional review board (no. 4-2018-0040) of the Yonsei University Health System (Seoul, Republic of Korea) with waived obtainment of consent, the electronic medical records of 1,360 patients were reviewed (**Figure**).

Data Collection Including Perioperative Hb Levels

Perioperative Hb concentrations were serially assessed at the following time points: immediately before surgery; during grafting; at sternum closure; immediately after surgery; and 24 h after surgery. The lowest Hb level was assessed during OPCAB and 24 h after OPCAB.

The assessed preoperative data were as follows: demographic data; the presence of co-existing disease including left main CAD, hypertension, diabetes mellitus, chronic obstructive lung disease, congestive heart failure, chronic renal failure, prior acute coronary syndrome (including unstable angina and/or myocardial infarction [MI] within 1 month); prior cerebrovascular accident or cardiac surgery; EuroSCORE; left ventricular ejection fraction; preoperative use of intra-aortic balloon pump; emergency surgery; and cardiovascular medications. Mean blood pressure and cardiac index were collected prior to anesthesia and at the time of coronary artery anastomosis with the greatest hemodynamic instability.

The assessed perioperative data were the amount of postoperative blood loss (chest tube drainage for 24 h), and transfusion requirements of packed erythrocytes (pRBC), fresh frozen plasma (FFP), and platelets during surgery and 24 h after surgery. The lengths of hospital and intensive care unit (ICU) days were also recorded. The postoperative composite morbidity/mortality endpoints included MI, stroke, acute kidney injury (AKI), sternal infection, reoperation, prolonged mechanical ventilation, and in-hospital mortality. MI was defined as the elevations of creatine kinase-MB level ≥50 ng/mL (10-fold more than the upper reference limit) during the first 48 h after surgery. In addition, either (1) new pathological Q waves or new left bundle branch block; or (2) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality was considered as diagnostic of a postoperative MI. Postoperative AKI was defined as an increase in serum creatinine ≥0.3 mg/dL from baseline, or to 50% from baseline, or an oliguria $<0.5\,mL\cdot kg^{-1}\cdot h^{-1}$ for ≥6 h, within postoperative 48 h. Other complications were assessed according to Society of Thoracic Surgeons' morbidity definition (https://www.sts.org/quality-safety/performance-measures).

Endpoints

The primary endpoint for this study was to examine the association between perioperative degree of acute anemia represented by the nadir Hb and occurrence of the composite of morbidity/mortality endpoints.

The secondary endpoint was to identify risk factors for the nadir Hb to further depict potentially modifiable preoperative risk factors.

Clinical Management

Institutional standardized anesthetic and surgical management was provided to all patients. In brief, standard monitoring included a Swan-Ganz catheter and transesophageal echocardiography. Anesthesia was maintained with sevoflurane and sufentanil.

Intraoperatively, patients received balanced crystalloid at approximately $6\,mL\cdot kg^{-1}\cdot h^{-1}$, and balanced synthetic colloid (Volulyte; Fresenius Kabi, Bad Homburg, Germany) was infused to replace estimated blood loss at a maximum dose of 1,000 mL. Intraoperative blood loss was estimated by the amount of collected blood through a cell salvage device. Target mean arterial pressure (MAP) was >70 mmHg, which was achieved first by norepinephrine infusion (up to $0.3\,\mu g\cdot kg^{-1}\cdot min^{-1}$) with the addition of vasopressin (up to 4 IU/h) thereafter. Milrinone ($0.5\,\mu g\cdot kg^{-1}\cdot min^{-1}$) was infused when there was a persistent decrease in mixed venous oxygen saturation (<60% for >10 min) or newly developed mitral regurgitation (grade ≥3). Perioperative transfusion was conducted at Hb concentrations <8 g/dL at the discretion of the attending physician.

After surgery, all participants were managed in the ICU by using the institutional standardized protocols, which are as follows. When bleeding exceeded >200 mL/h for 2 consecutive hours after surgery, FFP and/or platelets were transfused, in case of international normalized ratio (INR) >1.3 and/or platelet count $<50\times10^3/\mu L$. Reoperation was

Table 1. Predictive Power of Chosen Variables for Postoperative Composite of Major Morbidity/Mortality Endpoints According to Logistic Regression Analyses

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Female	1.323 (1.042–1.68)	0.021	0.949 (0.72–1.25)	0.708
Age	1.051 (1.037–1.066)	<0.001	1.033 (1.017–1.049)	<0.001
Preoperative				
Anemia	2.453 (1.949–3.087)	<0.001	1.313 (0.985–1.75)	0.063
Congestive heart failure	2.041 (1.474–2.826)	<0.001	1.207 (0.833–1.75)	0.32
Diabetes	2.131 (1.699–2.673)	<0.001	1.599 (1.249–2.046)	<0.001
Hypertension	1.927 (1.491–2.492)	<0.001	1.442 (1.089–1.91)	0.011
Prior cerebrovascular accident	1.54 (1.102–2.153)	0.012	1.214 (0.844–1.747)	0.296
Chronic renal disease	4.072 (2.729–6.075)	<0.001	2.287 (1.476–3.543)	<0.001
Chronic obstructive lung disease	2.206 (1.182–4.119)	0.013	1.45 (0.74–2.842)	0.279
Prior cardiac surgery	0.617 (0.124–3.071)	0.558	0.449 (0.077–2.609)	0.373
Acute coronary syndrome	1.411 (1.128–1.765)	0.003	1.139 (0.889–1.46)	0.302
Preoperative IABP use	2.809 (0.789–10.002)	0.111	1.14 (0.285–4.577)	0.853
Emergency operation	4.109 (1.552–10.881)	0.004	3.497 (1.193–10.253)	0.023
LVEF	0.978 (0.97–0.986)	<0.001	0.985 (0.976–0.994)	0.001
Perioperative				
Transfusion	2.284 (1.819–2.869)	<0.001	1.299 (0.98–1.721)	0.068
Nadir hemoglobin	0.709 (0.647–0.777)	<0.001	0.878 (0.776–0.994)	0.04

CI, confidence interval; IABP, intraaortic balloon pump; LVEF, left ventricular ejection fraction; OR, odds ratio.

performed when postoperative bleeding exceeded 200 mL/h for ≥6 h or ≥400 mL for the first 1 h. Final decisions for transfusion and reoperation were made at the discretion of the attending anesthesiologist and cardiac surgeon in the ICU.

Statistical Analyses

SPSS 23.0 (SPSS Inc., Chicago, IL, USA) was used. Data are shown as mean±standard deviation, median (interquartile range, IQR), or number of patients (percentage). Normality was assessed with the Shapiro-Wilk test. Comparisons between patients with postoperative composite of morbidity/mortality endpoints and those without were analyzed by using an independent t-test, χ^2 test, Fisher's exact test, or Mann-Whitney U-test, as appropriate. In the case of serial changes in perioperative Hb concentration, the differences between groups were analyzed using linear mixed models with unstructured covariance matrix. Multivariable logistic regression analysis was used to detect independent risk factors of the composite of morbidity/mortality endpoints and of perioperative nadir Hb concentration. The known risk factors and variables with statistical significance from the intergroup comparisons were included in the multivariable logistic regression analysis, and it was confirmed that there was no multicollinearity among these independent variables. Odds ratios (OR) and associated 95% confidence intervals (CI) were calculated. The optimal cut-off values for the continuous variables were determined by receiver operating characteristic (ROC) analysis. In all analyses, P<0.05 was considered statistically significant, except for the Bonferroni-corrected P value in the post-hoc test for serial Hb value analysis.

Results

Among the assessed 1,360 patients, the composite of morbidity/mortality endpoints occurred in 476 (35%) patients (morbidity group). Preoperative comorbidities were more frequent in the morbidity group, except for the number of patients with left main coronary disease, preoperative intraaortic balloon pump, and prior cardiac surgery. The use of aspirin and clopidogrel and their durations of discontinuation before surgery were similar between the groups (**Supplementary Table 1**). There was no significant difference in mean blood pressure and cardiac index between the groups, not only before anesthesia but also during the coronary artery anastomosis (**Supplementary Table 1**).

Preoperative Hb level was significantly lower (12.4 [11.1–13.7] g/dL vs. 13.4 [12.3–14.4] g/dL, P<0.001) in patients with composite of morbidity/mortality endpoints than in those without. The percentage of patients with preoperative anemia (247 [52%] vs. 270 [31%], P<0.001) was significantly greater in the morbidity group than in the non-morbidity group. Overall, the decrease in Hb concentration occurred by 4.3 (3.3–5.2) g/dL, and the degree of maximum decrease in Hb concentration was similar between the groups. Serially measured mean Hb concentrations during the study period were all significantly lower in the morbidity group than in the non-morbidity group (P<0.001). The perioperative nadir Hb level was significantly lower in the morbidity group (8.1 [7.4–9.1] vs. 8.8 [7.9–9.8], P<0.001). Nadir Hb was observed during the intraoperative and postoperative periods in 40% and 60% of patients, respectively, in both groups. The percentage of patients requiring transfusion during the perioperative period was significantly greater in the morbidity group (256 [54%] vs. 301 [34%], P<0.001; **Supplementary Table 2**).

In the multivariable analysis, to identify risk factors regarding the composite of morbidity/mortality endpoints, nadir Hb remained as an independent risk factor of the composite of morbidity/mortality endpoints (OR: 0.878, 95% CI: 0.776–0.994, P=0.04) together with age, diabetes, hypertension, chronic renal disease, emergency operation,

Table 2. Preoperative and Intraoperative Data for Patients Divided by the Perioperative Nadir Hemoglobin

	Nadir hemoglobin ≤8 g/dL (n=483)	Nadir hemoglobin >8 g/dL (n=877)	P value
Female sex, %	233 (48)	185 (21)	<0.001
Age, years	67±8	63±9	<0.001
Body surface area	1.62 (1.51–1.72)	1.75 (1.65–1.87)	<0.001
Left main art. >50%	305 (63)	440 (50)	<0.001
Hypertension	361 (75)	582 (66)	0.001
Diabetes mellitus	254 (53)	361 (41)	<0.001
Chronic obstructive lung disease	15 (3)	26 (3)	0.884
Prior cerebrovascular accident	62 (13)	97 (11)	0.329
Congestive heart failure	84 (17)	84 (10)	<0.001
Chronic renal failure	81 (17)	36 (4)	<0.001
Acute coronary syndrome	227 (47)	403 (46)	0.711
Preoperative LVEF (IQR), %	58 (45–68)	59 (47–67)	0.445
EuroSCORE (IQR)	4 (3–5)	3 (2–4)	<0.001
NYHA functional classification			<0.001
I	75 (23)	206 (34)	
II	171 (53)	331 (54)	
III	64 (20)	71 (12)	
IV	13 (4)	4 (0.7)	
Preoperative IABP use, %	3 (0.6)	7 (0.8)	>0.999
Prior cardiac surgery, %	3 (0.6)	5 (0.6)	>0.999
Emergency operation, %	9 (2)	10 (1)	0.277
Preoperative medication			
β-blockers	234 (48)	460 (53)	0.157
Calcium channel blockers	175 (36)	283 (32)	0.139
Renin-angiotensin system blockers	213 (44)	363 (41)	0.333
Diuretics	101 (21)	118 (14)	<0.001
Statin	259 (54)	503 (57)	0.185
Prior heparin use	186 (39)	427 (49)	<0.001
Aspirin use	409 (85)	753 (86)	0.554
Aspirin pause days (IQR)	0 (0–2)	1 (0–2)	0.003
Clopidogrel use	348 (72)	607 (69)	0.274
Clopidogrel pause days (IQR)	1 (0–2)	1 (0–2)	0.008
Perioperative hemodynamic parameters			
Baseline			
Mean blood pressure, mmHg	94 (84–104)	91 (82–102)	0.014
Cardiac index, $L \cdot min^{-1} \cdot m^{-2}$	3 (2.5–3.6)	2.9 (2.4–3.4)	0.172
During coronary artery anastomosis			
Mean blood pressure, mmHg	74 (69–79)	75 (71–82)	<0.001
Cardiac index, $L \cdot min^{-1} \cdot m^{-2}$	1.9 (1.6–2.2)	1.9 (1.6–2.2)	0.153

Data are presented as mean±standard deviation (SD), median (interquartile range, IQR), or number of patients (%). IABP, intraaortic balloon pump; LVEF, left ventricular ejection fraction; NYHA, the New York Heart Association.

and preoperative left ventricular ejection fraction (**Table 1**).

The optimal cut-off value of nadir Hb for predicting detrimental outcome was 8.05 g/dL (area under the ROC [AUROC]: 0.627, 95% CI: 0.595–0.657, P<0.001). Using logistic regression analysis with a binary value divided by this cut-off value, nadir Hb of ≤8 g/dL showed an independent association with a 1.4-fold increased risk of composite of morbidity/mortality endpoints (OR: 1.446, 95% CI: 1.07–1.954, P=0.016). Comparing patients with a nadir Hb level <8 g/dL and those with a nadir Hb level >8 g/dL, there were significant differences in sex, age, body surface area, and the number of patients with preoperative comorbidities, including left main coronary disease, hypertension, diabetes mellitus, congestive heart disease, chronic renal failure, and anemia (**Table 2**). When comparing the prognosis of patients with perioperative nadir Hb ≤8 g/dL and those of patients with perioperative nadir Hb >8 g/dL, the ICU/hospital days and postoperative myocardial enzyme values also showed significant differences (**Table 3**).

In the multivariable analysis, to identify risk factors regarding the lower perioperative Hb ≤8 g/dL, preoperative anemia remained as an independent risk factor together with female sex, age, body surface area, chronic renal disease and left main disease (**Table 4**). The optimal cut-off value of preoperative Hb level for predicting nadir Hb ≤8 g/dL was 13.1 g/dL (AUROC: 0.82, 95% CI: 0.797–0.843, P<0.001).

Table 3. Postoperative Data According to Nadir Hemoglobin Concentration

	Perioperative nadir hemoglobin ≤8 g/dL (n=483, 36%)	Perioperative nadir hemoglobin >8 g/dL (n=877, 64%)	P value
Intensive care unit days (IQR)	3 (3–4)	3 (2–3)	<0.001
Hospital days, (IQR)	15 (12–20)	13 (11–15)	<0.001
Maximum postoperative CK-MB during 48 h after surgery (ng/mL, IQR)	7.5 (5.5–11.6)	6.8 (5.1–10.5)	0.002
Composite morbidity endpoint, %	232 (48)	244 (28)	<0.001
Postoperative myocardial infarction	13 (3)	16 (2)	0.289
Acute kidney injury	162 (34)	133 (15)	<0.001
Postoperative cerebrovascular accident	7 (1)	9 (1)	0.489
Deep sternal infection	39 (8)	63 (7)	0.551
Re-operation	13 (3)	23 (3)	0.94
Prolonged mechanical ventilation >24 h	64 (13)	66 (8)	0.001
In-hospital mortality	15 (3)	9 (1)	0.005

Data are presented as median (interquartile range, IQR), or number of patients (%). CK-MB, creatine kinase-myocardial band.

Table 4. Predictive Power of Chosen Variables for Lower Perioperative Hemoglobin Below 8 g/dL According to Logistic Regression Analyses

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Female	3.486 (2.739–4.437)	<0.001	2.348 (1.714–3.215)	<0.001
Age	1.06 (1.045–1.075)	<0.001	1.027 (1.009–1.045)	0.003
Body surface area	0.006 (0.003–0.013)	<0.001	0.034 (0.013–0.091)	<0.001
Preoperative				
Congestive heart failure	1.987 (1.435–2.752)	<0.001	1.451 (0.972–2.167)	0.069
Diabetes	1.585 (1.268–1.983)	<0.001	1.11 (0.836–1.473)	0.471
Hypertension	1.5 (1.17–1.923)	0.001	1.075 (0.785–1.472)	0.651
Chronic renal disease	4.707 (3.123–7.094)	<0.001	3.351 (2.049–5.48)	<0.001
Left main disease	1.702 (1.356–2.136)	<0.001	1.797 (1.343–2.404)	<0.001
Anemia	6.776 (5.296–8.67)	<0.001	6.301 (4.694–8.459)	<0.001

CI, confidence interval; OR, odds ratio.

Discussion

Although accruing evidence points in favor of restrictive transfusion strategies at Hb concentrations of approximately 7 g/dL, the effect of perioperative acute anemia still remains a critical issue in patients with cardiovascular diseases.[1] Acute anemia may especially be dangerous to patients with limited coronary reserve exposed to conditions of increased myocardial oxygen consumption.[11] Thus, the threshold Hb concentration causing adverse outcome was questioned to be higher in CAD patients.[3,12]

In observational studies involving CAD patients with acute coronary syndrome undergoing PCI, the threshold Hb concentration was found to be approximately 8 g/dL.[4,13,14] Likewise, a meta-analysis involving a similar subset of patients also depicted that transfusion was beneficial at Hb levels <8 g/dL, whereas it was harmful only when performed at Hb levels >10 g/dL.[6]

In cardiac surgical patients, observational studies showed somewhat permissive threshold Hb values linked to detrimental outcome than in the setting of PCI, approximately 7–8 g/dL.[15–17] In support of these findings, a recent large, randomized controlled trial with an additive analysis of 6-month follow-up data depicted that a Hb threshold of <7.5 g/dL was non-inferior to a more liberal threshold of <9.5 g/dL.[7,18] Of note, consensus gathered through previous studies highlighted the complexity underlying recommendations for a uniformly applicable transfusion trigger,[19] and tolerating nadir Hb concentration should be specified based on the characteristics of the studied population.[3,12,20] As yet, no comprehensive evidence exists in that regard in patients undergoing OPCAB.

Off-pump coronary bypass is essentially not intimidated by the risk of CPB-induced hemodilution and coagulopathy. Still, it is accompanied by a substantial amount of perioperative blood loss resulting in acute anemia and transfusion.[9] During OPCAB, the heart must generate sufficient cardiac output under normothermia even during the inevitable period of mechanical heart and coronary flow interruption, resulting in fragile oxygen consumption/supply balance.[10] These unique features of OPCAB are clearly distinct from the PCI or on-pump CABG settings. Therefore, we postulated that the nadir Hb concentration conveying poor postoperative outcome should be different in OPCAB patients when compared to patients undergoing PCI or on-pump CABG.

According to our results, the overall decrease in median Hb concentration during the perioperative period was by

4.3 g/dL, exposing the majority of patients to moderate-to-severe acute anemia (Hb <10 g/dL). Unlike cardiac surgery using CPB, in which the Hb concentration is the lowest during CPB, nadir Hb developed during the postoperative period in 60% of patients, showing a different course of perioperative acute anemia. In the present study, the nadir Hb concentration was significantly lower in the morbidity group and it remained as an independent risk factor for the composite of morbidity/mortality endpoints when adjusted for possible confounders with a critical cut-off value of 8.05 g/dL. Accordingly, we could also observe significantly longer lengths of ICU and hospital stay in patients with nadir Hb values ≤8 g/dL, which yielded an 1.4-fold increased risk of adverse outcome.

Preoperative anemia and perioperative transfusion are closely interlinked variables that have been shown to exert adverse influences on outcome.[11] However, most of the previous studies about cardiac surgery have not properly addressed the confounding effects of these variables on the perioperative nadir Hb, let alone that no evidence existed for OPCAB heretofore. In the current study, preoperative anemia and perioperative transfusion were both more frequent in the morbidity group than in the non-morbidity group. However, when accounting for those variables in the multivariable analysis, we could still observe the independent prognostic importance of perioperative nadir Hb, whereas the significance of preoperative anemia and perioperative transfusion disappeared. Thus, based on our results, it seems that the nadir Hb concentration conveys more adverse influence on outcome than preoperative anemia or perioperative transfusion. Moreover, we can also assume that transfusion of Hb <8 g/dL may be necessary to support oxygen-carrying capacity, as transfusion did not remain an independent risk factor of adverse outcome, whereas our transfusion practice guideline coincided with the critical cut-off value of our analysis. If it were to be otherwise, our analysis would have revealed a different critical cut-off value of Hb or transfusion as an independent risk factor. However, based on the retrospective nature of our analyses, we can only speculate so until these findings can be confirmed through a randomized controlled trial.

The threshold nadir Hb concentration of 8 g/dL, which was congruent to the results from PCI settings, was an unexpected value as we expected it to be somewhat higher considering the supposed risk of surgery-related factors in OPCAB. This seems to be associated with advances in surgical technique related to cardiac displacement and grafting, and also with the anesthetic management to optimize cardiac output while maintaining the oxygen supply/demand balance. When compared to on-pump CABG, it would be advisable not to apply restrictive transfusion strategies at Hb thresholds of approximately 7 g/dL in OPCAB patients until proven otherwise.

We could also confirm the prognostic importance of other well-known risk factors of detrimental outcome, such as advanced age, diabetes, hypertension, chronic renal disease, emergency operation, and low preoperative left ventricular ejection fraction, which are all non-modifiable risk factors. Thus, to further provide clinical significance, we have analyzed the risk factors of nadir Hb ≤8 g/dL that may prove to be modifiable before surgery. In that context, preoperative anemia was the strongest predictor indicating that optimization of preoperative Hb concentration could prevent nadir Hb to decrease below a critical level in patients undergoing OPCAB. Considering the avoidance of CPB and the relative consistency in the degree of decrease in the median Hb concentrations by 4.3 g/dL, the cut-off value of preoperative Hb concentration to predict nadir Hb ≤8 g/dL was 13 g/dL. Thus, the preoperative goal should be targeted to correct anemia according to its cause to reach a Hb level of >13 g/dL to potentially improve patients' outcome.

This study is inherently limited by its retrospective nature, although all analyzed data could be retrieved from the electronic medical recording system without any missing sets. The strengths of this study are as follows: it is the first study to address the perioperative changes in Hb levels and the association of nadir Hb with adverse outcome in a fairly large number of patients undergoing multivessel OPCAB; and it is the first of its kind to concomitantly address the confounding effects of preoperative anemia and perioperative transfusion to clarify the independent role of nadir Hb on adverse outcome.

In conclusion, we found a significant association between perioperative nadir Hb and adverse outcome in patients undergoing isolated, multivessel OPCAB with a critical cut-off value of 8 g/dL. Transfusion based on a target Hb level of 8 g/dL did not seem to be harmful. Although preoperative anemia was not association with poor prognosis, it was the only modifiable risk factor that was closely linked to nadir Hb, suggesting the importance of preoperative anemia correction whenever possible.

Sources of Funding

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Disclosures

The authors declare that they have no conflicts of interest.

IRB Information

This retrospective study was sanctioned by the Institutional Review Board (no. 4-2018-0040) of the Yonsei University Health System (Seoul, Republic of Korea) with waived obtainment of consent.

Data Availability

The deidentified participant data will be shared upon request. Please contact directly the corresponding author to request data sharing.

A. What data in particular will be shared: Individual participant data that underlie the results reported in this article, after deidentification.
B. What additional, related documents will be available: Study protocol, statistical analysis plan will be available.
C. When the data will become available and for how long: Beginning 3 months and ending 3 years following article publication.
D. By what access criteria the data will be shared (including with whom): Researchers who provide a methodologically sound proposal.
E. For what types of analyses, and by what mechanism the data will be available: For individual participant meta-analysis. Proposals should be directed to ylkwak@yuhs.ac.

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Supplementary Files

Please find supplementary file(s);
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