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Association of hemoglobin levels with clinical outcomes in acute coronary syndromes in Koreans

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Abstract

Anemia is a well-known risk factor for cardiovascular disease. However, there are limited data on whether anemia on admission is a long-term prognostic factor in acute coronary syndrome (ACS) patients undergoing percutaneous coronary intervention. We sought to evaluate the prevalence and prognostic consequences of anemia in patients with ACS treated with percutaneous coronary intervention in Korea. We retrospectively enrolled 1930 consecutive patients. Among the anemic population (hemoglobin [Hb] < 13 g/dL in men, and < 12 g/dL in women), we classified patients with Hb ≥ 7 g/dL, <10 d/dL as moderate anemia, other cases classified as mild anemia. Among patients with normal hemoglobin levels, we classified those with Hb > 16.5 g/dL in men, and > 16.0 g/dL in women, as having high hemoglobin. We examined the relationship between anemia with all-cause mortality and secondary outcomes – including cardiovascular mortality, myocardial infarction, stroke, and repeat revascularization. We classified 3.3%, 21.5%, and 5.3% of patients as moderate anemia, mild anemia, and high hemoglobin, respectively. During a median follow-up of 67.2 (interquartile range; 46.8–88.5) months, 74 (3.8%) patients died. Compared with patients with normal hemoglobin, we detected a significantly increased risk for all-cause mortality in patients with anemia (adjusted hazard ratios for moderate and mild anemia, respectively: 8.26 [95% confidence interval: 3.98–17.15], $P < .001$ and 2.60 [1.54–4.40], $P < .001$). Among patients with ACS, anemia is prevalent and is strongly associated with increased mortality and cardiovascular events. Clinical trials will prospectively evaluate the efficacy of treatment for anemia on the outcomes of patients with ACS.

Abbreviations: ACS = acute coronary syndrome, CI = confidence interval, DES = drug-eluting stent, Hb = hemoglobin, HR = hazard ratio, MI = myocardial infarction, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction.

Keywords: acute coronary syndrome, anemia, coronary artery disease, mortality

1. Introduction

Anemia is a well-known risk factor for cardiovascular disease.[1–3] Anemia occurs in 15% of all acute myocardial infarction (MI) patients and 43% of elderly acute MI patients,[4] Anemia exacerbates myocardial damage by decreasing myocardial oxygen supply in patients with acute coronary syndromes (ACS) and increasing myocardial oxygen demand to increase cardiac output to maintain adequate oxygen delivery.[5,6] Anemia in patients with heart failure has been shown to be an independent risk factor for poor clinical outcomes in a community-based cohort study.[7–9] However, there are limited data on whether anemia on admission is a long-term prognostic factor in ACS patients undergoing percutaneous coronary intervention (PCI) with a drug-eluting stent (DES). We therefore examined the association between baseline hemoglobin and clinical outcomes in patients with ACS treated with PCI in Korea.

2. Methods

2.1. Study design and population

We based our retrospective observational study on the registry of patients who had undergone PCI with new-generation DESs for ACS at CHA Bundang Medical Center, admitted consecutively between August 2008 and December 2015. For this study, patients with a history of coronary artery bypass graft surgery, a history of PCI, patients who treated with various DES during the procedure, bifurcation lesions requiring side branch stent implantation, patients with cardiogenic shock or other diseases whose life expectancy was < 1 year, patients who were scheduled to discontinue antiplatelet agents for surgery within 6 months or who underwent concurrent valve or aortic surgery were excluded. The Institutional Review Board, CHA Bundang Medical Center, approved the study, which conformed to the principles outlined in the Declaration of Helsinki (approval

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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2.2. Definitions

We defined ST-elevation MI (STEMI) as the presence of chest pain with persistent ST-segment elevation of at least 0.1 mV in at least 2 contiguous leads or a new left bundle-branch block on electrocardiography. Non-ST-segment elevation MI (NSTEMI) was defined as the presence of chest pain during the previous 48 hours with a positive troponin test with or without ST-segment changes on electrocardiography, indicating ischemia. We established a diagnosis of unstable angina in patient with suggestive symptoms, or evidence of myocardial ischemia on the stress test, accompanied by a culprit lesion in coronary angiography. Based on initial pre-procedure blood samples taken at admission, we classified patients as anemic using the definition of the World Health Organization: hemoglobin (Hb) < 13 g/dL in men, and < 12 g/dL in women.[10] Among the anemic population, we classified patients with Hb ≥ 7 g/dL, <10 d/dL were classified as moderate anemia, and other cases as mild anemia.[11] Among patients with normal hemoglobin levels, we classified those who met the polycythemia criteria – Hb > 16.5 g/dL in men, and > 16.0 g/dL in women as high hemoglobin.[12]

2.3. Procedure and follow-up

PCI was performed at the discretion of the treating physician and according to standard techniques. Since the procedure method was not specified, the overall operation was performed according to the decision of the interventional cardiologists according to the guidelines.[13] All patients were loaded with dual antiplatelet agents before the procedure, and aspirin was continuously administered after the procedure, and adenosine diphosphate receptor antagonists were administered for 6 to 12 months.[14] Thereafter, the administration of adenosine diphosphate receptor antagonists was subject to the physician's decision. Data was collected using a dedicated case report form, and information on baseline characteristics and clinical outcome was collected based on the patient's medical records.

2.4. Endpoints and follow-up

We defined our primary endpoint as all-cause mortality, and our secondary outcomes as death from cardiac cause, MI, stroke, or repeat revascularization. We considered death as cardiac unless an unequivocal noncardiac cause could be established. MI was defined based on the universal definition of MI.[15,16] Stroke was diagnosed by a neurologist as a case of neurological defect based on imaging tests. Repeat revascularization included percutaneous or surgical revascularization procedures after index procedure, which was not planned at the time of index procedure. Clinical events were identified based on the diagnosis of the attending physician, and an independent clinicians adjudicated them on the basis of medical records.

2.5. Statistical methods

We express continuous data as mean ± standard deviation, and categorical data as counts or percentages. Analysis of variance (continuous variables) and chi-square statistics (categorical variables) were used to analyze baseline characteristics between groups. Analysis of clinical outcome was performed using the Kaplan-Meier curve estimate and compared using the log-rank test. In order to confirm the effect of hemoglobin level on clinical outcome, multivariable Cox proportional hazards regression modeling was used. Based on this analysis, the analysis was carried out including the following factors as factors that can affect clinical outcome; age, sex, history of chronic renal failure, atrial fibrillation, history of diabetes, history of hypertension, clinical presentation (unstable angina, NSTEMI, or STEMI), left ventricular ejection fraction, femoral approach, extent of coronary artery disease, use of intravascular ultrasound, and complete revascularization. In the Cox model with stepwise backward elimination method (retention threshold; $P < .05$) was used. We assessed the proportionality assumptions by the Schoenfeld residual test, detecting no relevant violations. All our p values were 2 sided, and we considered values < 0.05 significant. We performed all statistical analyses using SPSS software, version 22.0 (SPSS, Inc, Chicago, IL) and R, version 3.6.3 software (R Foundation for Statistical Computing, Vienna, Austria)

3. Results

3.1. Patient characteristics

We enrolled a total of 1930 patients with ACS treated with PCI with DES, among whom 1012 had unstable angina (52.4%), 433 had NSTEMI (22.4%), and 485 had STEMI (25.1%). One quarter of the patients met the criteria for anemia – 415 patients for mild anemia (21.5%) and 63 for moderate anemia (3.3%). We detected high hemoglobin in 103 patients (5.3%).

In Table 1 we present the baseline clinical, angiographic, and laboratory characteristics of the study population, sorted by anemia status. Patients with anemia were more likely to be older, to be female, and to have more comorbidities – including hypertension, diabetes, chronic renal failure, and prior heart failure. We observed a significantly lower left ventricular ejection fraction and higher extent of coronary artery disease in anemic patients. In patients with anemia, a complete revascularization rate was less often achieved. At discharge, almost all patients received dual-antiplatelet agent. In patients with anemia, the P2Y12 inhibitor was less commonly prescribed.

3.2. Anemia and clinical presentation

In Figure 1, we show the incidence of anemia according to the clinical presentation. Among patients in all patient groups, about 2-thirds had normal hemoglobin. We found the frequency of moderate anemia to range from 2.8% to 3.9% depending on the clinical presentation, and that of mild anemia to be high in unstable angina (24.1%) and low in STEMI (14.6%). Conversely, we found the frequency of high hemoglobin in unstable angina to be low (2.2%) and that in STEMI patients to be high (10.7%), with statistically significant differences.

3.3. Anemia and clinical outcomes

The period leading up to median follow-up of 67.2 (interquartile range; 46.8–88.5) months occasioned the death of 74 (3.8%) patients. Regarding secondary outcomes, cardiac death, MI, stroke, and repeat vascularization accounted for 29 (1.5%), 24 (1.2%), 28 (1.5%), and 317 (16.4%), respectively. We have followed up 1138 patients at 5 years. In Table 2, we present 5-year event rates of clinical outcomes in patients categorized by baseline hemoglobin. The event rates of moderate anemia and mild anemia were highest and second highest, respectively, for all-cause death and cardiac death. We detected no statistically significant differences – in both all-cause death and cardiac death – between the normal hemoglobin and high hemoglobin groups. Kaplan-Meier survival estimates are shown in Figure 2.

The occurrence of MI, stroke, and repeat revascularization did not differ significantly among the normal hemoglobin group, the anemia group, and the high hemoglobin group. Given imbalances in important baseline characteristics, we used multivariable logistic regression to evaluate the independence of the relationship between hemoglobin and clinical outcomes

Table 1

Baseline characteristics of the patients stratified by baseline hemoglobin.

Variables	Moderate anemia (N = 63)	Mild anemia (N = 415)	Normal hemoglobin (N = 1349)	High hemoglobin (N = 103)	*P* value
Demographic data					
Age, yr	67.3 ± 11.2	66.8 ± 11.8	62.2 ± 11.3	55.5 ± 11.9	<.001
Male	33 (52.4%)	254 (61.2%)	936 (69.4%)	87 (84.5%)	<.001
Height, cm	160.4 ± 8.5	161.2 ± 9.0	163.4 ± 9.1	166.0 ± 8.0	<.001
Weight, kg	61.1 ± 10.3	63.1 ± 11.2	66.2 ± 11.2	70.0 ± 11.7	<.001
Body mass index, kg/m^2	23.7 ± 3.2	24.2 ± 3.5	24.7 ± 3.2	25.4 ± 3.5	.001
CV risk factors and prior CV disease					
Hypertension	42 (66.7%)	273 (65.8%)	761 (56.4%)	45 (43.7%)	<.001
Diabetes mellitus	34 (54.0%)	159 (38.3%)	373 (27.7%)	26 (25.2%)	<.001
Dyslipidemia	3 (4.8%)	25 (6.0%)	92 (6.8%)	4 (3.9%)	.603
Peripheral artery disease	1 (1.6%)	3 (0.7%)	4 (0.3%)	0 (0.0%)	.268
Chronic renal failure	20 (31.7%)	42 (10.1%)	21 (1.6%)	1 (1.0%)	<.001
Prior heart failure	9 (14.3%)	17 (4.1%)	22 (1.6%)	2 (1.9%)	<.001
Atrial fibrillation	2 (3.2%)	16 (3.9%)	31 (2.3%)	1 (1.0%)	.236
Prior stroke	7 (11.1%)	31 (7.5%)	79 (5.9%)	3 (2.9%)	.115
Chest pain presentation					<.001
Unstable angina	28 (44.4%)	244 (58.8%)	718 (53.2%)	22 (21.4%)	
NSTEMI	17 (27.0%)	100 (24.1%)	287 (21.3%)	29 (28.2%)	
STEMI	18 (28.6%)	71 (17.1%)	344 (25.5%)	52 (50.5%)	
Laboratory data					
Hemoglobin, g/dL	8.8 ± 0.8	11.6 ± 0.8	14.3 ± 1.0	17.0 ± 0.6	<.001
Albumin, g/dL	3.4 ± 0.7	3.9 ± 0.5	4.2 ± 0.4	4.3 ± 0.4	<.001
Cholesterol, mg/dL	154.2 ± 45.9	168.5 ± 44.3	183.1 ± 44.6	195.0 ± 46.2	.043
Echocardiographic and angiographic data					
LV EF	46.2 ± 16.6	53.0 ± 14.8	56.2 ± 13.0	53.5 ± 10.7	<.001
Extent of CAD					<.001
1VD	16 (25.4%)	145 (34.9%)	583 (43.2%)	45 (43.7%)	
2VD	17 (27.0%)	120 (28.9%)	431 (31.9%)	34 (33.0%)	
3VD	30 (47.6%)	150 (36.1%)	335 (24.8%)	24 (23.3%)	
Use of IVUS	35 (55.6%)	265 (63.9%)	900 (66.7%)	65 (63.1%)	.222
Complete revascularization	20 (31.7%)	173 (41.7%)	680 (50.4%)	57 (55.3%)	<.001
Femoral approach	34 (54.0%)	202 (48.7%)	597 (44.3%)	57 (55.3%)	.045
Stent					.939
Sirolimus-eluting stent	1 (1.6%)	19 (4.6%)	45 (3.3%)	3 (2.9%)	
Everolimus-elutin stent	43 (68.3%)	266 (64.1%)	885 (65.6%)	69 (67.0%)	
Zotarolimus-eluting stent	13 (20.6%)	78 (18.8%)	269 (19.9%)	19 (18.4%)	
Biolimus-eluting stent	6 (9.5%)	52 (12.5%)	150 (11.1%)	12 (11.7%)	
Medical therapy					
Aspirin	61 (96.8%)	415 (100.0%)	1340 (99.3%)	102 (99.0%)	.023
Clopidogrel	60 (95.2%)	413 (99.5%)	1327 (98.4%)	102 (99.0%)	.045
Prasugrel	0 (0.0%)	0 (0.0%)	8 (0.6%)	1 (1.0%)	.352
Ticagrelor	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	.934
Beta-blocker	36 (57.1%)	205 (49.4%)	679 (50.3%)	68 (66.0%)	.012
ACE inhibitor or ARB	21 (33.3%)	134 (32.3%)	428 (31.7%)	20 (19.4%)	.092
Statin	41 (65.1%)	288 (69.4%)	848 (62.9%)	77 (74.8%)	.014
Calcium channel blocker	55 (87.3%)	381 (91.8%)	1253 (92.9%)	101 (98.1%)	.053

ACE = angiotensin-converting enzyme, ACS = acute coronary syndrome, ARB = angiotensin receptor blocker, CAD = coronary artery disease, CV = cardiovascular, LV EF = left ventricular ejection fraction, NSTEMI = non–ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction, VD = vessel disease.

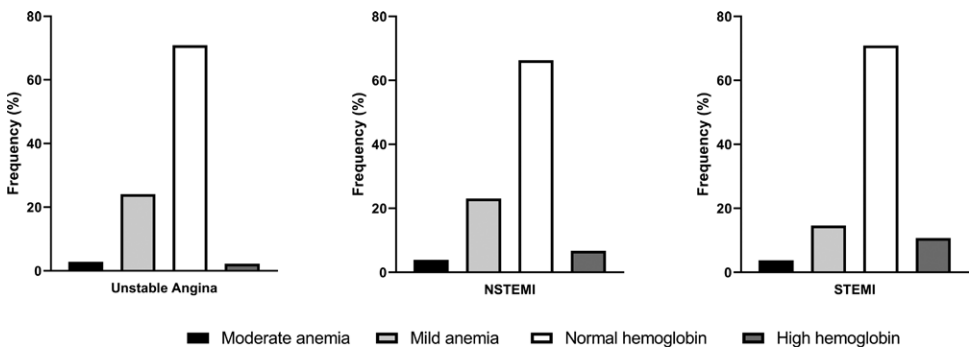

Figure 1. Prevalence of anemia according to acute coronary syndrome presentation. NSTEMI: non–ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

Table 2

Five-year event rates of primary and secondary clinical outcomes stratified by baseline hemoglobin.

	Moderate anemia (n = 63)	Mild anemia (n = 415)	Normal hemoglobin (N = 1349)	High hemoglobin (n = 103)	
	Event rate (%,95% CI)	Event rate (%,95% CI)	Event rate (%,95% CI)	Event rate (%,95% CI)	*P* value
Primary outcomes					
All-cause death	23.43 (10.9–35.96)*	6.89 (4.13–9.65)*	2.06 (1.24–2.87)	2.57 (–1.05 to 6.19)	<.001
Secondary outcomes					
Cardiac deaths	12.36 (2.88–21.85)*	2.18 (0.68–3.69)*	1.05 (0.45–1.64)	0.23 (–0.03 to 0.48)	<.001
Myocardial infarction	2.33 (–2.18 to 6.83)	0.79 (–0.10 to 1.68)	0.97 (0.40–1.54)	3.48 (–0.39 to 7.34)	.290
Stroke	2.27 (2.13 to 6.68)	1.25 (0.02–2.48)	0.89 (0.37–1.41)	1.72 (–1.63 to 5.07)	.874
Repeat revascularization	26.41 (12.27–40.54)	14.18 (10.51–17.85)	16.92 (14.76–19.09)	21.71 (13.22–30.19)	.229

CI = confidence interval.

*Statistically significant different compared with normal hemoglobin group.

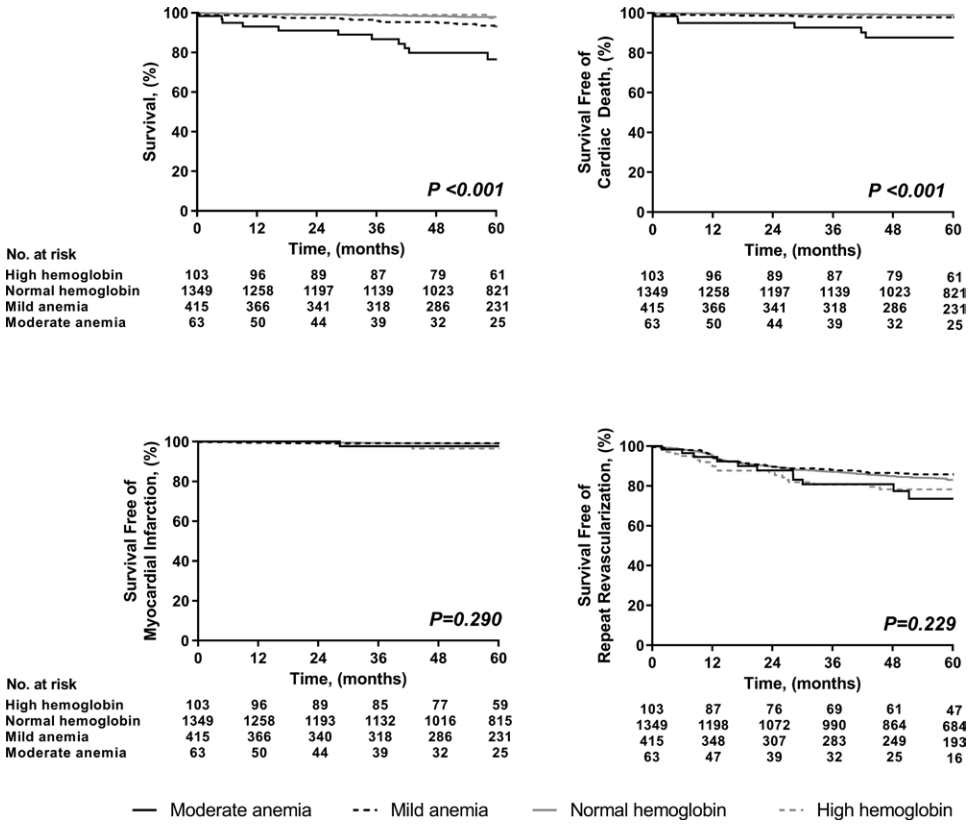

Figure 2. Kaplan–Meier curves of clinical outcomes the patients stratified by baseline hemoglobin level.

after adjustment for a wide range of covariables. In Figure 3 we show a plot of the adjusted hazard ratio and 95% confidence interval for all-cause mortality and cardiac deaths in study patients categorized by hemoglobin level. Using patients with normal hemoglobin as the reference, we found moderate anemia and mild anemia to be significantly higher risks factors for all-cause death (hazard ratio [HR]: 8.26, 95% confidence interval [CI]: 3.98–17.15, $P < .001$; HR: 2.60, 95% CI: 1.54–4.40, $P < .001$, respectively, Table S1, Supplemental Digital Content, http://links.lww.com/MD/I270). These results were consistently observed in major clinical subgroups except patients with chronic renal failure. (Figure S1, Supplemental Digital Content, http://links.lww.com/MD/I271). The high hemoglobin group showed an increased but statistically insignificant risk of death (HR: 1.20, 95% CI: 0.37–3.92, $P = .763$). Patients with moderate anemia showed a statistically significantly higher risk for cardiac death than that for those with normal hemoglobin after adjustment (HR: 6.63, 95% CI: 2.17–20.29, $P = .001$). Compared with patients with normal hemoglobin, there was no statistical difference in the risk of cardiac death in patients with mild anemia (HR: 1.95, 95% CI: 0.79–4.81, $P = .149$) and high hemoglobin (HR: 0.25, 95% CI: 0.09–6.45, $P = .863$).

4. Discussion

Here, we observed that about 1 in 4 patients presenting with ACS and treated using PCI met the criteria for anemia. Such patients were more likely to be female, had a higher prevalence of comorbidities, and were less likely to achieve complete revascularization. Additionally, we identified statistically significant and independent associations between anemia on admission and clinical outcomes in patients with ACS treated with PCI. Compared with patients with normal hemoglobin, those with moderate anemia were associated with higher mortality and cardiac deaths, and in patients with mild anemia there was an increased risk of mortality.

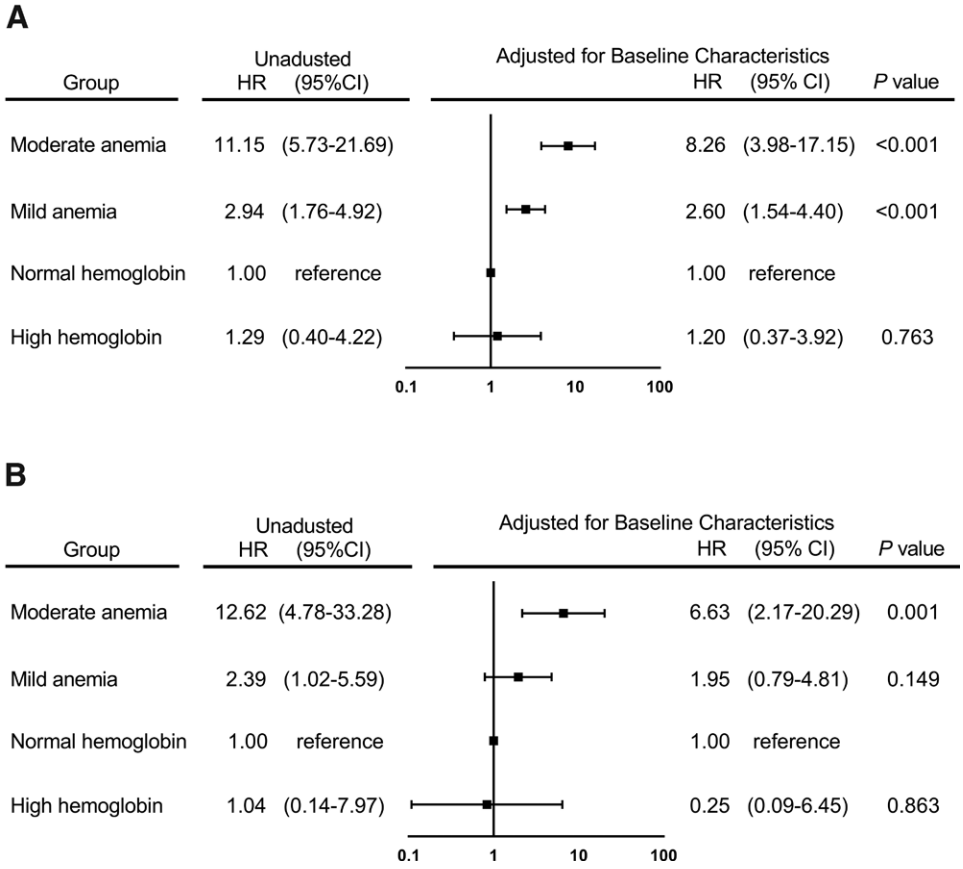

Figure 3. Unadjusted and adjusted hazard ratios and 95% confidence intervals for association be-tween baseline hemoglobin level and (A) all-cause mortality, and (B) cardiac deaths. Adjusted for age, sex, history of chronic renal failure, atrial fibrillation, history of diabetes, history of hypertension, clinical presentation (unstable angina, NSTEMI, or STEMI), left ventricular ejection fraction, femoral approach, extent of coronary artery disease, use of intravascular ultrasound, and complete revascularization. 95% CI = 95% confidence interval, HR = hazard ratio.

Our observed 24.8% prevalence of anemia is similar to that reported in data derived from randomized controlled trials reporting rates of between 10% and 25%.[17,18] As in our study, patients with anemia were older and had a higher prevalence of some comorbidities – including hypertension, diabetes mellitus, and chronic renal failure. The left ventricular ejection fraction of patients with anemia was significantly lower, and the extent of coronary artery disease, significantly higher, and a complete revascularization rate was less often achieved in patients with anemia, and their frequency of complete revascularization was statistically significantly lower, indicating that patients with anemia were treated more conservatively.

There are several mechanisms proposed for the association of anemia with poor clinical outcome in patients with ACS. In the presence of anemia, the heart must maintain a high stroke volume and heart rate to maintain adequate systemic oxygen delivery, thereby increasing myocardial oxygen demand. However, in the presence of anemia, it has a negative effect of decreasing oxygen delivery to the blood vessels with coronary stenosis.[19] These series of processes might contribute to poor clinical outcome in ACS patients with anemia. Clinically, due to bleeding concerns, patients with anemia are often under-prescribed antiplatelet therapy; for instance, in our current analysis clopidogrel was prescribed in 99.9%% of patients with high hemoglobin and 95.2% of those with moderate anemia ($P < .001$).

In our study, as the clinical presentation progressed from unstable angina to NSTEMI and STEMI, the frequency of moderate anemia remained more or less constant. The frequency of mild anemia, however, decreased, while the frequency of high hemoglobin increased significantly. Previous studies have reported a correlation of revere J-shape between baseline hemoglobin and clinical outcomes – including short term mortality and major adverse cardiac events.[20,21] The mechanism for this result is that when hemoglobin level is high, coronary perfusion is decreased due to increase in blood viscosity, which increases the risk of myocardial workload and thrombosis. However, we have not demonstrated such statistically significant relationships between all-cause mortality and cardiac death, and hemoglobin. A recent study analyzing the effects of anemia on elderly ACS reported that the prognostic effect was explained by the accompanying risk factors rather than the anemia itself.[22]

Considering that the extent of coronary artery disease is generally severe and the achievement of complete revascularization is low, it can be expected that there are more myocardial infarctions in patients with anemia. However current study did not detect a significant difference in the rate of myocardial infarction at follow-up according to anemia status. The higher rate of repeat revascularization may also have had an effect on the low rate of myocardial infarctions. The use of antiplatelet agents after the procedure may also have had an effect on the rate of myocardial infarctions, which did not differ significantly depending on the degree of anemia.

Our analysis suggests that anemia is independently associated with adverse clinical outcomes in patients presenting with ACS. Our study also demonstrates that the severity of anemia is associated with long-term outcome. Considering the results of previous studies, the current practice guidelines suggest identifying and correcting anemia in patients with ACS.[23] They do not, however, specify the desired hemoglobin target level. There are insufficient data on the level of hemoglobin to which anemic patients should be corrected.[24,25]

Our study had some limitations. This was a single-center, retrospective study with subsequent inherent disadvantages. In addition, data were limited, lacking information regarding educational status or socioeconomic characteristics that may have informed an understanding of the contributing factors of anemia. Considering that anemia is a marker of frailty in patients, there is also a lack of information about conditions that can cause anemia and affect the patient's clinical outcome. Data on the procedure results of staged PCI and duration of dual antiplatelet therapy are lacking. Although the study included patients with ACS, most patients were treated with clopidogrel. In addition, half of the patients had unstable angina, and patients with a history of revascularization therapy or cardiogenic shock were excluded, which may have influenced the low mortality rate of current study. Hemoglobin evaluation was performed only at a single time point, additional bleeding and subsequent changes in hemoglobin status over time could not be investigated and could affect clinical outcomes. As most of the patients in our registry were Asian, the applicability of these findings to other ethnic or social groups with different patient and procedural characteristics remains uncertain.

In conclusion, approximately 1 in 4 patients receiving PCI for ACS had anemia on admission in Korea. After adjusting for baseline prognostic factors and PCI, patients with anemia showed a higher risk for all-cause death and cardiac death than those without anemia. Meticulous treatment might be needed to improve clinical outcomes in anemic patients with ACS receiving PCI.

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References

[1] Nikolsky E, Aymong ED, Halkin A, et al. Impact of anemia in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention: analysis from the controlled abciximab and device investigation to lower late angioplasty complications (CADILLAC) trial. J Am Coll Cardiol. 2004;44:547–53.
[2] Al Falluji N, Lawrence-Nelson J, Kostis JB, et al. Effect of anemia on 1-year mortality in patients with acute myocardial infarction. Am Heart J. 2002;144:636–41.
[3] Kurek T, Lenarczyk R, Kowalczyk J, et al. Effect of anemia in high-risk groups of patients with acute myocardial infarction treated with percutaneous coronary intervention. Am J Cardiol. 2010;105:611–8.
[4] Wu WC, Rathore SS, Wang Y, et al. Blood transfusion in elderly patients with acute myocardial infarction. N Engl J Med. 2001;345:1230–6.
[5] Salisbury AC, Alexander KP, Reid KJ, et al. Incidence, correlates, and outcomes of acute, hospital-acquired anemia in patients with acute myocardial infarction. Circ Cardiovasc Qual Outcomes. 2010;3:337–46.
[6] Hasin T, Sorkin A, Markiewicz W, et al. Prevalence and prognostic significance of transient, persistent, and new-onset anemia after acute myocardial infarction. Am J Cardiol. 2009;104:486–91.
[7] Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in The Atherosclerosis Risk in Communities (ARIC) study. J Am Coll Cardiol. 2002;40:27–33.
[8] Al-Ahmad A, Rand WM, Manjunath G, et al. Reduced kidney function and anemia as risk factors for mortality in patients with left ventricular dysfunction. J Am Coll Cardiol. 2001;38:955–62.
[9] Ezekowitz JA, McAlister FA, Armstrong PW. Anemia is common in heart failure and is associated with poor outcomes: insights from a cohort of 12 065 patients with new-onset heart failure. Circulation. 2003;107:223–5.
[10] Zakai NA, Katz R, Hirsch C, et al. A prospective study of anemia status, hemoglobin concentration, and mortality in an elderly cohort: the cardiovascular health study. Arch Intern Med. 2005;165:2214–20.
[11] Ducrocq G, Gonzalez-Juanatey JR, Puymirat E, et al. Effect of a restrictive versus liberal blood transfusion strategy on major cardiovascular events among patients with acute myocardial infarction and anemia: The REALITY randomized clinical trial. JAMA. 2021;325:552–60.
[12] Campo E, Harris NL, Jaffe ES, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 2017.
[13] Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: executive summary: a report of the American college of cardiology foundation/American heart association task force on practice guidelines and the society for cardiovascular angiography and interventions. Circulation. 2011;124:2574–609.
[14] Park DW, Kim YH, Song HG, et al. Long-term comparison of drug-eluting stents and coronary artery bypass grafting for multivessel coronary revascularization: 5-year outcomes from the Asan medical center-multivessel revascularization registry. J Am Coll Cardiol. 2011;57:128–37.
[15] Moussa ID, Klein LW, Shah B, et al. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the society for cardiovascular angiography and interventions (SCAI). J Am Coll Cardiol. 2013;62:1563–70.
[16] Park SJ, Ahn JM, Kim YH, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. N Engl J Med. 2015;372:1204–12.
[17] Anker SD, Voors A, Okonko D, et al. Prevalence, incidence, and prognostic value of anaemia in patients after an acute myocardial infarction: data from the OPTIMAAL trial. Eur Heart J. 2009;30:1331–9.
[18] Kunadian V, Mehran R, Lincoff AM, et al. Effect of anemia on frequency of short- and long-term clinical events in acute coronary syndromes (from the acute catheterization and urgent intervention triage strategy trial). Am J Cardiol. 2014;114:1823–9.
[19] Most AS, Ruocco NA Jr, Gewirtz H. Effect of a reduction in blood viscosity on maximal myocardial oxygen delivery distal to a moderate coronary stenosis. Circulation. 1986;74:1085–92.
[20] Sabatine MS, Morrow DA, Giugliano RP, et al. Association of hemoglobin levels with clinical outcomes in acute coronary syndromes. Circulation. 2005;111:2042–9.
[21] Mamas MA, Kwok CS, Kontopantelis E, et al. Relationship between anemia and mortality outcomes in a national acute coronary syndrome cohort: insights from the UK myocardial ischemia national audit project registry. J Am Heart Assoc. 2016;5:e003348.
[22] De Luca G, Verdoia M, Morici N, et al. Impact of hemoglobin levels at admission on outcomes among elderly patients with acute coronary syndrome treated with low-dose Prasugrel or clopidogrel: a sub-study of the ELDERLY ACS 2 trial. Int J Cardiol. 2022;369:5–11.
[23] Ryan TJ, Antman EM, Brooks NH, et al. 1999 update: ACC/AHA guidelines for the management of patients with acute myocardial infarction: executive summary and recommendations: a report of the American college of cardiology/American heart association task force on practice guidelines (committee on management of acute myocardial infarction). Circulation. 1999;100:1016–30.
[24] Hébert PC, Yetisir E, Martin C, et al. Is a low transfusion threshold safe in critically ill patients with cardiovascular diseases? Crit Care Med. 2001;29:227–34.
[25] Rao SV, Jollis JG, Harrington RA, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. JAMA. 2004;292:1555–62.