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Impact of Anemia and Acquired Anemia on in-Hospital Mortality of Acute Coronary Syndrome Patients

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Objective: To investigate the associations of anemia-related parameters, with in-hospital mortality after acute coronary syndrome (ACS), as well as factors associated with prior anemia (PA) and hospital-acquired anemia (HAA) in patients with ACS.

Methods: This was a retrospective cohort study conducted between June 2021 and May 2023. The data of patients diagnosed with ACS who were hospitalized and treated in our hospital were recorded, including age and sex, smoking and comorbidity status, laboratory findings, CHA2DS2-VASc scores, prior medication use, left ventricular ejection fraction, ACS type, the synergy between percutaneous intervention with taxus drug-eluting stents and cardiac surgery (SYNTAX) scores, stent thrombosis status and mortality status. Mortality was assessed according to in-hospital death. Patients were grouped based on anemia presence (PA and HAA).

Results: A total of 329 patients were included in the study. Of these, 219 (66.56%) were in the no anemia group, 58 (17.63%) in the PA group, and 52 (15.81%) in the HAA group. The mean age of all participants was 61.27±12.45 years and 76.29% of them were male. 14 (4.26%) patients died during hospitalization. Multivariable logistic regression analysis had revealed that, prior coronary artery disease (OR: 3.779, 95% CI: 1.141–12.508, p=0.030), PA (OR: 7.043, 95% CI: 1.574–31.517, p = 0.011), HAA (OR: 5.857, 95% CI: 1.260–27.236, p=0.024) and high WBC (OR: 1.190, 95% CI: 1.028–1.378, p=0.020) were independently associated with the increased risk of in-hospital mortality.

Conclusion: Consequently, the risk of in-hospital mortality is higher in patients with a previous history of coronary artery disease, PA, HAA and high WBC, and additional precautions should be taken in these patients.

Keywords: acute coronary syndrome, anemia, mortality

Introduction

Cardiovascular diseases, most often the result of atherosclerosis, are the leading cause of death worldwide.[1] Atherosclerotic plaques can become unstable, leading to thrombosis and acute coronary syndromes (ACS). ACS, which includes unstable angina pectoris (USAP), non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI), is one of the most common causes of hospital admission.[2] Despite the implementation of guideline-recommended treatments, ACS still has a poor prognosis and there is therefore a need for early risk stratification.[1]

Adult anemia is defined as hemoglobin value less than 13 g/dL in men and <12 g/dL in women.[3] The main role of hemoglobin is to ensure that sufficient oxygen is delivered to body tissues.[4] The prevalence of anemia present at the time of ACS diagnosis in patients with ACS is estimated to range between 10% and 43%.[5–10] Hospital-acquired anemia (HAA), defined as anemia onset during hospitalization, is frequently seen in patients admitted for ACS.[4] Its overall prevalence was estimated to be 57%.[11,12] It has been shown in many studies that the presence of anemia, whether it exists before the diagnosis of ACS or develops during hospitalization or during follow-up, is associated with poor ACS prognosis.[5–9,13] However, the negative impact of anemia on short- and long-term morbidity and mortality is unclarified. It

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has been suggested that this relationship could be a reflection of poor clinical conditions that cause both anemia and poor ACS prognosis.[4] Moreover, it is not yet clear whether mild anemia directly leads to poor ACS outcomes.[14] On the other hand, systemic inflammation plays an important role in the pathophysiology of both atherosclerosis and ACS.[1,15] Several studies have demonstrated that inflammatory parameters are associated with ACS prognosis, left ventricular function and cardiac enzymes.[16–20] However, the inter-relationship between anemia and inflammation markers in the context of myocardial injury markers has not been adequately investigated. Another important issue is that there are very few studies which have investigated the relationship between ACS prognosis and predictors of in-hospital mortality.[1]

Therefore, in this study, we aimed to investigate the associations of some clinicodemographic and laboratory variables, especially anemia-related parameters, with in-hospital mortality after acute myocardial infarction and indicators of myocardial injury, as well as factors associated with previous anemia and HAA in ACS patients.

Methods

Study Design and Ethics

This retrospective study was carried out at Ankara City Hospital ana Istanbul Medipol University, Turkey. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Non-invasive Clinical Research Ethics Committee of Istanbul Medipol University (Decision date: 04.01.2024, decision no: 20). In accordance with the retrospective design of the study, the local ethics committee waived the requirement for informed consent, as no identifiable patient information was included in the analysis.

Study Population and Data Collection

The data of patients diagnosed with ACS, hospitalized and treated in our hospital between June 2021 and May 2023 were retrospectively investigated. Patients diagnosed with USAP, those with incomplete or missing data regarding the variables included in the study, and those with a history of coronary artery bypass grafting were excluded from the study.

According to odds ratio data reported by Vrsalovic et al, a total sample size of 152 was found to achieve 90% power for a two-sided 0.05 significance level.[21] Sample size was calculated using logistic regression power analysis (Hintze, J. (2011). PASS 11. NCSS, LLC. Kaysville, Utah, USA. www.ncss.com).

Patients' age and sex data, smoking and comorbidity status, laboratory findings (detailed below), CHA2DS2-VASc scores, prior acetyl salicylic acid (ASA) and statin use, left ventricular ejection fraction (LVEF), ACS type, the presence of more than 50% stenosis in the left main coronary artery, cases of multivessel disease, the use and type of P2Y12 inhibitors and anticoagulants, the type of treatment administered (medical, percutaneous coronary intervention, or coronary artery bypass graft), the location of intervention (radial or femoral), the type according to the Bleeding Academic Research Consortium (BARC) scale, and the occurrence of blood transfusions, the synergy between percutaneous intervention with taxus drug-eluting stents and cardiac surgery (SYNTAX) scores, stent thrombosis status, statin use during hospitalization and mortality status were obtained from the hospital database and patient charts. Mortality was assessed according to in-hospital death. As mentioned previously, patients were grouped based on anemia presence [no anemia, prior anemia (PA) before event, or HAA].

Data from a total of 624 patients diagnosed with ACS were analyzed. A total of 210 were excluded due to missing data, 60 due to a diagnosis of USAP, and 35 due to a history of coronary artery bypass graft surgery. A total of 329 patients were included in the study (Figure 1). Of these, 219 (66.56%) were in the no anemia group, 58 (17.63%) in the PA group, and 52 (15.81%) in the HAA group.

ACS Management

The management of diagnosis, classification and treatment of ACS were performed in line with the current ESC guidelines.[22–24] STEMI and NSTEMI were diagnosed according to electrocardiography and cardiac biomarkers. STEMI was defined as myocardial ischaemia in association with persistent electrocardiographic ST elevation. Positive ST segment elevation (2 mm; 0.2 mv) was described as an ST elevation at the J point in at least two adjacent leads in males or 1.5 mm (0.15 mv) in females (leads v2–v3) and/or 1-mm elevation (0.1 mv) in other adjacent chest leads or the

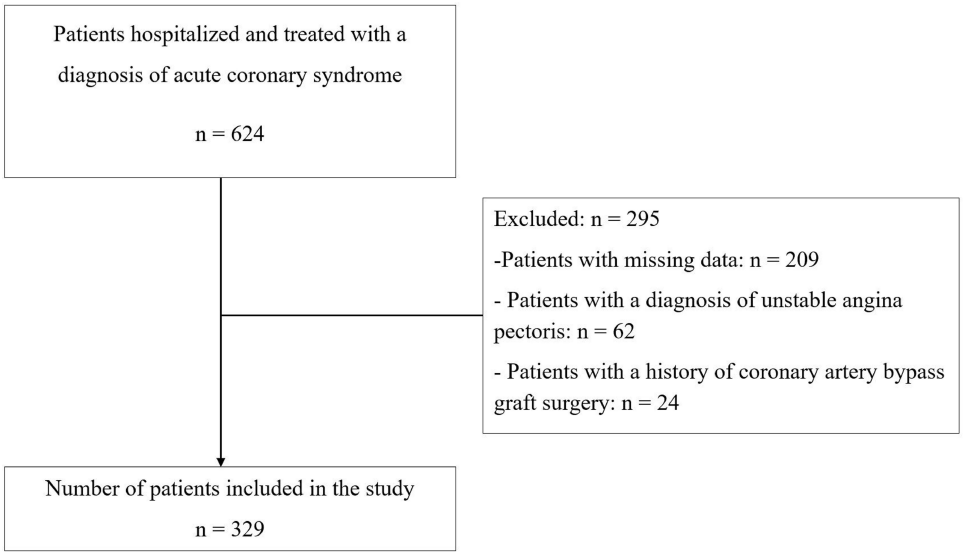

Figure 1 Flowchart of the study.

limb lead.[24,25] NSTEMI was described by electrocardiographic ST depression or prominent T-wave inversion and/or positive cardiac biomarkers in the absence of ST elevation, given that the findings fulfilled ACS criteria with positivity for cardiac enzymes.[26]

USAP cases were identified through electrocardiographic ST-segment depression or prominent T-wave inversion, given presence of an appropriate clinical setting (chest discomfort or anginal equivalent) for ACS. The presence of negative cardiac enzymes was defined as USAP.[26]

Following the diagnosis of ACS, coronary angiography was performed on the same day using standard Judkins techniques or radial approach.[27] Baseline LVEF values acquired from echocardiography results performed and recorded before angiography were included in the study. CHA2DS2-VASc score was calculated for each patient based on demographic and echocardiographic characteristics at baseline. Patients received 1 point each for congestive heart failure, hypertension, age of 65–74 years, diabetes, vascular disease and female sex, and 2 points for age ≥75 years and previous stroke or transient ischemic attack.[28] All patients received at least 1 point because they all had vascular atherosclerosis.

The baseline SYNTAX scores were calculated by viewing the patients' coronary angiography images registered on the computer system using the website (http://www.syntaxscore.com). A higher score indicates more severe vascular disease.

The Bleeding Academic Research Consortium scale was used to classify bleeding events observed during the study period.[29]

Laboratory Analysis

All measurements were performed in the clinical chemistry department of Ankara City Hospital via use of routine devices. The following laboratory parameters studied from blood samples taken at first admission and before angiography were included in the study: hemoglobin (baseline and pre-discharge), hematocrit (baseline and pre-discharge), mean platelet volume (MPV), platelet distribution width (PDW), creatinine, C-reactive protein (CRP), gamma glutamyltransferase (GGT), albumin, total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglyceride, fasting blood glucose, troponin and creatine kinase-MB (CK-MB) levels, platelet and white blood cell (WBC) counts. The lowest hemoglobin and hematocrit levels and the highest troponin levels of the patients during their hospitalization were also included in the study. Peak to baseline troponin ratio was calculated by dividing the peak troponin level by the baseline troponin level. Estimated glomerular filtration rate (eGFR; in mL/min per 1.73 m^2) was calculated for each patient using the modification of Diet in Renal Disease study equation.[30]

PA was defined as anemia present before hospital admission, with hemoglobin levels less than 13 g/dL in men and less than 12 g/dL in women.[31] HAA was defined as a decrease in hemoglobin levels of at least 2 g/dL from baseline

during hospitalization, or the development of anemia (hemoglobin levels below 13 g/dL in men and 12 g/dL in women) during the hospital stay in patients who were not anemic at admission.[32]

Statistical Analysis

All analyses were performed on IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Distribution of continuous variables were evaluated with the histograms and Q-Q plots. Descriptive statistics were represented with the frequency (percentage) for categorical variables, mean ± standard deviation for normally distributed continuous variables and median (25th percentile - 75th percentile) for non-normally distributed continuous variables. Repeated measurements of hemoglobin and hematocrit were analyzed with the paired samples *t* test. Between groups analysis of categorical variables were performed with the chi-square test or Fisher-Freeman-Halton test. Between groups analysis of continuous variables were performed with the one-way analysis of variances (ANOVA) for normally distributed variables and were performed with the Kruskal Wallis test for non-normally distributed variables. Pairwise comparisons were adjusted by Bonferroni correction. Pearson or Spearman correlation coefficients were calculated to evaluate relationships between continuous variables. Logistic regression analyses were performed to determine significant factors independently associated with the mortality. Variables were analyzed with the univariable regression analysis and statistically significant variables were included into the multivariable analysis (forward conditional selection method). The statistical significance value was accepted as $p < 0.05$.

Results

Overall mean age was 61.27 ± 12.45 years and 76.29% of the participants were males. The PA and HAA groups were significantly older than the no anemia group ($p < 0.001$). The percentage of males and smokers in the no anemia group was significantly higher than in the PA group ($p < 0.001$, $p = 0.010$). The CHA2DS2–VASc scores of the PA and HAA groups were significantly higher compared to the no anemia group ($p < 0.001$) (Table 1).

The percentage of patients requiring blood transfusion was significantly higher in the PA group compared to the no anemia group ($p < 0.001$). Both baseline hemoglobin, in-hospital hemoglobin, baseline hematocrit, and in-hospital hematocrit levels in the PA and HAA groups were significantly lower relative to the no anemia group ($p < 0.001$).

Table 1 Summary of Patient Characteristics with Regard to Anemia Status

	Total (n=329)	Anemia status			p
		No Anemia (n=219)	Prior Anemia (n=58)	Hospital-Acquired Anemia (n=52)	
Age (years)	61.27 ± 12.45	58.47 ± 11.45	68.03 ± 11.91*	65.56 ± 13.18*	**<0.001**
Sex					
Male	251 (76.29%)	181 (82.65%)	34 (58.62%)*	36 (69.23%)	**<0.001**
Female	78 (23.71%)	38 (17.35%)	24 (41.38%)*	16 (30.77%)	
Smoking	90 (27.36%)	71 (32.42%)	8 (13.79%)*	11 (21.15%)	**0.010**
Peripheral artery disease	6 (1.82%)	3 (1.37%)	2 (3.45%)	1 (1.92%)	0.479
Prior coronary artery disease	91 (27.66%)	52 (23.74%)	21 (36.21%)	18 (34.62%)	0.080
Hypertension	120 (36.47%)	77 (35.16%)	19 (32.76%)	24 (46.15%)	0.271
Diabetes mellitus	76 (23.10%)	48 (21.92%)	17 (29.31%)	11 (21.15%)	0.462
Stroke	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Atrial fibrillation	6 (1.82%)	3 (1.37%)	1 (1.72%)	2 (3.85%)	0.306
Prior ASA use	96 (29.18%)	55 (25.11%)	23 (39.66%)	18 (34.62%)	0.062
Prior statin use	65 (19.76%)	38 (17.35%)	14 (24.14%)	13 (25.00%)	0.301

Notes: Descriptive statistics are represented with the frequency (percentage) for categorical variables, mean ± standard deviation for normally distributed continuous variables and median (25th percentile - 75th percentile) for non-normally distributed continuous variables. *: Significantly different from "No anemia" group, #: Significantly different from "Prior anemia" group. Statistically significant p values are shown in bold.
Abbreviations: ASA, Acetyl salicylic acid; N/A, Non-applicable.

Additionally, the baseline hemoglobin, in-hospital hemoglobin, baseline hematocrit, and in-hospital hematocrit levels in the HAA group were significantly higher than those in the PA group, as anticipated ($p < 0.001$). The eGFR of the no anemia group was significantly higher than both the PA group and the HAA group ($p < 0.010$). While CRP ($p = 0.002$) of the PA group was significantly higher than the no anemia group, GGT ($p = 0.029$), albumin ($p < 0.001$) and total cholesterol ($p = 0.036$) values were significantly lower. Fasting blood glucose of the HAA group was significantly higher than that of the no anemia group ($p = 0.006$) (Table 2).

In total, 136 (41.34%) were diagnosed with STEMI and 193 (58.66%) with NSTEMI. Fourteen (4.26%) patients died during hospitalization. The CHA2DS2–VASc scores of the PA and HAA groups were significantly higher compared to the no anemia group ($p < 0.001$). In the PA group, the percentage of patients using clopidogrel was significantly higher than in the no anemia group, while the percentage of those using prasugrel was significantly lower (p = 0.001). In the HAA group, the percentage of patients using Glycoprotein IIb/IIIa antagonists was significantly higher than in the other two groups (p < 0.001). The percentage of patients with a BARC score indicating no bleeding was significantly lower in the PA and HAA groups compared to the no anemia group, while the percentage of those with a Type 1 BARC score was significantly higher (p < 0.001). The percentage of patients requiring blood transfusion was significantly higher in the PA group compared to the no anemia group (p < 0.001). The in-hospital mortality rate of both the PA and HAA groups was significantly higher than the no anemia group ($p = 0.001$) (Figure 2) (Table 3).

Univariable logistic regression analysis revealed that in hospital mortality was associated with advanced age, female sex, prior coronary artery disease, diabetes mellitus, high CHA2DS2–VASc score, prior ASA use, low LVEF, prior

Table 2 Summary of Laboratory Measurements with Regard to Anemia Status

	Total (n=329)	Anemia Status			p
		No Anemia (n=219)	Prior Anemia (n=58)	Hospital-Acquired Anemia (n=52)	
Hemoglobin, baseline (g/dL)	14.10 ± 1.76	14.97 ± 1.12	11.33 ± 1.16*	13.54 ± 0.81*#	**<0.001**
Hemoglobin, in-hospital (g/dL)	13.26 ± 1.69	14.19 ± 1.02	10.93 ± 1.31*	11.99 ± 0.64*#	**<0.001**
Hematocrit, baseline (%)	42.51 ± 4.88	44.84 ± 3.40	35.34 ± 3.23*	40.70 ± 2.61*#	**<0.001**
Hematocrit, in-hospital (%)	40.21 ± 4.96	42.89 ± 3.19	33.94 ± 4.03*	36.33 ± 2.20*#	**<0.001**
Platelet ($x10^3$)	242 (206–287)	236 (205–285)	241 (192–291)	256 (215.5–295)	0.291
MPV (fL)	9.67 ± 1.15	9.67 ± 1.17	9.87 ± 1.09	9.47 ± 1.09	0.179
PDW (fL)	12.9 (11.15–16.5)	13.6 (11.1–16.5)	12.2 (11.4–16.5)	12.35 (10.6–16.35)	0.447
WBC ($x10^3$)	11.00 (8.75–13.12)	11.20 (8.98–13.20)	10.30 (8.12–12.83)	10.80 (8.28–12.80)	0.390
Creatinine, baseline (mg/dL)	0.92 (0.78–1.06)	0.91 (0.79–1.06)	0.92 (0.76–1.26)	0.93 (0.77–1.05)	0.382
eGFR (mL/min/1.73 m^2)	86.20 ± 26.49	91.02 ± 23.63	70.72 ± 30.13*	83.37 ± 26.96#	**<0.001**
CRP (mg/L)	4.74 (2.10–10.57)	4.13 (2.06–7.30)	8.64 (2.50–30.18)*	5.73 (2.12–13.70)	**0.002**
GGT (U/L)	25 (17–40)	27 (19–41)	18.5 (14–33)*	25 (17–38)	**0.029**
Albumin (g/dL)	3.86 ± 0.42	3.94 ± 0.41	3.63 ± 0.43*	3.80 ± 0.39	**<0.001**
Total cholesterol (mg/dL)	175 (150–202)	178 (155–207)	165 (135–192)*	172 (148.5–193.5)	**0.036**
HDL-C (mg/dL)	40 (33–47)	40 (34–48)	38.5 (31–47)	39 (32.5–45.5)	0.210
LDL-C (mg/dL)	110.81 ± 33.90	113.13 ± 33.81	105.67 ± 33.56	106.85 ± 34.30	0.217
Triglyceride (mg/dL)	116 (75–182)	121 (79–190)	105.5 (67–161)	104.5 (67–167.5)	0.073
Fasting blood glucose (mg/dL)	101 (93–131)	99 (90–123)	101 (94–159)	108.5 (98.5–141.5)*	**0.006**
Troponin, baseline (ng/mL)	0.289 (0.051–2.900)	0.265 (0.050–2.200)	0.330 (0.089–4.460)	0.425 (0.060–3.230)	0.196
Troponin, peak (ng/mL)	3.450 (1.010–10.000)	3.250 (1.070–11.200)	3.750 (0.898–9.760)	4.960 (1.800–20.070)	0.355
Peak to baseline troponin ratio	5.415 (1.729–27.403)	6.750 (1.751–32.667)	3.913 (1.667–12.288)	6.577 (1.866–25.445)	0.304
CK-MB (ng/mL)	49.8 (25.2–116.0)	44.8 (25–109)	62.8 (24.4–112.1)	51 (31.4–155)	0.391

Notes: Descriptive statistics are represented with the frequency (percentage) for categorical variables, mean ± standard deviation for normally distributed continuous variables and median (25th percentile - 75th percentile) for non-normally distributed continuous variables. *: Significantly different from "No anemia" group, #: Significantly different from "Prior anemia" group. Statistically significant p values are shown in bold.

Abbreviations: CK-MB, Creatine kinase-MB; CRP, C-reactive protein; eGFR, Estimated glomerular filtration rate; GGT, Gamma glutamyltransferase; HDL-C, High density lipoprotein cholesterol; LDL-C, Low density lipoprotein cholesterol; MPV, Mean platelet volume; PDW, Platelet distribution width; WBC, White blood cell.

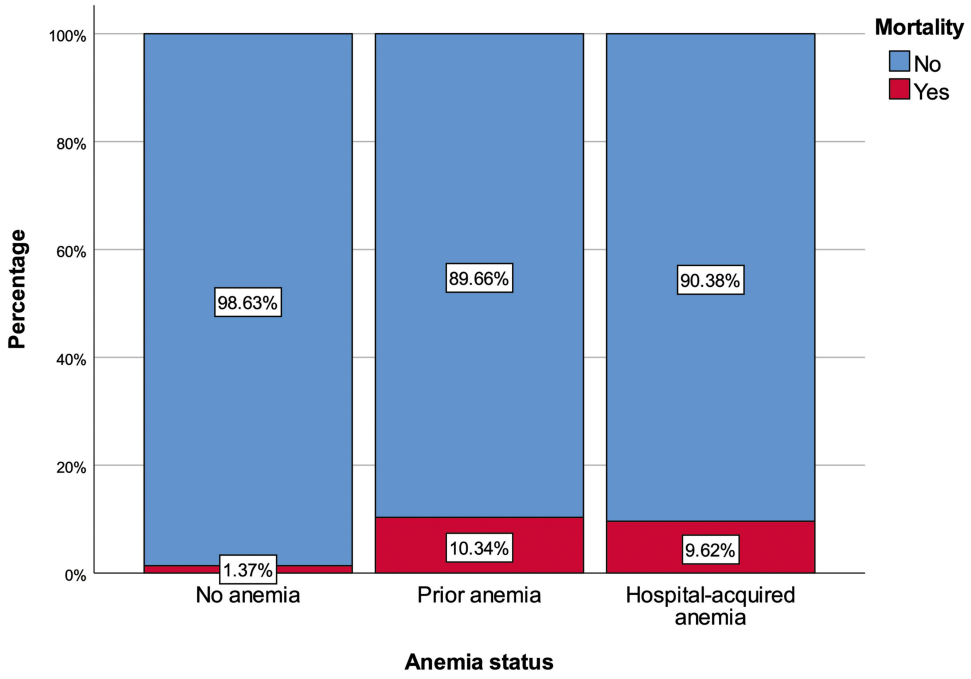

Figure 2 In-hospital mortality according to the anemia status.

presence of anemia, high WBC, high creatinine, low eGFR, high CRP, high GGT, low albumin, high total cholesterol, high fasting blood glucose, high baseline troponin and CK-MB, and high SYNTAX score. However, multivariable logistic regression revealed that patients with prior coronary artery disease had 3.779-fold higher risk of mortality (OR: 3.779, 95% CI: 1.141–12.508, $p = 0.030$). Patients with prior anemia had 7.043-fold higher risk of mortality than patients without anemia (OR: 7.043, 95% CI: 1.574–31.517, $p = 0.011$) and patients with HAA had 5.857-fold higher risk of mortality than patients without anemia (OR: 5.857, 95% CI: 1.260–27.236, $p = 0.024$). In addition, higher WBC was associated with increased risk of mortality (OR: 1.190, 95% CI: 1.028–1.378, $p = 0.020$) (Table 4).

Table 3 Summary of Diagnosis, Hospitalization, Intervention and Follow-Up Data with Regard to Anemia Status

	Total (n=329)	Anemia status			p
		No Anemia (n=219)	Prior Anemia (n=58)	Hospital-Acquired Anemia (n=52)	
LVEF (%)	45.74 ± 8.97	46.40 ± 8.50	44.88 ± 9.79	43.94 ± 9.77	0.150
Diagnosis					
STEMI	136 (41.34%)	92 (42.01%)	20 (34.48%)	24 (46.15%)	0.436
NSTEMI	193 (58.66%)	127 (57.99%)	38 (65.52%)	28 (53.85%)	
CHA_2DS_2–VASc score	2 (1–3)	2 (1–3)	3 (2–4)*	3 (1–4)*	**<0.001**
LMCA occlusion, >50%	12 (3.65%)	6 (2.74%)	2 (3.45%)	4 (7.69%)	0.223
Multivessel disease	23 (6.99%)	14 (6.39%)	6 (10.34%)	3 (5.77%)	0.525
$P2Y_{12}$ inhibitors					
Clopidogrel	99 (30.09%)	54 (24.66%)	29 (50.00%)*	16 (30.77%)	**0.001**
Ticagrelor	138 (41.95%)	92 (42.01%)	20 (34.48%)	26 (50.00%)	
Prasugrel	92 (27.96%)	73 (33.33%)	9 (15.52%)*	10 (19.23%)	
Anticoagulant					
Heparin	323 (98.18%)	214 (97.72%)	57 (98.28%)	52 (100%)	0.833
Enoxaparin	6 (1.82%)	5 (2.28%)	1 (1.72%)	0 (0.00%)	
Glycoprotein IIb/IIIa	17 (5.17%)	6 (2.74%)	0 (0.00%)	11 (21.15%)*#	**<0.001**

(*Continued*)

Table 3 (Continued).

	Total (n=329)	Anemia status			p
		No Anemia (n=219)	Prior Anemia (n=58)	Hospital-Acquired Anemia (n=52)	
Location of intervention					
Radial	276 (83.89%)	195 (89.04%)	44 (75.86%)*	37 (71.15%)*	**0.001**
Femoral	53 (16.11%)	24 (10.96%)	14 (24.14%)*	15 (28.85%)*	
Treatment					
Medical	4 (1.22%)	3 (1.37%)	1 (1.72%)	0 (0.00%)	0.313
PCI	317 (96.35%)	211 (96.35%)	57 (98.28%)	49 (94.23%)	
CABG	8 (2.43%)	5 (2.28%)	0 (0.00%)	3 (5.77%)	
BARC Scale					
No bleeding	308 (93.62%)	214 (97.72%)	49 (84.48%)*	45 (86.54%)*	**<0.001**
Type 1	11 (3.34%)	2 (0.91%)	5 (8.62%)*	4 (7.69%)*	
Type 2	7 (2.13%)	2 (0.91%)	2 (3.45%)	3 (5.77%)	
Type 3	3 (0.91%)	1 (0.46%)	2 (3.45%)	0 (0.00%)	
Blood transfusion	14 (4.26%)	3 (1.37%)	9 (15.52%)*	2 (3.85%)	**<0.001**
Duration of hospitalization, hours	48 (48–72)	48 (48–72)	48 (48–72)	48 (48–72)	0.717
SYNTAX score	18 (12–24.5)	17 (11.5–23.5)	21.5 (15–27)	19 (11–27)	0.070
Stent thrombosis	11 (3.34%)	6 (2.74%)	2 (3.45%)	3 (5.77%)	0.469
In-hospital statin use	309 (93.92%)	211 (96.35%)	52 (89.66%)	46 (88.46%)	0.051
Mortality	14 (4.26%)	3 (1.37%)	6 (10.34%)*	5 (9.62%)*	**0.001**

Notes: Descriptive statistics are represented with the frequency (percentage) for categorical variables, mean ± standard deviation for normally distributed continuous variables and median (25th percentile - 75th percentile) for non-normally distributed continuous variables. *: Significantly different from "No anemia" group, #: Significantly different from "Prior anemia" group. Statistically significant p values are shown in bold.

Abbreviations: BARC, Bleeding Academic Research Consortium; CABG, Coronary artery bypass graft; LVEF, Left ventricular ejection fraction; LMCA, Left main coronary artery; NSTEMI, Non-ST-elevation myocardial infarction; PCI, Percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; SYNTAX, The synergy between percutaneous intervention with taxus drug-eluting stents and cardiac surgery.

Table 4 Odds Ratios for Mortality, Logistic Regression Analysis Results

	Univariable		Multivariable[(a)]	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.093 (1.041–1.147)	**<0.001**	–	0.282
Sex, Female	3.437 (1.167–10.124)	**0.025**	–	0.371
Smoking	0.195 (0.025–1.515)	0.118		
Peripheral artery disease	0.000 (0.000 - N/A)	0.999		
Prior coronary artery disease	5.115 (1.666–15.704)	**0.004**	3.779 (1.141–12.508)	**0.030**
Hypertension	1.788 (0.612–5.225)	0.289		
Diabetes mellitus	3.565 (1.209–10.510)	**0.021**	-	0.121
Atrial fibrillation	4.769 (0.519–43.806)	0.167		
CHA_2DS_2–VASc score	2.068 (1.469–2.910)	**<0.001**	-	0.235
Prior ASA use	3.439 (1.160–10.196)	**0.026**	-	0.843
Prior statin use	2.361 (0.764–7.300)	0.136		
LVEF	0.903 (0.849–0.961)	**0.001**	-	0.333
Diagnosis, STEMI	1.442 (0.494–4.210)	0.503		
LMCA occlusion, >50%	9.273 (2.200–39.076)	**0.002**	-	0.629
Multivessel disease	1.024 (0.128–8.197)	0.982		
$P2Y_{12}$ inhibitors [(b)]		0.244		
Ticagrelor	0.494 (0.152–1.605)	0.241		

(*Continued*)

Table 4 (Continued).

	Univariable		Multivariable[a]	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Prasugrel	0.292 (0.059–1.444)	0.131		
Anticoagulant, Enoxaparin	0.000 (0.000 - N/A)	0.999		
Glycoprotein IIb/IIIa	5.864 (1.469–23.413)	**0.012**	-	0.645
Location of intervention, Femoral	3.090 (0.993–9.620)	0.051		
Treatment [c]		1.000		
Medical	0.000 (0.000 - N/A)	0.999		
CABG	0.000 (0.000 - N/A)	0.999		
BARC Scale [d]		0.104		0.789
Type 1	2.700 (0.317–22.992)	0.363	-	0.368
Type 2	4.500 (0.498–40.648)	0.180	-	0.694
Type 3	13.500 (1.136–160.362)	**0.039**	-	0.999
Blood transfusion	4.208 (0.846–20.933)	0.079		
Duration, hours	1.008 (0.988–1.028)	0.445		
Anemia status [e]		**0.007**		**0.024**
Prior anemia	8.308 (2.011–34.321)	**0.003**	7.043 (1.574–31.517)	**0.011**
Hospital-acquired anemia	7.660 (1.769–33.171)	**0.006**	5.857 (1.260–27.236)	**0.024**
Platelet ($x10^3$)	0.999 (0.992–1.007)	0.857		
MPV	1.131 (0.727–1.762)	0.585		
PDW	1.032 (0.856–1.243)	0.744		
WBC ($x10^3$)	1.195 (1.056–1.352)	**0.005**	1.190 (1.028–1.378)	**0.020**
Creatinine, baseline	3.249 (1.597–6.607)	**0.001**	-	0.996
eGFR	0.950 (0.928–0.972)	**<0.001**	-	0.257
CRP	1.014 (1.001–1.027)	**0.037**	-	0.818
GGT	1.013 (1.004–1.022)	**0.005**	-	0.757
Albumin	0.177 (0.050–0.634)	**0.008**	-	0.889
Total cholesterol	0.981 (0.966–0.997)	**0.022**	-	0.536
HDL-C	0.997 (0.962–1.032)	0.846		
LDL-C	0.983 (0.966–1.000)	0.055		
Triglyceride	0.992 (0.982–1.002)	0.126		
Fasting blood glucose	1.006 (1.001–1.012)	**0.034**	-	0.078
Troponin, baseline	1.027 (1.010–1.045)	**0.001**	-	0.533
Troponin, peak	1.013 (1.000–1.027)	0.058		
Peak to baseline troponin ratio	0.991 (0.970–1.012)	0.391		
CK-MB	1.005 (1.001–1.008)	**0.015**	-	0.689
SYNTAX score	1.075 (1.005–1.151)	**0.037**	-	0.820
Nagelkerke R^2	-		0.266	

Notes: (a) Multivariable analysis was performed via forward conditional selection method, (b) Reference category is "Clopidogrel", (c) Reference category is "Percutaneous coronary intervention", (d) Reference category is "No bleeding", (e) Reference category is "No anemia". Statistically significant p values are shown in bold.

Abbreviations: ASA, Acetyl salicylic acid; BARC, Bleeding Academic Research Consortium; CABG, Coronary artery bypass graft; CI, Confidence interval; CK-MB, Creatine kinase-MB; CRP, C-reactive protein; eGFR, Estimated glomerular filtration rate; GGT, Gamma glutamyltransferase; HDL-C, High density lipoprotein cholesterol; LDL-C, Low density lipoprotein cholesterol; LMCA, Left main coronary artery; LVEF, Left ventricular ejection fraction; N/A, Non-applicable; OR, Odds ratio; STEMI, ST-elevation myocardial infarction; SYNTAX, The synergy between percutaneous intervention with taxus drug-eluting stents and cardiac surgery; WBC, White blood cell.

Discussion

The current retrospective cohort study revealed that a PA rate was 17.63% and HAA rate was 15.81% in patients diagnosed with ACS. In-hospital mortality rate was 4.26%. In ACS patients, anemia at the time of admission, HAA, and high WBC at the time of admission are independent risk factors for in-hospital cardiac deaths. Additionally, as previously

shown,[33] the presence of prior coronary artery disease was another independent predictor of mortality in our study. Older age, high CHA2DS2–VASc score, low eGFR and high fasting blood glucose were associated with HAA.

Anemia is a frequent comorbidity in patients with ACS and may negatively impact cardiovascular outcomes in these patients.[13] The 3 determinants of anemia are increased plasma volume relative to erythrocyte mass or hemodilution, decreased erythropoietin production and bone marrow failure.[4] All these pathogenetic determinants may be disrupted in patients with ischemic heart disease, resulting in decreases in hemoglobin levels.[4] In the current study, the PA rate was 17.63% and HAA rate was 15.81%. In-hospital mortality rate was 4.26%. Both anemia at admission and HAA were independent risk factors for in-hospital deaths in ACS patients. HAA was associated with advanced age, high CHA2DS2–VASc score, low eGFR, and high fasting blood glucose. Anemia at admission was associated with older age, female sex, lower smoking rates, high CHA2DS2–VASc score, low eGFR, GGT, albumin and total cholesterol and high CRP. In both randomized trials and meta-analyses, anemia at presentation was almost always associated with worse short- and long-term outcomes and increased mortality.[5–9,13] On the other hand, some comprehensive studies have reported no significant association between anemia and coronary heart disease mortality after adjustment for traditional cardiovascular disease risk factors and other covariates.[34,35] They argued that this effect of anemia is a reflection of other risk factors. Several preexisting factors including smoking, hyper-lipidemia, angina, previous myocardial infarction, previous heart failure, previous stroke, peripheral vascular disease, diabetes mellitus, chronic obstructive pulmonary disease, renal disease and previous coronary intervention were shown to be independently associated with anemia.[36] However, according to the multivariate analysis results in our study, anemia was determined to be a risk factor for in-hospital mortality in ACS, independent of other factors. In any anemic patient at risk for cardiovascular disease, or in a patient hospitalized and treated for ACS who has the factors associated with anemia found in our study, addressing the mechanisms underlying the development of anemia, taking measures to prevent anemia from occurring, and ameliorating anemia that does occur may help overcome or reduce the potential adverse prognostic impact of anemia in the ACS setting.

It has long been known that inflammation can contribute to vascular damage, atherogenesis, atherosclerotic plaque rupture and thrombosis.[19] Several studies have reported that various markers of inflammation can predict poor short- and long-term prognosis in ACS patients.[19,20] In this presented study, among the included laboratory parameters, only WBC elevation was found to be an independent risk factor for increased in-hospital mortality. In addition to many inflammatory blood parameters, blood leukocyte count has been reported in many previous studies to be an important biomarker for these disease processes and a risk factor for acute myocardial infarction, coronary artery disease, coronary heart disease and stroke, and to be associated with mortality from all these causes.[19,20] For example, one study showed that WBC was an important predictor of death between the first 30 days and 6 months following acute myocardial infarction.[20] In another study, high WBC was associated with in-hospital mortality.[1] On the other hand some studies did not find the initial WBC count to be associated with short-term mortality in patients with ACS.[21] When the results of the current study are considered together with those of most previous studies, patients with elevated WBC at the time of ACS diagnosis may be considered to be at higher risk for mortality and additional precautions may be required for these patients.

In light of the findings from this study, it is important to consider the implications for clinical practice. The identification of anemia at admission, as well as HAA, as independent risk factors for in-hospital mortality in ACS patients is indicative that monitoring and early intervention for these properties would be beneficial. Addressing anemia, whether present at admission or acquired during hospitalization, may improve patient outcomes. Clinicians should be aware of the risks associated with these conditions, particularly in patients with advanced age, elevated CHA2DS2-VASc scores, and impaired renal function. Furthermore, the association of high WBC count with mortality emphasizes the need to assess inflammatory markers as part of routine care in ACS. Therefore, we believe the comprehensive and individualized approach to managing ACS should consider anemia-related complications as well as traditional risk factors.

Some limitations of the study are as follows. It is a two-center study. Therefore, the generalizability of the results is limited. The fact that the data was obtained retrospectively limited the investigation of new variables. As the most important outcome of the study, only in-hospital mortality was investigated. Short-, medium- and long-term mortality rates after discharge and their relationship with anemia and other variables have not been investigated. Since there was no control group, anemia rates could not be compared with rates in the normal population. To ensure temporal standardization between patients, laboratory data were included in the study using blood samples taken before angiography.

Therefore, the fasting state of the patients at the time of blood collection could not be guaranteed. Consequently, the reliability of glucose and lipid values may be questionable. In-hospital mortality occurred in only 14 patients. Therefore, the analysis of variables associated with mortality may have been affected by this low number.

Conclusion

In patients diagnosed with ACS, the PA rate was 17.63% and the HAA rate was 15.81%. Previous history of coronary artery disease, presence of anemia at admission, HAA, and high WBC were the independent risk factors for in-hospital mortality. Older age, high CHA2DS2–VASc score, low eGFR and high fasting blood glucose were associated with HAA. It is therefore conceivable that in-hospital mortality rates due to ACS can be reduced if management is based on the assessment of risks with respect to current anemia at the time of ACS diagnosis and other risk factors for HAA.

Data Sharing Statement

The datasets generated and analyzed during the current study are not publicly available because of further study in this area but are available from the corresponding author upon reasonable request.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Non-invasive Clinical Research Ethics Committee of Istanbul Medipol University (Decision date: 04.01.2024, decision no: 20).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare in this work.

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