Patients with anemia on admission who have undergone primary angioplasty for ST elevation myocardial infarction: in-hospital and long-term clinical outcomes

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Objective **We investigated the in-hospital and long-term follow-up (mean 21 months) results of patients with and without anemia on admission and who have undergone primary angioplasty for ST elevation myocardial infarction (STEMI).**

Study design **A total of 2509 patients (616 patients with anemia on admission, 1893 patients without anemia on admission), who were treated with primary angioplasty due to STEMI, were included in this study. Demographics and basic clinical features of the patients, outcomes of the primary angioplasty procedures, and clinical course of the patients during and a mean period of 21-month follow-up after hospitalization were retrospectively evaluated. All the parameters were compared between anemic and nonanemic groups.**

Results **The mean age of the patients in anemic group was found to be higher than nonanemic group (61.5 ± 11.4 vs. 54.8 ± 11.4, $P < 0.001$). The rates of death, major cardiac events, and severe cardiac insufficiency were significantly higher in anemic patients during hospitalization period. Moreover, frequency of death was also higher in anemic patients when compared with the nonanemic ones after a mean follow-up period of 21 months ($P < 0.001$). Anemia on admission is an independent predictive factor for mortality in patients with STEMI who were treated with primary angioplasty (odds ratio: 2.2; 95% confidence interval: 1.2–4.0; $P < 0.009$).**

Conclusion **Patients with anemia on admission initially have high-risk profiles regarding their worse clinical outcomes during and 21 months after hospitalization. In accordance with the suggestion of the evidence-based medicine we conclude that etiology of anemia should be meticulously investigated and the oxygenization of the tissue should be provided with the appropriate treatment.** *Coron Artery Dis* **22:375–379 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Anemia is a common problem among patients with ST elevation myocardial infarction (STEMI) and is associated with a poor prognosis [1–3]. As myocardial ischemia is expected to occur along with elevated need for oxygen in anemic patients, anemia can induce arrhythmias and may lead to enlargement of the infarct area [4]. Lower hemoglobin levels have been consistently associated with adverse cardiovascular outcomes in patients with congestive heart failure [5–7], in patients undergoing a percutaneous coronary intervention (PCI) [8] or coronary artery bypass surgery [9].

To date, only a few data exist on the role of anemia on admission in patients with STEMI treated with PCI [1,4]. In this study, we aimed to evaluate in-hospital and long-term mortality in anemic patients who were admitted with STEMI and received primary percutaneous treatment.

Patients and methods

Patient population

In this study, 2509 patients who were diagnosed with STEMI in emergency department of our hospital and received coronary angiography within the first 12 h of the onset of symptoms (within 18 h of the onset of symptoms for patients with hemodynamic instability and persistent chest pain) were included. The following criteria were used for the diagnosis of STEMI: (i) elevated ST segment in more than or equal to two contiguous leads (≥ 2 mm in precordial leads and ≥ 1 mm in extremity leads) or left bundle branch block with a new onset, (ii) ischemic chest pain lasting for more than 30 min, and

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(iii) treatment with primary PCI (angioplasty and/or stent deployment). The study protocol was approved by the ethics committee of the hospital.

Coronary angiography, primary angioplasty, and stent implantation

All patients received chewable aspirin (300 mg, unless contraindicated), and clopidogrel (300-mg loading dose) before coronary angiography. Angiographic data of the patients were obtained from the cardiac catheterization laboratory records. Emergency coronary angiography was performed by the percutaneous femoral approach. After femoral artery punction, each patient received a bolus dose of heparine (10 IU). Blood flow in the infarct-related artery was assessed according to the Thrombolysis in Myocardial Infarction (TIMI) classification (TIMI 0, 1, 2, 3). Primary angioplasty (balloon angioplasty and/or stent implantation) was applied only on the infarct-related artery depending on the lesion type. After angioplasty, all patients were admitted to the coronary care unit where 500 IU/h of intravenous heparin infusion or subcutaneous enoxaparin of 1 mg/kg per day was given; 100 mg of aspirin and 75 mg of clopidogrel were continued in all patients. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the operator. Concomitant medical treatment with β-blockers, angiotensin-converting enzyme inhibitors, and statins was prescribed according to American College of Cardiology/American Heart Association guidelines. Laboratory values of the patients were evaluated by analyzing the blood collected before the primary PCI.

Follow-up

Follow-up data were obtained from hospital records or by interviewing (directly or by telephone) patients, their families, or their personal physicians.

Definitions

Successful procedure was defined as establishing TIMI-III flow in the infarct-related artery along with a residual stenosis below 50%. Target vessel revascularization (TVR) was defined as an angioplasty or a coronary artery bypass surgery operation due to restenosis or reocclusion in the infarct-related artery. Major cardiac events (MACE) were defined as cardiovascular death, reinfarction, and repeat TVR (percutaneous or surgical). Reinfarction was defined as elevation of serum CK-MB enzyme levels by twice the upper limit of normal and ST-segment re-elevations. Cardiovascular mortality was defined as unexpected sudden death or death associated with acute myocardial infarction, heart failure, or arrhythmia. Advanced heart failure was defined as New York Heart Association classification of more than or equal to 3. Multivessel disease was defined by a stenosis of more than 50% in three major epicardial coronary arteries.

Contrast nephropathy was defined as an increase in the baseline serum creatinine level higher than 25% or more than or equal to 0.5 mg/dl within the first 72 h of contrast agent delivery. Renal failure was defined as a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2, which was estimated by the simplified Modification of Diet in Renal Disease equation. The diagnosis of diabetes mellitus was defined as having a history of antidiabetic drugs use or insulin therapy, whereas history of antihyperlipidemic drug use or a total cholesterol level more than or equal to 200 mg/dl was identified as hypercholesterolemia. Major hemorrhage was defined as a bleeding, which requires more than or equal to 2 units of blood transfusion. On the basis of the definition of the World Health Organization, anemia was described as the presence of a hemoglobin level of less than 13 g/dl in men and 12 g/dl in women.

Statistical analysis

Quantitative variables were expressed as mean value ± standard deviation, and qualitative variables were expressed as percentage. Comparison of parametric values between two groups was performed by means of the two-tailed Student *t*-test. Categorical variables were compared by the likelihood ratio χ^2-test or the Fisher exact test. Backward stepwise multivariate Cox regression analysis was performed to identify independent predictors of long-term cardiovascular mortality. The cumulative survival curves for long-term cardiovascular mortality were constructed with the use of the Kaplan–Meier method with differences assessed with the log-rank test. A P value of less than 0.05 was considered statistically significant. All statistical studies were carried out with SPSS program (version 15.0; SPSS, Chicago, Illinois, USA).

Results

Clinical and demographic characteristics

Clinical and demographic characteristics of the patients are shown in Table 1. In view of both groups (616 patients with anemia on admission, 1893 patients without anemia on admission), anemic patients were observed to be older (mean age: 61.5 ± 11.4 vs. 54.8 ± 11.4, $P < 0.001$). Although women were more anemic than men, the incidences for

Table 1 Baseline characteristics of study patients

	Anemia (n=616)	Nonanemia (n=1893)	P value
Age [years (SD)]	61.5 ± 11.4	54.8 ± 11.4	<0.001
Women sex [n (%)]	161 (26.1)	259 (13.6)	<0.001
DM [n (%)]	166 (26.9)	446 (23.5)	0.09
Hypertension [n (%)]	302 (49)	726 (38.3)	<0.001
Family history for CAD [n (%)]	95 (15.4)	342 (18)	0.15
Hypercholesterolemia [n (%)]	177 (28.8)	740 (39.1)	<0.001
Current smoker [n (%)]	327 (53)	1235 (65.2)	<0.001
Dialysis history [n (%)]	5 (0.8)	3 (0.1)	0.01
Bypass [n (%)]	16 (2.6)	57 (3)	0.6
MI history [n (%)]	86 (13.9)	185 (9.7)	0.04
PCI [n (%)]	73 (11.8)	122 (6.4)	<0.001
Anterior MI [n (%)]	274 (44.4)	939 (49.6)	0.03

CAD, coronary artery disease; DM, diabetes mellitus; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation.

history of hypertension, dialysis, myocardial infarction, and angioplasty were higher in the anemic patients. As we found similar anemia frequencies for diabetes mellitus, family history for coronary artery disease, and infarct localization (particularly anterior wall infarction), current smoker demonstrated a lower anemia frequency.

Angiographic and procedural characteristics

Angiographic and procedural characteristics for both of the groups are shown in Table 2. Regarding infarct-related artery localization; left anterior descending artery, circumflex coronary artery, and right coronary artery lesions were observed to have significantly higher incidences among the anemic patients, whereas we found no significant difference with regard to left main coronary artery, intermediary artery, and saphenous vein graft lesions. Multivessel disease and unsuccessful procedure were more common in the anemic patients. There was no significant difference between the two groups in terms of contrast nephropathy and tirofiban use.

Biochemical parameters

Biochemical parameters are shown in Table 3.

In-hospital and long-term results

In-hospital results are shown in Table 4. A total of 66 of the STEMI patients who received primary angioplasty, developed mortality due to cardiovascular events. Cardiovascular mortality was 5% ($n = 31$) in the anemic and 1.8% ($n = 35$) in the nonanemic patients. Similarly, MACE, cardiopulmonary resuscitation, serious ventricular arrhythmia (ventricular tachycardia/fibrillation), advanced heart failure, need for inotropic agents, use of intra-aortic balloon pump, major hemorrhage, and atrioventricular complete block were more common in the anemic patients. Length of hospital stay was significantly longer in the anemic patients. Long-term results are shown in Table 5. During the 21-month follow-up period, while the incidence of mortality and advanced heart failure was found to be significantly higher in anemic patients, other parameters such as TVR, MACE, and reinfarction were found to be similar in the two groups.

Table 2 Angiographic and procedural characteristics of patients

	Anemia ($n=616$)	Nonanemia ($n=1893$)	*P* value
LMCA [*n* (%)]	0 (0)	2 (0.1)	0.34
LAD [*n* (%)]	276 (44.8)	946 (49.9)	0.02
CX [*n* (%)]	73 (11.8)	263 (13.8)	0.02
RCA [*n* (%)]	261 (42.3)	666 (35.2)	0.02
Intermediate artery [*n* (%)]	0 (0)	4 (0.2)	0.36
Bypass graft [*n* (%)]	6 (0.9)	12 (0.6)	0.27
Multivessel disease [*n* (%)]	195 (31.7)	440 (23.2)	<0.001
CIN [*n* (%)]	156 (25.4)	459 (24.2)	0.57
Tirofiban [*n* (%)]	297 (48.3)	939 (49.6)	0.58
Stent [*n* (%)]	507 (82.3)	1625 (85.8)	0.03
Success of the procedure [*n* (%)]	551 (89.4)	1746 (92.2)	0.03

CIN, contrast-induced nephropathy; CX, circumflex coronary artery; LAD, left anterior descending coronary artery; LMCA, left main coronary artery; RCA, right coronary artery.

Table 3 Laboratory findings of patients

	Anemia ($n=616$)	Nonanemia ($n=1893$)	*P* value
Creatinine (mg/dl; SD)	1.06 ± 0.65	0.94 ± 0.23	<0.001
Glucose (mg/dl; SD)	158 ± 75	153 ± 71	0.12
Platelet (10^3/μl; SD)	261 ± 81	260 ± 69	0.72
Leukocyte (10^3/μl; SD)	11.1 ± 3.6	12.9 ± 3.8	<0.001
Hemoglobin (g/dl; SD)	11.4 ± 1.3	14.3 ± 1.1	<0.001
Hematocrit (%; SD)	33.9 ± 3.7	41.9 ± 3.5	<0.001
Mean platelet volume (fl; SD)	8.5 ± 1.0	8.5 ± 1.0	0.91
GFR (MDRD) <60 ml/min/1.73 m^2 (SD)	81 ± 26	90 ± 22	<0.001

GFR, glomerular filtration rate; MDRD, modification of diet in renal disease; SD, standard deviation.

Table 4 In-hospital cardiac events and complications

	Anemia ($n=616$)	Nonanemia ($n=1893$)	*P* value
In-hospital mortality [*n* (%)]	31 (5.0)	35 (1.8)	<0.001
Reinfarction [*n* (%)]	14 (2.2)	36 (1.9)	0.56
Target-vessel revascularization [*n* (%)]	33 (5.3)	76 (4.0)	0.15
MACE [*n* (%)]	61 (9.9)	104 (5.4)	<0.001
Cardiopulmonary resuscitation [*n* (%)]	34 (5.5)	46 (2.4)	<0.001
Renal failure requiring dialysis [*n* (%)]	7 (1.1)	9 (0.4)	0.07
Serious ventricular arrhythmia [*n* (%)]	31 (5.0)	56 (2.9)	0.01
Advanced heart failure [*n* (%)]	94 (15.2)	212 (11.1)	0.007
Inotropic agents [*n* (%)]	56 (9.0)	111 (5.8)	0.005
Intra-aortic balloon pump [*n* (%)]	29 (4.7)	47 (2.4)	0.005
Complete atrioventricular block requiring transient pacemaker [*n* (%)]	37 (6.0)	50 (2.6)	<0.001
New atrial fibrillation [*n* (%)]	9 (1.4)	24 (1.2)	0.71
Major bleeding requiring blood transfusion [*n* (%)]	65 (10.5)	27 (1.4)	<0.001
Time of hospital stay (days; SD)	7.8 ± 4.8	6.9 ± 3.4	<0.001

MACE, major adverse cardiac events (cardiovascular death, reinfarction, target vessel revascularization); SD, standard deviation.

Table 5 Long-term cardiac events

	Anemia ($n=574$)[a]	Nonanemia ($n=1823$)[b]	*P* value
Cardiovascular mortality [*n* (%)]	56 (9.7)	72 (3.9)	<0.001
Advanced heart failure [*n* (%)]	66 (11.5)	136 (7.4)	0.005
Reinfarction [*n* (%)]	47 (8.3)	175 (9.6)	0.39
Target-vessel revascularization [*n* (%)]	107 (18.7)	333 (18.2)	0.73
MACE [*n* (%)]	157 (27.3)	430 (23.6)	0.08

MACE, major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization).
[a]There is no follow-up for 11 patients and 31 patients died in hospital.
[b]There is no follow-up for 35 patients and 35 patients died in hospital.

Univariate and multivariate predictors of long-term mortality

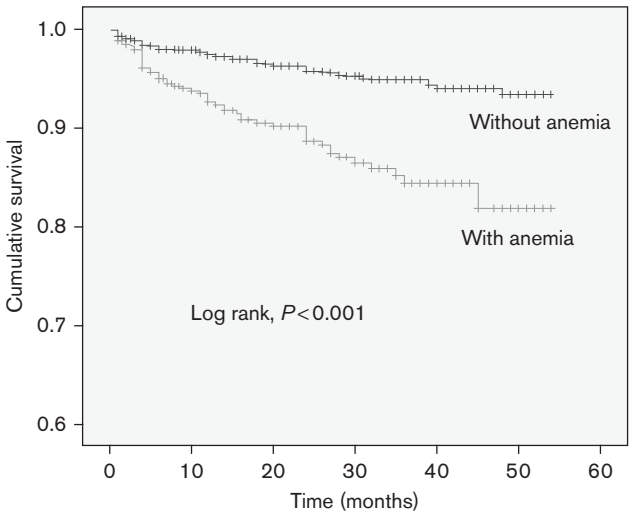
Univariate and independent predictors of long-term mortality are shown in Table 6. Multivariate analysis revealed unsuccessful procedure, GFR of less than 60 ml/min/1.73 m^2, diabetes mellitus, and anemia on admission, as the independent predictors of long-term mortality. The presence of anemia on admission was found to increase the mortality independently (odds rate: 2.2; 95% confidence interval: 1.2–4.0; $P < 0.009$). Long-term survival curves for both groups are shown in Fig. 1.

Table 6 Predictors of long-term cardiovascular mortality

	Odds ratio	95% CI	*P* value
Univariate predictors			
Unsuccessful procedure	9.68	5.81–16.1	<0.001
GFR (MDRD) <60 ml/min/1.73 m^2	9.44	5.66–15.81	<0.001
DM	5.16	3.07–8.67	<0.001
Age >75 (years)	4.89	2.97–8.07	<0.001
Anemia at admission	2.81	1.72–4.60	<0.001
Multivessel disease	2.08	1.26–3.43	0.004
MI history	1.88	0.97–3.67	0.06
Tirofiban	0.59	0.35–0.98	0.04
Independent predictors			
Unsuccessful procedure	6.2	3.3–11.4	<0.001
GFR (MDRD) <60 ml/min/1.73 m^2	6.1	3.3–11.4	<0.001
DM	3.8	2.1–7.0	<0.001
Anemia at admission	2.2	1.2–4.0	0.009

CI, confidence interval; DM, diabetes mellitus; GFR, glomerular filtration rate; MDRD, modification of diet in renal disease; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Fig. 1



Kaplan–Meier curve for long-term cardiovascular mortality in patients with anemia versus without anemia.

Discussion

Our study, in which anemic and nonanemic patients with STEMI were followed up for a period of 21 months, revealed the following principal results: (i) in STEMI, anemic patients were observed to be older and have a high-risk profile; (ii) in-hospital events (death, advanced heart failure) were more common among anemic patients; and (iii) cardiovascular mortality occurred more frequently in the long-term follow-up in anemic patients.

Similar to other studies conducted on myocardial infarction, anemic patients were older [3,4,10,11] and accompanying comorbid conditions (e.g. hypertension) had a higher incidence [3,11] in our study, as well. As shown by other studies, our study found higher blood creatinine levels and lower GFR in anemic patients [3,10,12]. This may be explained by the fact that anemic patients were more aged; hypertension and history of dialysis were more common in them.

Studies that evaluate the influence of anemia over in-hospital mortality among patients with myocardial infarction show contentious results, which may be due to a low number of patients with STEMI and inclusion of low-risk patients [4]. Similar to our study, Nikolsky *et al.* [1] found that anemia increased the in-hospital mortality. Anemia may show its effect on in-hospital mortality by increasing the oxygen need of myocardium, activating the sympathetic nerve system, and enlarging the infarct area [4,10,13] as well as causing arrhythmias such as ventricular tachycardia and ventricular fibrillation due to reduced blood oxygen level. In our study, enlargement of the infarct area induced by anemia may explain advanced heart failure.

In our study, the success rate of PCI was found to be lower in the anemic patients, which was a finding consistent with the literature [4] and it became the most powerful predictor of mortality during the 21-month follow-up (odds ratio: 6.2, 95% confidence interval: 3.3–11.4; $P < 0.001$). Higher incidence of accompanying diseases and multivessel disease, advanced age, inclusion of more women than men, and lower incidence of stent placement, may be the underlying causes of unsuccessful procedure.

Higher mortality rate during 21-month follow-up period may be stemming from the high incidence of accompanying comorbid conditions (e.g. advanced age and hypertension), higher mortality rate in women populations [14], persistence of the heart failure during the postdischarge period due to diffuse infarct area, persistent myocardial ischemia due to inadequate treatment of factors causing anemia, and reduced use of required drugs such as aspirin and clopidogrel among anemic patients due to their gastrointestinal and hemorrhagic effects.

In conclusion, patients with STEMI who were anemic on admission and received primary angioplasty demonstrated a higher rate of mortality at the end of a 21-month follow-up comprising the in-hospital and postdischarge periods. Therefore, being anemic on admission was observed to be a predictor of mortality. Therefore, in compliance with the evidence-based medical recommendations, etiology of anemia should be screened in the hospital and the proper treatment should be started without delay, complications that would lead to anemia should be avoided, and tissue oxygenation should be increased by blood transfusion in case of need. As a result mortality due to anemia could be prevented.

Limitations of the study

Several limitations should be taken into consideration while assessing the results of our study. First, our single-center study had a retrospective design; therefore, it has certain disadvantages of a retrospective study. Second, the effect of etiology of anemia over prognosis of patients

with a history of myocardial infarction was ignored. Therefore, the real etiology of the anemia may have affected the prognosis in a more influential way.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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