The relationship between admission hemoglobin level and left ventricular systolic functions in patients with first ST-segment elevated myocardial infarction

İlk ST yükselmeli miyokart enfarktüslü hastalarda başvuru sırasındaki hemoglobin düzeyi ile sol ventrikül sistolik fonksiyonu arasındaki ilişki

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Objectives: The goal of this study was to evaluate the relationship between admission hemoglobin levels and left ventricular systolic functions in patients admitted with first ST-segment elevated myocardial infarction (STEMI).

Study design: The study was conducted prospectively in three centers in 483 consecutive patients (402 men, 81 women; mean age 56.5±11.2 years; range 24 to 74 years) with first STEMI. All patients were evaluated by echocardiography after a mean of 2.4 days of admission. Evaluation of left ventricular systolic functions included measurements of ejection fraction (EF), wall motion score index (WMSI), and tissue Doppler S wave velocities at four different localizations (anterior, inferior, lateral, posterior septum). Hemoglobin levels were measured within one hour of admission. Anemia was defined according to the World Health Organization criteria (hemoglobin <13.0 g/dl in men and <12.0 g/dl in women). Echocardiographic characteristics of the patients with and without anemia were compared.

Results: Anemia was detected in 67 patients (13.9%). There were no significant differences between patients with and without anemia with respect to left ventricular end-systolic and end-diastolic diameters, wall thickness, WMSI, and EF. The mean EF in the anemic group (47.5%) was lower than that of the patients without anemia (48.5%), but this difference was not significant. All Sm velocities were lower in the anemic group, but only septal mitral annular Sm velocity reached statistical significance (p=0.048). There was no correlation between hemoglobin levels and EF (r=0.027, p=0.55).

Conclusion: Our findings suggest that mild to moderate anemia has no deleterious effect on systolic function in patients with first STEMI.

Key words: Anemia/complications; hemoglobins; myocardial infarction; ventricular dysfunction, left.

Amaç: Bu çalışmada, ilk ST yükselmeli ME (STYME) nedeniyle yatırılan hastalarda başvuru sırasındaki hemoglobin düzeyi ile sol ventrikül sistolik fonksiyonları arasındaki ilişki değerlendirildi.

Çalışma planı: Çalışmaya, ileriye dönük olarak, üç farklı merkezde ilk STYME tanısıyla yatırılan 483 hasta (402 erkek, 81 kadın; ort. yaş 56.5±11.2; dağılım 24-74) alındı. Tüm hastalar, yatıştan ortalama 2.4 gün sonra ekokardiyografi ile değerlendirildi. Sol ventrikül sistolik fonksiyonlarının değerlendirilmesi için ejeksiyon fraksiyonu (EF), duvar hareket skor indeksi (DHSİ) ve sol ventrikülün dört farklı noktasından (anteriyor, inferiyor, lateral, posteriyor septum) doku Doppler S dalga hızları ölçüldü. Hemoglobin düzeyleri yatışın ilk saati içinde belirlendi. Anemi, Dünya Sağlık Örgütü ölçütlerine göre tanımlandı (hemoglobin erkeklerde <13 gr/dl, kadınlarda <12 gr/dl). Anemi olan ve olmayan hastaların ekokardiyografik özellikleri karşılaştırıldı.

Bulgular: Anemi 67 hastada (%13.9) saptandı. Anemi olan ve olmayan hastalar arasında sol ventrikül sistol ve diyastol sonu çapları, duvar kalınlıkları, DHSİ ve EF açısından anlamlı farklılık saptanmadı. Anemisi olanların EF değeri (%47.5) anemisi olmayanlardan (%48.5) daha düşüktü, fakat aradaki fark istatistiksel anlamlılık göstermedi. Miyokart S dalga hızlarının tümü anemi olan hastalarda daha düşük bulundu, fakat sadece septal bölgeden yapılan ölçümlerde sonuç anlamlı farklılık gösterdi (p=0.048). Hemoglobin düzeyi ile EF arasında ilişki bulunmadı (r=0.027, p=0.55).

Sonuç: Bulgularımız. ilk STYME geçiren hastalarda hafif ve orta derecede aneminin sol ventrikül sistolik fonksiyonları üzerinde zararlı etkisi olmadığını göstermektedir.

Anahtar sözcükler: Anemi/komplikasyon; hemoglobin; miyokart enfarktüsü; ventrikül disfonksiyonu, sol.

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Anemia is common in patients with acute coronary syndrome admitted to cardiac intensive care units and has been shown to be present in 6.4% to 43% of patients presenting with acute myocardial infarction (AMI).[1-4] It has been demonstrated that anemia increases adverse cardiovascular outcomes and risk for death in patients with myocardial infarction both in the short- and long-term.[2-5]

The degree of left ventricular (LV) systolic dysfunction is strongly associated with poor prognosis after myocardial infarction.[6,7] Anemia worsens myocardial ischemia in AMI as a result of decreased oxygen content of the blood supplied to the myocardium in the setting of increased myocardial oxygen demand for a higher cardiac output to maintain adequate systemic oxygen delivery.[8-10] Anemia is an important predictor for the development of heart failure after myocardial infarction.[11] In patients with anemia, more severe LV systolic dysfunction can be expected after myocardial infarction.

The goal of our study was to evaluate the relationship between admission hemoglobin levels and the degree of LV systolic dysfunction in patients admitted to the coronary intensive care unit with first ST-segment elevation myocardial infarction (STEMI).

PATIENTS AND METHODS

Study population. This study was conducted prospectively in three centers in 498 consecutive patients who were admitted with first STEMI between May 2004 and January 2007. Ethical committee approval from each center and informed consent from each patient were obtained. All patients were treated according to the decision of the pursuing physician.

Acute myocardial infarction was defined as the presence of ST-segment elevation of more than 1 mm in two contiguous leads and increased serum troponin level (at least threefold above the upper normal limit) in the setting of clinical symptoms.[12]

First STEMI was accepted as the inclusion criterion of the study. Exclusion criteria were previous myocardial infarction, cardiogenic shock, inadequate echocardiographic imaging, malignant disease, and previous cerebrovascular disease. Fifteen patients who met one or more of the exclusion criteria were not included in the assessments and data on 483 patients (402 men, 81 women; mean age 56.5±11.2 years; range 24 to 74 years) were analyzed.

Echocardiographic assessment. Echocardiographic examination was made as soon as clinical stability of the patients was achieved after admission to the coronary intensive care unit (mean 2.4 days). All patients were evaluated by two-dimensional and pulsed-wave tissue Doppler echocardiography using the Vivid 7 or 5 echocardiography machine system (General Electric, Horten, Norway) with a 2.5-5 MHz transducer. Left ventricular systolic functions were assessed by measurements of ejection fraction (EF), wall motion score index (WMSI), and tissue Doppler S wave velocities measured at different localizations in the left ventricle.[13]

Wall motion score index (WMSI) was calculated as recommended by the American Society of Echocardiography using a 16-segment model. Regional wall motion in each segment was graded visually using a four-point scoring system: 1=normal (normal wall motion); 2=hypokinesia (marked decrease in endocardial motion); 3=akinesia (absence of inward wall motion); 4=dyskinesia (paradoxical wall motion away from the LV lumen in systole). Patients in whom evaluation of more than two segments in the infarct zone or four or more of the 16 segments could not adequately be visualized were not included in the study. Wall motion score index was derived by dividing the sum of all scores by the number of segments visualized. Ejection fraction was determined from apical two- and four-chamber views using the Simpson's modified biplane formula and taking the mean values. Pulsed tissue Doppler samples were recorded from four different locations by placing 2.9-mm sample volumes at the level of the mitral annulus (anterior, inferior, lateral, posterior septum), using the apical two- and four- chamber and long-axis views. At each location of examination, peak systolic wave (S), peak early diastolic wave (E), and peak late diastolic wave (A) were determined. All echocardiographic examinations were performed in each center by one cardiologist who was blind to laboratory data of the patients.

Hematological and biochemical analysis. Hemoglobin levels were measured within one hour of admission to the cardiac intensive care unit. Anemia was defined according to the World Health Organization criteria (hemoglobin <13.0 g/dl in men and <12.0 g/dl in women).[14] The patients were recorded as anemic on admission based on the hemoglobin levels below the threshold value. Biochemical and hematological measurements were made on automated analyzers. Glomerular filtration rate was estimated using the Cockcroft-Gault formula.

Statistical analysis. Continuous variables were expressed as mean±standard deviation (SD) and categorical variables as percentages. Continuous vari-

Table 1. Baseline clinical and laboratory characteristics of the study groups

	All patients (n=483)			Anemic (n=67)			Nonanemic (n=416)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (years)			56.5±11.1			62.5±11.6			55.6±10.7	**<0.001**
Sex										**0.028**
Males	402	83.2		50	74.6		352	84.6		
Female	81	16.8		17	25.4		64	15.4		
Diabetes mellitus	84	17.4		20	30.0		64	15.4		**0.03**
Hypertension	150	31.1		25	37.3		125	30.1		0.23
Smoking	310	64.2		38	56.7		272	65.4		0.14
Myocardial infarction										
Anterior wall	257	53.2		34	50.8		223	53.6		0.36
Nonanterior wall	226	46.8		35	52.2		191	45.9		0.34
Thrombolytic treatment	200	41.4		21	31.3		179	43.0		0.88
Primary PCI	176	36.4		25	37.3		151	36.3		0.80
Complete ST resolution	347	71.8		43	64.2		304	73.1		0.16
Laboratory findings										
Baseline hemoglobin (g/dl)			14.4±1.6			11.8±1.0			14.9±1.2	**<0.001**
Baseline hematocrit (%)			42.5±4.4			35.9±3.6			43.6±1.5	**<0.001**
Creatinine (mg/dl)			1.0±0.3			1.1±0.4			1.0±0.2	0.08
Creatinine clearance (ml/min)			86.5±27.0			75.5±20.0			88.4±26.0	**<0.001**
Peak CK (u/l)			2435±1676			2089±1221			2491±1732	**0.049**
Peak CK-MB (u/l)			254±191			259±221			254±187	0.860
LDL-cholesterol (mg/dl)			125±37			115±32			127±37	**0.027**
HDL-cholesterol (mg/dl)			41±11			40±9			41±11	0.59
Triglycerides (mg/dl)			127±81			110±58			130±84	0.082
Time to echocardiography (days)			2.4±1.4			2.6±1.6			2.4±1.3	0.26

PCI: Percutaneous coronary intervention; CK: Creatine kinase.

ables were compared using the Student's t-test or Mann-Whitney U-test, where appropriate. Categorical variables were compared using the chi-square test. Correlations were sought using the Spearman test or Pearson test, where appropriate. For all tests, a *p* value of less than 0.05 was considered statistically significant. All statistical calculations were made using the SPSS statistical software package.

RESULTS

Anemia was detected in 67 patients (13.9%). Hemoglobin levels were greater than 8 g/dl in all the patients. The mean hemoglobin level was 14.3±1.7 (g/dl) in men and 13.2±1.5 g/dl in women. Anemia was more frequent in women (n=17/81, 21%) than in men (n=50/402, 12.4%). The characteristics of the patients with and without anemia are shown in Table 1. Older age, female gender, and diabetes mellitus were found to be more common in the anemic group.

Echocardiographic findings. Echocardiographic features of the patients with and without anemia are summarized in Table 2. There were no significant differences between the two groups with respect to LV end-systolic and end-diastolic diameters, wall

Table 2. Echocardiographic findings of the study groups

	All patients (n=483) (Mean±SD)	Anemic (n=67) (Mean±SD)	Nonanemic (n=416) (Mean±SD)	*p*
Ejection fraction (%)	48.4±9.5	47.5±8.3	48.5±9.8	0.46
Wall motion score index	1.58±0.35	1.59±0.38	1.58±0.35	0.78
End-diastolic diameter (cm)	5.0±0.5	5.1±0.5	5.0±0.5	0.6
End-systolic diameter (cm)	3.6±0.6	3.7±0.6	3.6±0.6	0.6
Systolic mitral annular velocity (Sm)				
Anterior Sm (cm/sec)	6.75±2.10	6.47±1.97	6.80±2.10	0.238
Inferior Sm (cm/sec)	7.10±1.80	6.65±1.92	7.10±1.80	0.064
Lateral Sm (cm/sec)	7.60±2.20	7.20±2.40	7.65±2.20	0.135
Septal Sm (cm/sec)	6.30±1.70	5.90±1.60	6.36±1.70	**0.048**

Table 3. Echocardiographic findings of the patients who received reperfusion treatment (primary percutaneous coronary intervention and thrombolytic treatment)

	All patients (n=376) (Mean±SD)	Anemic (n=45) (Mean±SD)	Nonanemic (n=331) (Mean±SD)	*p*
Ejection fraction (%)	48.6±9.6	48.1±8.2	48.7±9.8	0.7
Wall motion score index	1.57±0.35	1.55±0.36	1.57±0.35	0.7
End-diastolic diameter (cm)	5.0±0.5	5.0±0.5	5.0±0.5	0.4
End-systolic diameter (cm)	3.6±0.6	3.7±0.6	3.5±0.6	0.2
Systolic mitral annular velocity (Sm)				
Anterior Sm (cm/sec)	6.9±2.1	6.6±2.2	6.9±2.1	0.3
Inferior Sm (cm/sec)	7.2±1.8	6.7±1.9	7.3±1.8	0.06
Lateral Sm (cm/sec)	7.8±2.2	7.5±2.6	7.8±2.2	0.3
Septal Sm (cm/sec)	6.5±1.7	6.1±1.7	6.5±1.6	0.1

thickness, WMSI, and EF. The mean EF of the patients was 48.4±9.5%. The mean EF in the anemic group was lower than that of the patients without anemia, but this difference did not reach statistical significance. The Sm velocities were lower in the anemic group globally, but only septal mitral annular Sm velocities reached statistical significance. There was no correlation between hemoglobin levels and EF (r=0.027, p=0.55). Echocardiographic features of the patients with and without anemia, who received reperfusion treatment (primary percutaneous coronary intervention and thrombolytic treatment) are summarized in Table 3.

DISCUSSION

We investigated the effects of mild to moderate anemia on LV systolic functions in patients admitted with first STEMI. We found that mild to moderate anemia did not affect EF or WMSI significantly during the course of AMI.

The mean EF in the anemic group was lower than that of the patients without anemia, but this difference was not significant. Nikolsky et al.[4] examined STEMI patients undergoing primary percutaneous coronary intervention and determined EF angiographically. Similar to our results, they found no difference between the mean EFs of patients with and without anemia (50% *vs*. 50%, p=0.46). Wall motion score index is a quantitative and more objective measure of LV systolic dysfunction and has been shown to be correlated with the extent of the infarct area.[15] In our study, the mean WMSI did not differ significantly between the anemic and nonanemic groups.

The Sm velocities measured at the inferior, anterior, lateral, and septal mitral annular sites were lower in the anemic group, but only the septal mitral annular Sm velocity reached statistical significance. We thought that significantly lower Sm velocity measured from the septal mitral annulus was not sufficient to correlate an unfavorable effect of anemia with systolic function. However, we cannot completely exclude the possibility that lower Sm velocities in anemic patients might be of interest. The subendocardium is the most vulnerable portion of the myocardium to ischemia and the longitudinal fibers are affected more frequently than the circular fibers. Thus, wall motions along the longitudinal axis are affected more severely. Deterioration in LV systolic function is expected first in the longitudinal axis in anemic patients.[16]

Left ventricle systolic functions were found to be highly preserved in our study population. The main reasons for preserved systolic functions may be listed as follows: all the patients were admitted with the first STEMI, most of them were treated with reperfusion therapies (77.9%) with few comorbid diseases. The mean age (56.5 years) can be considered a relatively young age for AMI population. The early successful reperfusion rate based on ECG findings was 71.8%, implying that effective reperfusion therapies were available for most of the patients.

Detrimental factors for LV functions such as lower rate of reperfusion treatment and higher incidence of diabetes mellitus were more common in the anemic group, but it was interesting that LV systolic functions of both groups were similar. This is probably due to the fact that hemoglobin levels in mild-moderate anemia can provide sufficient oxygen required by the jeopardized myocardium. The undesirable effects of mild to moderate anemia can be reduced by the counter regulatory mechanisms of the cardiovascular system, preserving LV systolic functions despite the presence of anemia. It is also possible that the number of anemic patients in our study may be inadequate to show adverse effects of anemia.

The most important factor that determines LV systolic function after AMI is the success of reperfusion treatment.[17-19] Thus, we also investigated the effects of anemia on LV systolic functions in patients receiving reperfusion treatment and found that both anemic and nonanemic groups had similar LV systolic functions. The rate of successful reperfusion treatment was lower in anemic patients compared to nonanemic patients, but this difference was not statistically significant. Mild to moderate anemia had no deleterious effect on the success of reperfusion treatment. The success rates of reperfusion treatment were similar in both groups, suggesting that LV functions of both groups were similar.

Previous studies have demonstrated that mortality rate and the incidence of adverse cardiovascular outcomes after AMI are significantly increased in patients with anemia compared to nonanemic counterparts.[2,4,5] The mechanism underlying increased rates of mortality and adverse cardiovascular events in anemic patients might be associated with other factors rather than increased LV systolic dysfunction. Tachycardia and increased contractility induced by anemia together with increased afterload seen in anemic patients contribute to increased overall ventricular workload. In addition, impaired vasodilator reserve, increased sympathetic tonus, and possible LV hypertrophy induced by long-lasting anemia make LV myocardium more vulnerable to anemia. In addition, anemia itself is a marker of poor general health status. In several studies, anemic patients were found to be older and comorbid conditions like hypertension, diabetes mellitus, and chronic renal disease were more frequently seen in these patients.[4,5] These observations were consistent with our findings. In our study, the mean age was higher, diabetes mellitus was more frequent, and the mean creatinine clearance was lower in the anemic group.

Our study is the first to show the prevalence of anemia in patients with myocardial infarction in Turkish population. We detected anemia in 67 patients (13.9%) with myocardial infarction. The prevalence of anemia in AMI patients was similar to those reported in previous studies.[1,4]

There are some limitations to our study. First, the number of patients with anemia was relatively small (n=67). Second, we did not have a core laboratory to evaluate the hematologic and echocardiographic measurements. Third, medications of the patients were not recorded, but all the patients included in the study were treated according to the recent guidelines.

We concluded that mild to moderate anemia had no deleterious effect on LV systolic functions in patients presenting with first STEMI.

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