Effect of anemia on 1-year mortality in patients with acute myocardial infarction

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Background Limited data are available on the effect of anemia on mortality in patients with acute myocardial infarction (MI).

Methods We examined the association of anemia with mortality at 1 year among 30,341 patients hospitalized with acute MI in 1986 (prethrombolytic era, n = 15,584) and 1996 (thrombolytic era, n = 14,757). The records were obtained from the Myocardial Infarction Data Acquisition System, a database of all patients with MI admitted to nonfederal hospitals in New Jersey.

Results Anemia was present in 996 patients (6.4%) in 1986 and 1510 patients (10.2%, P < .0001) in 1996. In both years, patients with anemia were older, more frequently female and nonwhite, and more likely to have left ventricular dysfunction, non-Q MI and coronary artery bypass graft. In addition, in 1996, patients with anemia were more likely to undergo percutaneous transluminal coronary angioplasty and less likely to have a history of MI. One-year mortality was lower overall in 1996 compared with 1986 (1996 23.6%, 95% CI 22.9-24.3 vs 1986 24.9%, 95% CI 24.2-25.6, P = .0001). In both years, patients with anemia had significantly higher unadjusted risk for 1-year mortality (RR = 1.40, P = .0001 in both years). However, after controlling for demographics, left ventricular dysfunction, arrhythmias, Q versus non-Q MI, comorbid conditions, and revascularization procedures in a multivariable regression model, 1-year mortality in the anemia group was similar to the nonanemia group in both years.

Conclusion In the Myocardial Infarction Data Acquisition System database, anemia appears to have no significant direct effect on 1-year mortality. The higher unadjusted mortality observed among patients with acute MI and anemia is probably the result of older age, higher comorbidity, and more left ventricular dysfunction. (Am Heart J 2002;144:636-41.)

The association of anemia with short- and long-term mortality has been studied in patients with end-stage renal diseases, post-coronary artery bypass graft (CABG), in critically ill patients, and perioperatively, but not in patients with acute coronary syndromes. One recent study of Medicare beneficiaries with acute myocardial infarction (MI) found that transfusing patients with hematocrit values below 30% was associated with reduced 30-day mortality.1 The prognostic importance of anemia in the setting of acute MI is not well defined, and the impact of anemia on long-term survival after MI has not been studied.

A prospective observational study of 2202 patients undergoing CABG in the United States found higher postoperative hematocrit values (>34%) were associated with higher rates of postoperative MI, left ventricular dysfunction (LVD), and mortality.2 In patients with end-stage renal disease, anemia is associated with the development of left ventricular hypertrophy.2 Correction to near-normal hemoglobin values3 or to values above 10 g/dL1 was associated with fewer cardiovascular events, longer duration to first MI, regression of left ventricular hypertrophy, and decreased resting and exercise induced angina. However in a randomized, open-label prospective trial with 29-month follow-up of 1233 patients with end-stage renal disease and history of heart disease, administration of erythropoietin to maintain a normal hematocrit (>42%) was associated with higher rates of acute nonfatal MI and a higher mortality rate compared to low hematocrit of 30%.5 The above studies assessed the association of anemia with short-term mortality and were not conducted in the setting of acute MI.

This retrospective cohort study was conducted to evaluate the effect of anemia on 1-year mortality in patients with acute MI admitted to nonfederal hospitals in New Jersey. Two patient cohorts were investi-
Data source and study population

The study was conducted with the use of the Myocardial Infarction Data Acquisition System (MIDAS). This statewide database provided discharge abstract information on index admissions of all patients (n = 30,341) who were hospitalized with the diagnosis of acute MI in nonfederal hospitals in New Jersey in the years 1986 (n = 15,584) and 1996 (n = 14,757). Patient discharge abstract data (UB-82 and UB-92) were obtained from the New Jersey hospital discharge data system. Hospital discharge records from administrative files were included in the MIDAS database if an International Classification of Diseases, 9th Revision, diagnosis code in the range 410.0-410.9 (acute MI) was either the principal diagnosis or one of the secondary diagnoses. The MIDAS records included codes for procedures and comorbid conditions, and other relevant patient information such as age, sex, race, insurance status, admission, and discharge dates. Composite indices of complications were constructed for LVD and arrhythmia. Anemia was defined as the presence of the disease codes 280.00-281.30, 281.90, 282.00, and 283.00-285.99. The confidentiality of hospital patient records was maintained and the State and Robert Wood Johnson Institutional Review Boards approved MIDAS.

Survival follow-up was performed by matching the MIDAS records with New Jersey death registration files, through the use of specifically designed automated record linkage software (Automatch, Matchware Technologies, Inc, Burtonsville, Md). Patients with the diagnosis of cancer (International Classification of Diseases-9 codes 140.00-208.00) and those hospitalized in another state or federal hospital were excluded from the study. Only the first recorded (index) infarction that occurred in this database was considered.

Statistical analysis

Key baseline demographic and clinical characteristics among patients with and without anemia were compared by the chi-squared test for proportions and the t test for means for each year. Strength of association of the presence of anemia with categorical variables (eg, sex, race, age group, etc) was analyzed with the use of the Mantel-Haenszel chi-squared relative risk. A probability level <.05 was considered significant. Comparison of the effect of anemia on survival at 1-year was performed for each year with the use of the LIFETEST procedure (SAS, Cary, NC) and the log-rank statistic. Univariate Cox regression analyses were used to identify significant explanatory variables for inclusion in a multivariable Cox regression model. If a variable was significantly associated with 1-year mortality in either year, it was included. To avoid collinearity problems, prior MI was not included because it is used in the composite LVD index.

Results

Anemia was included among the discharge diagnoses of 996 of the 15,584 MI patients (6.4%) in 1986 and 1510 of 14,757 patients (10.2%) in 1996 (Table I). The mean length of hospital stay was longer in the anemia group (13.0 ± 6.2 vs 10.3 ± 5.5 days, P = .001 in 1986 and 9.5 ± 5.8 vs 6.4 ± 4.7 days, P = .001 in 1996) (Table I). Patients with anemia were older, less likely to be white, and more likely to be female and to have LVD, non-Q MI, and CABG in both years (Table II). In addition, in 1996, patients with anemia were less likely to have prior MI and more likely to have undergone percutaneous transluminal coronary angioplasty (PTCA). One-year mortality was lower overall in the 1996 cohort compared with 1986 (1986 23.6%, 95% CI 22.9-24.3, vs 1986 24.9%, 95% CI 24.2-25.6, P = .0001). One-year mortality in the nonanemia group was significantly lower in 1996 (22.7%, 95% CI 22.0—23.5) compared with 1986 (24.3%, 95% CI 23.6-25.0, P = .0002). There was a similar mortality decrease in the anemia group in 1996, but it did not reach statistical significance (30.9%, 95% CI 28.5-33.2, in 1996 vs 33.5%, 95% CI 30.6-36.5, in 1986, P = .16) (Figure 1).

Univariate Cox analysis revealed that age, female sex, LVD, arrhythmia, diabetes, anterior wall MI, chronic obstructive pulmonary disease (COPD), and anemia were all associated significantly with higher 1-year mortality in both 1986 and 1996 (Table III). The magnitude of the increase in 1-year mortality in patients with anemia was similar in the 2 years studied (1986...
RR = 1.395, 95% CI 1.247-1.560, and 1996 RR = 1.398, 95% CI 1.268-1.541, \( P = .0001 \) both years). However, in a multivariable Cox proportional hazard regression model controlling for demographics, LVD, arrhythmias, Q versus non-Q MI, comorbid conditions, and revascularization procedures, the 1-year mortality in the anemia groups was not significantly higher than that of the nonanemia groups in either year (RR = 1.005, \( P = .93 \) in 1986 and RR = 1.084, \( P = .11 \) in 1996) (Table IV). A significant interaction between anemia and the LVD index was observed, but inclusion of this term in the multivariate model did not improve the model score significantly. Age, female sex, LVD, arrhythmia, diabetes, and chronic liver disease remained significantly associated with a higher 1-year mortality after adjustment in both years.

**Discussion**

The impact of anemia in patients with acute MI has not been well characterized, as most previous investigations were small, had short duration follow-up, or focused on a specific group of patients. \(^1\) \(^5\) \(^8\) \(^9\) In this study, anemia was present in a higher percentage of patients with MI in 1996 than 1986, probably because of higher rates of CABG, use of primary PTCA, thrombolytic therapy, and older age of patients with acute MI.

Anemia was associated with higher unadjusted mortality rate, but this effect was lost in analyses controlling for demographics, comorbidities, complications, and revascularization. Thus, anemia predicted a negative outcome in patients through its association with other factors conferring high risk. Age, LVD, female sex, nonwhite race, and Q wave MI were associated with higher mortality in this and previous studies. \(^6\) \(^10\) \(^12\) Anemia was also associated with revascularization procedures, which may have given patients who developed anemia a survival advantage. However, only 14.4% of the anemia cases in MIDAS-audited charts had anemia develop during the hospitalization. Thus, the majority of the patients with anemia had anemia on admission.

Anemia may affect prognosis in acute MI in opposite directions. High hematocrit values may improve the short-term survival by improving the oxygen carrying capacity and counteracting free radical stress. \(^13\) \(^16\) In animal models, anemic dogs showed ischemic ST-segment changes and locally depressed cardiac function at higher hemoglobin levels with experimentally created coronary stenosis varying from 50% to 80%. \(^17\)
A retrospective analysis of 1958 surgical patients who refused blood transfusion for religious reasons, patients with cardiovascular disease had a much greater risk of death at 30 days than patients without cardiovascular disease when the preoperative hemoglobin level was \( \leq 10 \text{ g/dL} \). These results strongly suggest that patients with underlying cardiovascular disease are less tolerant of anemia than patients without cardiovascular disease.

Conversely, high viscosity associated with a high hematocrit value may worsen prognosis. In a retrospective analysis of 8787 patients aged \( \geq 60 \text{ years} \) undergoing hip fracture surgical repair, hemoglobin...
values ≥8.0 g/dL did not appear to influence the risk of 30- and 90-day mortality in that elderly population. In a prospective, randomized clinical trial of 838 critically ill patients in Canada, maintaining hemoglobin values of 10 to 12 g/dL through blood transfusion was not associated with a survival advantage when compared with patients with hemoglobin values of 7 to 9 g/dL.13 This study is limited in that it is a retrospective observational analysis, hemoglobin and hematocrit values are available only in the audited charts, data on the onset, treatment, duration, and severity of anemia are not available, and it is based on administrative data. However, the audit of a random sample of charts showed good accuracy, and the size of the sample is large and includes all MIs in the state of New Jersey (except federal hospitals). Another important limitation in this study was the lack of information about thrombolytic therapy and the timing of PTCA (primary vs elective). The presence of anemia on admission may have influenced the decision with regard to utilization of either modality in 1996. Neither primary PTCA nor thrombolytic therapy was used commonly in 1986.
Thus, it appears that anemia in the degree of severity that is encountered in the community does not have a significant direct effect on 1-year mortality in patients with acute MI. The higher unadjusted mortality in patients with anemia is probably caused by association with other factors (LVD, older age, etc) that confer worse prognosis.

References