



Outcomes of Percutaneous Coronary Interventions in Patients With Anemia Presenting With Acute Coronary Syndrome

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Abstract

Objective: To study the influence of anemia on long-term outcomes of patients with acute coronary syndrome undergoing percutaneous coronary intervention (PCI).

Patients and Methods: The study included 5668 consecutive unique patients with acute coronary syndrome who underwent PCI at Mayo Clinic from January 1, 2004, through December 31, 2014. The patients were stratified on the basis of the presence (hemoglobin [Hgb] level, <13 g/dL in men and <12 g/dL in women) and severity (moderate to severe Hgb level, <11 g/dL in men and women) of pre-PCI anemia and compared with patients without anemia. The primary outcomes were in-hospital and long-term all-cause mortality after balancing baseline comorbidities using the inverse propensity weighting method.

Results: Unadjusted all-cause in-hospital mortality (4.6% [84 of 1831] vs 2.0% [75 of 3837]) and 5-year follow-up mortality (44.4% [509] vs 15.4% [323]) were higher in patients with anemia than in those without anemia ($P<.001$ for both). After applying inverse propensity weighting analysis, the all-cause in-hospital mortality (2.0% [37] vs 2.0% [75]; $P=.85$) and 5-year mortality (17.8% [203] vs 15.4% [323]; $P=.05$) were not significantly different between patients with and without anemia; however, there were higher rates of all-cause 5-year mortality in patients with moderate to severe anemia (22.3% [113] vs 15.4% [323]; $P<.001$) compared with patients without anemia. The trend in 5-year mortality was driven by increased noncardiac mortality in patients with anemia (10.2% [91] vs 7.1% [148]; $P=.04$) and moderate to severe anemia (10.4% [52] vs 7.1% [148]; $P=.006$) when compared with nonanemic patients.

Conclusion: After accounting for differences in risk profiles of anemic and nonanemic patients, anemia appeared to be an independent risk factor for increased long-term all-cause and noncardiac mortality.

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The prevalence of anemia in patients with acute coronary syndrome (ACS) is high, ranging between 10% and 32%.¹⁻⁴ More so, multiple registries⁵⁻¹¹ and post hoc analyses of randomized controlled trials (RCTs)^{3,4,12-14} have reported that the presence of anemia in ACS is associated with worse clinical outcomes including death, ischemic events, and heart failure. In their pilot randomized controlled trial, Cooper et al¹⁵ found that treatment of anemia with liberal blood transfusion in ACS was associated with a 75% relative risk increase in cumulative in-hospital death, acute heart failure, and

recurrent infarction. Purported mechanisms for poor prognosis include reduced myocardial oxygen supply, increased myocardial oxygen demand and ischemia, volume expansion, and increased bleeding risk.^{4,16-18} Overt bleeding and need for blood transfusion in the setting of ACS are also more prevalent in anemic patients and associated with higher mortality and recurrent infarction.^{1,18-23} The causal role of anemia, however, is confounded by coexistent medical comorbidities,^{3,4,10,24-26} leading to the lack of firm recommendations on its management in the most recent ACS guidelines.^{1,2}

The need to reexamine anemia as a risk marker or independent risk factor for patients with coronary artery disease is underscored by changing demographic characteristics toward the elderly with higher prevalence of comorbidities (eg, malignancy, diabetes, gastrointestinal tract disorders, and chronic renal disease), a population seldom studied in previous randomized controlled trials.^{3,4,12-14} At Mayo Clinic, detailed records of the presence and severity of anemia and long-term data, including mortality, cause of death, and cardiovascular ischemic events, on all patients who undergo percutaneous coronary intervention (PCI) are available. An inverse propensity weighting (IPW) method was utilized for this study to account for extensive differences in baseline risk profiles of patients with and without anemia. With this background, we hypothesized that in patients presenting with ACS and undergoing PCI, anemia (and its severity) is associated with poor in-hospital and long-term outcomes, following adjustment by propensity scores.

PATIENTS AND METHODS

Data Collection

At the time of PCI, patient-specific data were entered into a prospective clinical registry.^{27,28} The Mayo Clinic PCI registry includes clinical, procedural, and angiographic data on all patients undergoing PCI. Patients were contacted at 6 months, 12 months, and yearly thereafter by a clinical research nurse. Medical records of all patients requiring hospitalization at Mayo Clinic, or elsewhere, were reviewed to further characterize any clinical events during follow-up. Separate approval for the current study was obtained from the Mayo Clinic Institutional Review Board. Patients who denied research authorization were excluded from the study in accordance with Minnesota law.

Study Population

Consecutive patients with ACS who underwent PCI from January 1, 2004, through December 31, 2014, were stratified on the basis of the presence (hemoglobin [Hgb] level, <13 g/dL in men and <12 g/dL in women; to convert values to g/L, multiply by 10.0) and severity (moderate to severe anemia Hgb level, <11 g/dL in men and women) of anemia detected on

hospital admission, before PCI, using the World Health Organization definition.²⁹ Baseline demographic characteristics; comorbid conditions defined by the Sachdev index (includes cigarette smoking, hypertension, diabetes mellitus, cerebrovascular accidents, chronic kidney disease, and malignancy and previously found to be associated with poor survival in patients with coronary artery disease)³⁰; Mayo Clinic risk score (MCRS) for adverse cardiovascular events^{27,28}; and type of ACS (unstable angina, non-ST-elevation myocardial infarction [NSTEMI] or ST-elevation myocardial infarction [STEMI]) presentations were extracted from the Mayo Clinic PCI registry. Angiographic data including the type, number, and locations of lesions as well as the type of stents deployed were compared between the 2 groups. The use of ACS guideline-directed medical therapy, including the use of dual antiplatelet therapy and glycoprotein IIb/IIIa inhibitor, was noted.^{1,2}

Clinical Outcomes

The primary outcomes were in-hospital and 5-year cause-specific (cardiac and noncardiac) mortality. Secondary outcomes were in-hospital and 5-year major adverse cardiac events (MACE) (composite of all-cause death, myocardial infarction [MI], stroke, or repeated revascularization), in-hospital bleeding, need for blood transfusion (≥ 1 U), and number of units transfused. Bleeding was defined as reported site hematoma (documented in medical record and required transfusion, surgery, or prolonged hospital stay), femoral bleeding (excessive bleeding from the femoral artery requiring treatment), gastrointestinal tract bleeding (hematemesis, melena, or hematochezia), cerebrovascular bleeding (documented radiographically), and retroperitoneal bleeding (bleeding postcatheterization into retroperitoneal space on the side of the puncture site, evidenced by flank pain and tenderness to palpation and ecchymosis on abdomen and flank, and documented by computed tomography or ultrasonography). In-hospital acute kidney injury was defined as documentation of "acute renal failure or acute kidney injury" of any severity as a complication in the medical record. Cause of death was further divided into cardiac and noncardiac using medical record review and death certificates of all patients and information from the

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