Prognostic Implication of Anemia on In-Hospital Outcomes After Percutaneous Coronary Intervention

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Background—Although prior studies have shown a relationship between anemia and in-hospital mortality after coronary artery bypass grafting and acute myocardial infarction (MI), the prognostic implication of anemia in patients undergoing percutaneous coronary intervention (PCI) is unknown. Therefore, we evaluated the relationship between anemia and outcomes of PCI.

Methods and Results—Clinical and outcome data on 48,851 consecutive PCIs were prospectively collected. Patients were classified as anemic using the World Health Organization definition (<12.0 g/dL in women and <13.0 g/dL in men). A total of 6471 men (21.7%) and 4659 women (30.4%) were anemic. Anemic men and women were older and had a higher percentage of comorbidities compared with their nonanemic cohorts (P<0.0001 for all comparisons). When compared with nonanemic patients, anemic patients had higher in-hospital mortality (3.0% versus 0.8% in men; 2.4% versus 1.5% in women; P≤0.0001) and postprocedural MI (2.0% versus 1.6% in men; 2.4% versus 1.6% in women; P≤0.02) and a higher combined major cardiovascular events end point, including death, MI, and cerebrovascular event (5.0% versus 2.6% in men; 5.1% versus 3.5% in women; P<0.0001). After adjustment for comorbidities, anemia was associated with a higher risk of in-hospital mortality (odds ratio [OR], 2.29; 95% CI, 1.79 to 2.92; P<0.0001) and MI (OR, 1.34; 95% CI, 1.05 to 1.72; P=0.02) and major cardiovascular events (OR, 1.2; 95% CI, 1.05 to 1.34). Significant gender interactions were observed for death in men and for MI in women.

Conclusions—Preprocedural anemia is associated with increased adverse in-hospital outcomes after PCI. Whether optimization of hemoglobin before PCI is of clinical benefit will need to be determined in a randomized clinical trial. (Circulation. 2004;110:271-277.)

Key Words: anemia ■ mortality ■ angioplasty

The presence of anemia in critically ill patients and in patients undergoing surgical procedures has been associated with worse clinical outcomes.1–3 Similar results have been described in patients with heart failure and in the setting of acute myocardial infarction.4,5 However, the prognostic implication of anemia in patients undergoing percutaneous coronary intervention (PCI) is unknown. Consequently, we evaluated the implication of anemia in patients undergoing contemporary PCI for any indication.

Methods

Study Patients

The study sample consisted of 48,851 consecutive PCIs performed between July 1997 and May 2003 in a consortium of 18 hospitals. The consortium included 3 academic centers, 4 tertiary referral centers, and 11 community hospitals. Eight hospitals contributed to the consortium since 1998, whereas the remaining 10 hospitals joined the consortium in 2001 to 2002. Clinical, procedural, and outcome data were collected prospectively by use of a standardized form. Details of the data collection and of the data quality-assurance process have been described previously.6 Preprocedure hemoglobin values were missing in 7.4% (n=3597) of cases. Additional hemoglobin values that were felt to be implausible were excluded (<5 g/dL, n=42; >20 g/dL, n=47). There were 45,165 patients for analysis after exclusions. Excluded patients had similar clinical characteristics and adverse outcome rates to the analysis population.

Patients were classified as anemic based on preprocedural hemoglobin levels using the World Health Organization (WHO) definition (<12.0 g/dL in women and <13.0 g/dL in men).7 We chose this definition because of its use in prior international comparisons, acknowledging that different cutoff levels to define anemia have also been described. The primary end point was in-hospital mortality; secondary end points evaluated included in-hospital cerebrovascular event (defined as abrupt loss of neurological function with either complete return of function in 24 hours or persistence of deficit.
greater than 24 hours); in-hospital postprocedural myocardial infarction (MI) (defined as either rise in creatine phosphokinase [CPK-MB] fraction above normal with new Q waves on ECG or development of new Q waves on ECG with subsequent elevation of CPK-MB 3 times the baseline level with a >5% MB subtraction over baseline); and a combined end point of major cardiovascular events (MACEs) including in-hospital mortality, in-hospital cerebrovascular event, and in-hospital postprocedural MI.

Statistical Analysis

Baseline characteristics are expressed as mean±SD and as percentages. Data were stratified by gender and by the presence or absence of anemia. The Student t test and analysis of variance for continuous variables and the χ² test for categorical variables were used to compare baseline anemia status data for men and women strata.

To further investigate the relationship between the severity of anemia and outcomes, baseline characteristics and end points were evaluated after stratifying anemic patients by gender and by quartiles of preprocedure hemoglobin in units of grams per deciliter. The quartiles in women were 5.4 to 9.5 g/dL, 9.6 to 10.6 g/dL, 10.7 to 11.2 g/dL, and 11.3 to 11.9 g/dL; and in men were 6.6 to 10.1 g/dL, 10.2 to 11.6 g/dL, 11.7 to 12.3 g/dL, and 12.4 to 12.9 g/dL. Differences across quartiles of hemoglobin level were evaluated using the Cochran-Armitage trend test for significance.

Logistic regression was used to adjust for covariates in models with in-hospital death, other individual end points, and MACE. Those variables with P<0.2 in univariate analysis were included in stepwise regression models for each outcome. Two different sets of models were developed. The first set was developed in the overall patient population. The WHO definition of anemia uses a different hemoglobin cutoff for men and women. Therefore, to assess whether there were dissimilar gender effects with respect to anemia and outcome, a single gender interaction term was then brought into the analysis. In addition, a logistic regression model was developed using hemoglobin as a continuous variable in increments of 1 g/dL rather than as a dichotomous variable.

The second set of models was developed to assess the prognostic implication of the severity of anemia according to quartiles of low hemoglobin versus normal hemoglobin. Gender-specific odds ratios (ORs) for each quartile versus nonanemic patients were estimated. The following variables were evaluated in the stepwise regression process: age, hypertension, myocardial infarction, diabetes mellitus, extracardiac vascular disease, congestive heart failure, renal failure requiring dialysis, gastrointestinal bleeding, chronic obstructive pulmonary disease, atrial fibrillation, cardiac arrest, prior history of percutaneous intervention, prior history of coronary artery bypass surgery, creatinine ≥1.5 mg/dL, myocardial infarction within 7 days, myocardial infarction within 24 hours, cardiogenic shock, ventricular tachycardia or fibrillation, emergency angioplasty, rescue angioplasty after failed thrombolysis, unstable angina (requiring intravenous nitroglycerin and heparin treatment), number of diseased vessels (≥70% stenosis), and ventricular ejection fraction <50%.

Model discrimination was assessed using the c-statistic, and goodness of fit was assessed using the Hosmer-Lemeshow statistics. Statistical analysis was performed with SAS version 8.2.

Results

Baseline clinical characteristics are shown in Table 1. Anemia was present in 21.7% of men and 30.4% of women. Mean hemoglobin was 11.7±1.1 g/dL in anemic men and 10.8±0.9 g/dL in anemic women.

When compared with nonanemic patients, anemic men and women were older and more likely to have prior history of MI, PCI, coronary artery bypass grafting, diabetes mellitus, renal failure requiring dialysis, hypertension, congestive heart failure, prior gastrointestinal bleed, and extracardiac vascular disease (P<0.0001 for all) (Table 1). From a procedural standpoint, anemic men and women were also more likely to have 3-vessel disease, cardiac arrest, ejection fraction <50%, and need for intra-aortic balloon pump (P≤0.03 for all). As expected, in-hospital transfusion was more frequent in anemic men compared with nonanemic men (9.3% versus 1.9%, P<0.0001) and in anemic women compared with nonanemic women (15.5% versus 5.2%, P<0.0001).

Table 2 describes risk factor trends by hemoglobin quartiles in anemic men and women. There was a significant trend in anemic men from the highest to lowest quartile for increased age and a higher percentage of comorbidities (P≤0.01 for trend). There was also a reverse trend for use of preprocedural aspirin, concomitant thrombolysis, and glycoprotein IIb/IIIa inhibitors (P≤0.04 for trend).

The same trends were observed in anemic women for age, comorbidities (P<0.05 for trend), preprocedural aspirin use, and glycoprotein IIb/IIIa inhibitors use (P<0.05).

Clinical Outcomes

Anemic men had higher rates of in-hospital mortality, cerebrovascular events, postprocedural MI, and MACE compared with nonanemic men. Anemic women also had higher rates of in-hospital mortality, postprocedural MI, and MACE compared with nonanemic women (Figure 1).

Table 3 describes clinical outcomes stratified by hemoglobin quartile and gender in anemic patients. In anemic men, there was a significant trend from highest to lowest quartile for higher rates of in-hospital mortality, cerebrovascular events, and MACE (P<0.0001 for trend for all). In anemic women, this trend was only significant for in-hospital mortality (P=0.02 for trend).

After adjusting for comorbidities, anemia remained an independent predictor of in-hospital mortality, with a significant gender interaction term (P=0.0004) (adjusted OR for men, 2.29; 95% CI, 1.8 to 2.9; P<0.0001; and adjusted OR for women, 1.19; 95% CI, 0.9 to 1.6; P=0.21) (Table 4). The fitted model had high discrimination, with a c-statistic of 0.92 (Hosmer-Lemeshow χ² 9.05, P=0.24). Model fitting using hemoglobin as a continuous variable revealed a similar gender-specific relationship between decreasing hemoglobin levels and risk of in-hospital mortality (adjusted OR for men, 1.21; 95% CI, 1.14 to 1.28; P<0.001; adjusted OR for women, 1.05; 95% CI, 0.97 to 1.14; P=0.24 for 1-g/dL decrement of hemoglobin level).

To determine the potential effect of blood transfusion on the risk of in-hospital death associated with anemia, a third model was developed with inclusion of blood transfusion as an explanatory variable. After adjustment for comorbidities and for blood transfusion, anemia remained an independent predictor of in-hospital mortality in men (adjusted OR for men, 1.91; 95% CI, 1.48 to 2.45; P<0.0001; adjusted OR for women, 1.01; 95% CI, 0.76 to 1.35; P=0.95).

No independent effect of anemia was observed in men or women on the risk of cerebrovascular events. Similar models were developed for postprocedural MI and for MACE. There was a significant association between anemia and increased risk of postprocedural MI in women (adjusted OR for women, 1.35; 95% CI, 1.06 to 1.72; P=0.02), but not in men (adjusted OR, 1.05; 95% CI, 0.9 to 1.3; P=0.63) (gender interaction
TABLE 1. Baseline Characteristics of the Study Population Stratified by Gender and Presence or Absence of Anemia

<table>
<thead>
<tr>
<th>Demographics</th>
<th>All Patients</th>
<th>Men</th>
<th>Women</th>
<th>P*</th>
<th>All Patients</th>
<th>Men</th>
<th>Women</th>
<th>P*</th>
</tr>
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<td>67.7</td>
<td>61.7</td>
<td>62.0</td>
<td>60.0</td>
<td>68.6</td>
<td>65.4</td>
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<tr>
<td>Female gender</td>
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<td>41.9</td>
<td>31.3</td>
<td>33.9</td>
<td>31.3</td>
<td>36.7</td>
<td>30.0</td>
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</tr>
<tr>
<td>Current smoking, %</td>
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<td>18.7</td>
<td>29.5</td>
<td>20.2</td>
<td>30.4</td>
<td>16.6</td>
<td>27.4</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Historical variables

| Hypertension, %        | 69.0         | 76.2      | 66.7       | 72.7      | 63.1         | <0.0001   | 81.0       | 74.4      | <0.0001   |
| Myocardial infarction, % | 34.2         | 40.4      | 32.0       | 43.0      | 33.1         | <0.0001   | 36.7       | 30.0      | <0.0001   |
| Diabetes mellitus, %   | 28.7         | 40.4      | 25.0       | 38.0      | 22.3         | <0.0001   | 43.6       | 30.7      | <0.0001   |
| Extracardiac vascular disease, % | 18.4         | 28.3      | 15.2       | 28.2      | 13.4         | <0.0001   | 28.5       | 19.1      | <0.0001   |
| Congestive heart failure, % | 10.6         | 20.2      | 7.4        | 18.1      | 5.7          | <0.0001   | 23.1       | 11.2      | <0.0001   |
| Renal failure requiring dialysis, % | 1.4          | 4.5       | 0.4        | 4.4       | 0.2          | <0.0001   | 4.6        | 0.9       | <0.0001   |
| Gastrointestinal bleeding, % | 1.8          | 4.3       | 0.9        | 4.2       | 0.9          | <0.0001   | 4.5        | 1.0       | <0.0001   |
| COPD, %                | 13.9         | 18.0      | 12.6       | 19.2      | 11.3         | <0.0001   | 16.4       | 15.4      | 0.11      |
| Atrial fibrillation, % | 6.8          | 10.3      | 5.7        | 10.9      | 5.5          | <0.0001   | 9.4        | 6.2       | <0.0001   |
| Cardiac arrest, %      | 1.8          | 2.6       | 1.5        | 2.7       | 1.6          | <0.0001   | 2.4        | 1.3       | <0.0001   |
| Prior PCI, %           | 35.0         | 39.3      | 33.6       | 40.9      | 34.2         | <0.0001   | 36.9       | 32.3      | <0.0001   |
| Prior CABG, %          | 18.8         | 24.4      | 16.9       | 28.7      | 18.2         | <0.0001   | 18.4       | 14.3      | <0.0001   |

Periprocedural variables

| Hemoglobin, g/dL       | 13.6         | 11.3      | 14.4       | 11.7      | 14.8         | NA        | 10.8       | 13.5      | NA        |
| Creatinine, mg/dL      | 1.2          | 1.44      | 1.06       | 1.52      | 1.09         | <0.0001   | 1.34       | 0.99      | <0.0001   |
| Creatinine >1.5 mg/dL, % | 4.9          | 22.9      | 6.1        | 25.7      | 6.2          | <0.0001   | 19.0       | 5.7       | <0.0001   |
| Myocardial infarction within 7 days, % | 33.5         | 36.4      | 32.5       | 36.6      | 33.5         | <0.0001   | 36.1       | 30.4      | <0.0001   |
| Cardiogenic shock, %   | 2.3          | 3.1       | 2.0        | 3.2       | 1.8          | <0.0001   | 3.1        | 2.6       | 0.07      |
| Ventricular tachycardia/fibrillation, % | 1.9          | 2.2       | 1.9        | 2.5       | 1.9          | 0.004     | 1.8        | 1.6       | 0.37      |
| Acute myocardial infarction (within 24 hr), % | 16.3         | 12.2      | 17.6       | 12.6      | 18.6         | <0.0001   | 11.7       | 15.5      | <0.0001   |
| Emergency angioplasty, % | 15.9         | 12.5      | 17.1       | 12.7      | 17.8         | <0.0001   | 12.3       | 15.5      | <0.0001   |
| Rescue angioplasty, %  | 4.1          | 3.4       | 4.4        | 3.4       | 4.8          | <0.0001   | 3.2        | 3.3       | 0.78      |
| Unstable angina        | 35.4         | 43.2      | 32.8       | 42.9      | 32.1         | <0.0001   | 43.7       | 34.4      | <0.0001   |
| Cardiac arrest, %      | 3.5          | 4.1       | 3.3        | 4.3       | 3.3          | <0.0001   | 3.9        | 3.2       | 0.03      |
| Three-vessel disease (>70%), % | 19.3         | 25.6      | 17.2       | 29.3      | 18.5         | <0.0001   | 20.4       | 14.5      | <0.0001   |
| Ejection fraction <50%, % | 28.9         | 37.4      | 26.1       | 41.0      | 27.8         | <0.0001   | 32.4       | 22.6      | <0.0001   |
| Thromboliacs, %        | 4.9          | 3.9       | 5.3        | 4.0       | 5.9          | <0.0001   | 3.7        | 3.9       | 0.45      |
| Preprocedure aspirin, % | 91.0         | 90.3      | 91.3       | 91.1      | 91.7         | 0.16      | 89.1       | 90.4      | 0.02      |
| Glycoprotein IIb/IIIa, % | 64.0         | 61.1      | 64.9       | 61.9      | 66.0         | <0.0001   | 60.0       | 62.5      | 0.003     |
| Intra-aortic balloon pump, % | 3.7          | 4.6       | 3.4        | 5.0       | 3.4          | <0.0001   | 4.2        | 3.2       | 0.003     |
| Coronary stent, %      | 80.6         | 79.9      | 82.2       | 80.1      | 82.8         | <0.0001   | 79.7       | 80.6      | 0.19      |
| Transfusion, %         | 5.2          | 11.9      | 3.0        | 9.3       | 1.9          | <0.0001   | 15.5       | 5.2       | <0.0001   |

COPD indicates chronic obstructive pulmonary disease; CABG, coronary artery bypass grafting; and NA, not applicable.

*P value applies to anemic versus nonanemic for respective gender.

term, P=0.12). In addition, anemia was associated with an increased risk of MACE (adjusted OR, 1.2; 95% CI, 1.05 to 1.34; P<0.01), independently from gender (gender interaction term, P=0.60). The c-statistic for this last model was 0.72, consistent with good model discrimination, and the Hosmer-Lemeshow statistic was nonsignificant (χ², 9.37; P=0.31), indicating good model fit.

The adjusted ORs of death in anemic patients stratified by hemoglobin quartile are shown in Figure 2. Anemic men in each quartile had an increased adjusted OR of death compared with men with normal hemoglobin levels (range, 2.08 to 2.54; P=0.003), whereas this finding was not observed among anemic women.

Discussion

Our data indicate that anemic men and women have worse in-hospital outcomes after PCI compared with their respective nonanemic cohort. When anemic patients were addition-
ally stratified by hemoglobin quartile, the trend from highest to lowest quartile on in-hospital mortality was more pronounced, suggesting that anemia defined both as a threshold and as a range of severity beneath the WHO criteria has significant clinical implications. Furthermore, our findings suggest an impact of gender on specific in-hospital outcomes.

Similar untoward effects of anemia have been observed in cardiovascular patients in the intensive care unit setting, in patients undergoing cardiac or noncardiac surgical procedures, and in patients with heart failure or who have been hospitalized for acute MI.1–5 8–10 The presence of anemia in the general population has also recently been shown to be associated with worse cardiovascular outcomes.11 Proposed mechanisms for these relationships include (but are not limited to) impaired oxygen delivery to tissues causing hypoxia, as well as reduced coronary flow reserve and

![Table 2: Risk Factor Trends by Hemoglobin Quartiles in Anemic Men and Anemic Women](image)

**Demographics**

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
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<tbody>
<tr>
<td>69.0</td>
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**Historical variables**

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<tr>
<th>Hypertension, %</th>
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<th>Q4</th>
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<th>Atrial fibrillation, %</th>
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<th>Q3</th>
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<tr>
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<td>11.8</td>
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<th>Q4</th>
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<td>40.8</td>
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<td>11.6</td>
<td>12.3</td>
<td>12.8</td>
<td>NA</td>
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</table>

| Creatinine, mg/dL                  | 1.97| 1.53| 1.32| 1.21| <0.0001|

| Creatinine >1.5 mg/dL, %           | 40.8| 27.5| 18.6| 14.4| <0.0001|

<table>
<thead>
<tr>
<th>Myocardial infarction within 7 days, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
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<tbody>
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<td>40.6</td>
<td>36.7</td>
<td>35.1</td>
<td>33.5</td>
<td>&lt;0.0001</td>
<td></td>
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</table>

| Cardiac shock, %                     | 5.8 | 2.9 | 2.0 | 1.8 | <0.0001|

<table>
<thead>
<tr>
<th>Ventricular tachycardia/fibrillation, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.4</td>
<td>2.9</td>
<td>1.8</td>
<td>2.0</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute MI (within 24 hr), %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.8</td>
<td>11.9</td>
<td>12.9</td>
<td>12.5</td>
<td>0.96</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Emergency angioplasty, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.0</td>
<td>11.8</td>
<td>11.6</td>
<td>12.2</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rescue angioplasty, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2</td>
<td>2.9</td>
<td>3.7</td>
<td>4.0</td>
<td>0.16</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unstable angina, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>44.2</td>
<td>42.7</td>
<td>42.5</td>
<td>42.0</td>
<td>0.21</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiac arrest, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.9</td>
<td>4.4</td>
<td>4.0</td>
<td>3.6</td>
<td>0.07</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Three-vessel disease (&gt;70%), %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.7</td>
<td>31.4</td>
<td>27.3</td>
<td>24.0</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ejection fraction &lt;50%, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>51.3</td>
<td>41.7</td>
<td>36.9</td>
<td>32.6</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thrombolysis, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1</td>
<td>3.3</td>
<td>4.9</td>
<td>4.7</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preprocedure aspirin, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>89.3</td>
<td>90.5</td>
<td>92.2</td>
<td>91.8</td>
<td>0.02</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Glycoprotein III/IIIa, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>57.0</td>
<td>64.8</td>
<td>63.2</td>
<td>63.6</td>
<td>0.0003</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intra-aortic balloon pump, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.6</td>
<td>4.9</td>
<td>3.4</td>
<td>4.0</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coronary stent, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>79.3</td>
<td>79.2</td>
<td>80.4</td>
<td>81.5</td>
<td>0.11</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transfusion, %</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>21.2</td>
<td>6.6</td>
<td>4.3</td>
<td>4.0</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

COPD indicates chronic obstructive pulmonary disease; CABG, coronary artery bypass grafting; and NA, not applicable.

*Trend test over quartiles of low hemoglobin for gender stratum.

Quartiles in women: 5.4–9.5 g/dL, 9.6–10.6 g/dL, 10.7–11.2 g/dL, and 11.3–11.9 g/dL.

Quartiles in men: 6.6–10.1 g/dL, 10.2–11.6 g/dL, 11.7–12.3 g/dL, and 12.4–12.9 g/dL.
eventual myocardial ischemia. In addition, the higher frequency of comorbidities in our anemic population suggests that a lower hemoglobin level might be a marker of disease severity, and that as such it identifies patients at higher risk of complications after PCI.

The prevalence of anemia in our cohort was 24.6%, similar to estimates from other populations. The impact of anemia on in-hospital outcomes was substantial despite the high utilization of contemporary therapy, including coronary stents and glycoprotein IIb/IIIa inhibitors. This may reflect the higher percentage of comorbidities in an older, anemic population. Nonetheless, after adjustment for other confounders, the presence of anemia remained an independent predictor of in-hospital mortality and postprocedural myocardial infarction.

The observed interaction between anemia and gender on individual outcomes is perplexing. Previously, Brown et al described a relationship between lower hematocrit level and risk of cardiovascular death, particularly in men. Gender differences were also observed in the Framingham study, where men with lower than median hematocrit values had no evidence of altered risk of cardiovascular death, and women with lower hematocrit values had an increased risk of cardiovascular events, thus supporting our finding of increased postprocedural myocardial infarction in women. It is possible that anemia in women results in more ischemic outcomes, whereas anemia in men is a more potent marker of disease severity. In addition, a higher mortality rate was observed in women compared with men, regardless of the presence of anemia. Thus, it is also possible that in women anemia might contribute only marginally to an already higher risk of in-hospital mortality.

The overall transfusion rate in our population was 5.2%, similar to values observed in trials using glycoprotein IIb/IIIa inhibitors with PCI and low compared with rates observed in critically ill patients or in patients with acute MI. Although we observed a higher transfusion rate in both anemic men and women compared with their nonanemic counterparts, the differences were not statistically significant.

### Table 3. In-Hospital Outcome by Hemoglobin Quartile in Anemic Men and Anemic Women

<table>
<thead>
<tr>
<th>In-Hospital Outcome</th>
<th>Quartiles of Hemoglobin</th>
<th>Quartiles of Hemoglobin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1</td>
<td>Q2</td>
</tr>
<tr>
<td>Cerebrovascular event</td>
<td>1.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Death</td>
<td>5.0</td>
<td>2.8</td>
</tr>
<tr>
<td>MACE</td>
<td>7.3</td>
<td>4.8</td>
</tr>
</tbody>
</table>

MACE indicates cerebrovascular event, myocardial infarction, or death.

* Trend test over hemoglobin quartiles in anemic cohort for respective gender.
cohorts, the impact of blood transfusion on the risk of in-hospital death associated with anemia was insignificant. Yet we were unable to assess hemoglobin threshold, timing, indication, and appropriateness of transfusion.

Whether optimization of hemoglobin levels before PCI may be of clinical benefit remains to be determined, particularly in view of the current controversy on liberal use of blood transfusion in critically ill patients. Importantly, our data do not support a systematic use of blood transfusion in patients with anemia undergoing PCI. Besides transfusion, future options could include the use of erythropoietin prepro-

cedurally or, alternatively, the urgent use of synthetic blood substitutes.

Our study has an important limitation. Although a rigorous analysis was performed to adjust for other confounders, we cannot rule out the possibility that we were unable to adjust for other unknown confounders and that therefore anemia is just an indirect marker of disease severity.

**Conclusion**

Preprocedural anemia is associated with increased adverse in-hospital outcomes after PCI. Whether optimization of hemoglobin before PCI is of clinical benefit will need to be determined in a randomized clinical trial.

**Appendix**

**BMC Hospitals and Working Group Members**

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**TABLE 4. Multivariate Regression Model for In-Hospital Mortality**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender F:M</td>
<td>1.51</td>
<td>1.19–1.91</td>
<td>0.0008</td>
</tr>
<tr>
<td>Anemia</td>
<td>2.29</td>
<td>1.79–2.92</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender-hemoglobin</td>
<td>0.52</td>
<td>0.37–0.75</td>
<td>0.0004</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>1.71</td>
<td>1.31–2.23</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>70–79</td>
<td>2.7</td>
<td>2.10–3.47</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt;80</td>
<td>4.23</td>
<td>3.20–5.60</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Extracardiac vascular disease</td>
<td>1.51</td>
<td>1.23–1.84</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.34</td>
<td>1.11–1.63</td>
<td>0.0029</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>0.70</td>
<td>0.57–0.87</td>
<td>0.0013</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td>1.44</td>
<td>1.14–1.81</td>
<td>0.0019</td>
</tr>
<tr>
<td>Emergency PCI</td>
<td>3.56</td>
<td>2.81–4.51</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>2.22</td>
<td>1.70–2.90</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Creatinine ≥1.5 mg/dL</td>
<td>2.14</td>
<td>1.75–2.63</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ejection fraction ≤50%</td>
<td>1.91</td>
<td>1.55–2.36</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>7.78</td>
<td>6.26–9.67</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Myocardial infarction within 7 days</td>
<td>2.47</td>
<td>1.88–3.25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rescue PCI</td>
<td>1.44</td>
<td>1.12–1.85</td>
<td>0.0049</td>
</tr>
<tr>
<td>Ventricular tachycardia/fibrillation</td>
<td>1.46</td>
<td>1.09–1.96</td>
<td>0.0103</td>
</tr>
</tbody>
</table>

C-statistic = 0.915.

**Figure 2.** Gender-specific adjusted ORs of in-hospital mortality in anemic patients stratified by hemoglobin quartiles compared with their nonanemic cohort.
References


Prognostic Implication of Anemia on In-Hospital Outcomes After Percutaneous Coronary Intervention

for the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2)

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