Clin. Cardiol. 30 (Suppl. II), II-49–II-56 (2007)

Blood Transfusion and In-hospital Outcomes in Anemic Patients with Myocardial Infarction Undergoing Percutaneous Coronary Intervention

Sandeep M. Jani, m.p.h., Dean E. Smith, m.s., ph.d., David Share, m.d., m.p.h.,* Eva Kline-Rogers, r.n., m.s., Sanjaya Khanal, m.d.,† Michael J. O'Donnell, m.d.,‡ Julius Gardin, m.d.,§ Mauro Moscucci, m.d.

Division of Cardiology, University of Michigan Medical Centers, Ann Arbor; *Blue Cross Blue Shield of Michigan; †Henry Ford Hospital, Detroit; ‡St. Joseph Mercy Hospital, Ann Arbor; §St. John's Hospital and Medical Center, Detroit, Michigan, USA

Summary

Studies have shown poor prognostic implications of anemia in patients with myocardial infarction (MI) and in patients undergoing percutaneous coronary intervention (PCI). The impact of blood transfusion in these populations remains controversial. The objective of this study was to examine the effect of transfusion on in-hospital mortality in anemic patients undergoing PCI for MI.

Data from 67,051 PCIs (June 1, 1997 to January 31, 2004) were prospectively collected in a multicenter registry (Blue Cross Blue Shield of Michigan Cardiovascular Consortium). Of these, 4,623 patients who were classified as anemic according to the World Health Organization criteria underwent PCI within 7 days of presentation with acute MI. A propensity score for being transfused was estimated for each patient, and propensity matching and a prediction model for in-hospital death were developed.

The average age was 67.8 years, 57.7% of patients were men, and 22.3% of patients received a transfusion during hospitalization. Transfused patients, compared to nontransfused patients, were more likely to be older, female, have lower preprocedure hemoglobin levels, more comorbidities, and a higher unadjusted in-hospital mortality rate (14.52% vs. 3.01%, $p < 0.0001$). After adjustment for comorbidities and propensity for transfusion, blood transfusion was associated with a higher risk of in-hospital mortality (adjusted odds ratio = 2.02, 95% confidence interval 1.47–2.79, $p < 0.0001$).

In anemic patients undergoing PCI for MI, transfusion was associated with an increased crude and adjusted rate of in-hospital mortality. A randomized controlled trial is needed to determine the value of transfusion and the ideal transfusion criteria.

Key words: blood transfusion, myocardial infarction, percutaneous coronary intervention, mortality

Clin. Cardiol. 2007; 30 (Suppl. II): II-49–II-56.

Introduction

Previous studies have explored the effect of anemia on outcomes in patients undergoing PCI. Decreased hemoglobin levels prior to the procedure have been associated with increased in-hospital mortality in PCI patients.[1,2]

Other studies have examined the outcomes of transfusing critically ill patients and patients with cardiovascular disease (CVD). A randomized controlled trial evaluated transfusing critically ill patients to maintain a 10.0–12.0 g/dL hemoglobin level (liberal strategy) compared with a conservative strategy of maintaining hemoglobin levels between 7.0 and 9.0 g/dL. The trial found that a conservative strategy trended toward resulting in lower in-hospital mortality rates.[3] This study was both disputed and confirmed by observational studies. Vincent *et al*.[4] found that 28-day mortality rates were significantly higher in transfused critically ill patients, while Wu *et al*.[5] found that transfusion was associated with lower 30-day mortality rates in elderly patients with

Supported by an unrestricted grant from Blue Cross Blue Shield of Michigan, Detroit, Michigan, USA.

Address for reprints:
Mauro Moscucci, M.D.
University Hospital, TC B1-226
1500 E. Medical Center Drive
Ann Arbor, MI 48103-0311, USA
e-mail: moscucci@umich.edu

Received: June 19, 2007
Accepted: June 19, 2007

Published online in Wiley InterScience (www.interscience.wiley.com).
DOI:10.1002/clc.20236

acute MI. Finally, a recent analysis of acute coronary syndrome (ACS) patients from three major, randomized, controlled trials found that blood transfusion was associated with significantly higher 30-day mortality, even after adjustment for predictive variables.[6]

Despite this body of research, no studies have examined outcomes of transfusions in patients with MI and with anemia undergoing PCI. Thus, we sought to examine the effects of transfusions on in-hospital mortality in anemic patients undergoing PCI within 7 days of having an MI.

Methods

Data from 67,051 PCIs, performed between June 1, 1997 and January 31, 2004, were prospectively collected in a multicenter registry of contemporary PCIs (the Blue Cross Blue Shield of Michigan Cardiovascular Consortium—BMC^2) using a standardized data collection form and standardized definitions. Details of the data collection and quality assurance processes have been reported elsewhere.[7,8] In brief, data forms were reviewed for accuracy and completeness and any incomplete form was returned to the collecting site for clarification. In addition, all centers were audited twice a year. During the site visit, 2% of randomly selected cases and all major endpoints were reviewed.

The study population consisted of 21,521 patients undergoing PCI within 7 days of having an MI. Of these patients, 4,313 patients were excluded from the initial analysis because preprocedure hemoglobin and/or nadir hemoglobin values were missing. Another 31 patients were excluded because they had hemoglobin values that were thought to be implausible (<5 g/dL and >20 g/dL). Thus, 17,177 patients undergoing PCI within 7 days from an MI remained. Of these 17,177 patients, 4,623 patients (26.9%) had anemia prior to PCI and were the subject of this analysis.

To ensure that exclusion of patients with missing preprocedure and/or nadir hemoglobin values did not bias the results, an additional analysis was performed on the overall patient population, after imputation of missing hemoglobin values using linear regression analysis.

Patients were classified as anemic according to the WHO criteria.[9] According to this definition, men with preprocedure hemoglobin <13 g/dL and women with preprocedure hemoglobin <12 g/dL were classified as anemic. The median nadir hemoglobin in this group was 10 g/dL. To determine the impact of nadir hemoglobin on receiving a postprocedure transfusion, a dichotomous variable was created using the median value ($1 \leqslant 10$ g/dL; $0 \geqslant 10$ g/dL).

Transfusion was defined as postprocedure transfusion of red blood cells, platelets, fresh frozen plasma, or whole blood. Extra-cardiac vascular disease was defined as a history of cerebrovascular disease or peripheral vascular disease. Vascular complications were defined as any complication including pseudoaneurysm, arteriovenous fistula, femoral neuropathy, retroperitoneal hematoma, hematoma at the access site requiring transfusion/prolonged hospital stay/causing a drop in hemoglobin >3.0 g/dL, or any access site complication requiring surgical repair.

Statistical Analysis

Discrete variables were analyzed using Chi-square tests or Fisher's exact tests, while continuous variables were analyzed using Student's t-tests.

Propensity Matching

Demographics, comorbidities, in-hospital characteristics, and outcome differences between transfused anemic patients and nontransfused anemic patients were controlled for using propensity matching. Propensity matching uses logistic regression analysis to assign a propensity score between 0 and 1 for receiving a treatment vs. not receiving a treatment. Patients are then matched on the propensity score, thereby creating an equivalent treatment and control group.[10,11] We used this method to assign a propensity score to each patient, representing the relationship between undergoing a transfusion and the demographic, historical, in-hospital risk factors and outcomes included in the logistic regression model. The score was then used to match transfused anemic patients to nontransfused anemic patients by employing a greedy matching protocol (available at: http://www2.sas.com/proceedings/sugi26/p214-26.pdf). In this way, the independent variables used to determine the propensity score were equalized between the transfused anemic and nontransfused anemic populations. The variables included in the logistic regression model used to determine the propensity score included gender, age, nadir hemoglobin, history of smoking, hypertension, congestive heart failure (CHF), gastrointestinal bleeding, extra-cardiac vascular disease, renal failure requiring dialysis, diabetes, chronic obstructive pulmonary disease (COPD), atrial fibrillation, cardiac arrest, previous MI, previous PCI, and previous coronary artery bypass grafting (CABG). In-hospital characteristics and outcomes were also matched, including creatinine $\geqslant 2$ mg/dL, creatinine between 1.5 and 2 mg/dL, CHF on admission, left ventricular ejection fraction $<40\%$, undergoing a rescue PCI after failed thrombolysis, undergoing an emergency PCI, having an acute MI, cardiogenic shock, MI with ventricular tachycardia or fibrillation, in-hospital cardiac arrest, aspirin prior to procedure, intravenous heparin prior to procedure, low-molecular-weight heparin (LMWH) prior to procedure, ticlopidine or clopidogrel prior to procedure, and any glycoprotein (GP) IIb/IIIa receptor blocker. Postprocedural vascular complication, emergency CABG, and any CABG were also matched.

Multivariate Analysis

To further evaluate the role of potential confounders on receiving transfusions and in-hospital mortality in anemic patients with MI undergoing PCI, multivariate models with outcome transfusion and in-hospital death were developed. Variables with univariate p-values $\leqslant 0.2$ were included for selection into the stepwise multivariate regression models. Candidate variables in the transfusion model included gender, age, hemoglobin levels, history of smoking, history of hypertension, history of diabetes, history of CHF, history of extra-cardiac vascular disease, history of gastrointestinal bleeding, history of COPD, history of atrial fibrillation, history of renal failure requiring dialysis, history of cardiac arrest, prior MI, prior PCI, prior CABG, cardiogenic shock, MI with ventricular tachycardia or fibrillation, left ventricular ejection fraction <40%, emergency PCI, acute MI, cardiac arrest, rescue PCI after failed thrombolysis, creatinine $\geqslant$ 2 mg/dL, creatinine between 1.5 and 2 g/dL, CHF on admission, aspirin prior to procedure, heparin prior to procedure, LMWH prior to procedure, ticlopidine/clopidogrel prior to procedure, and GP IIb/IIIa receptor blocker any time. The in-hospital mortality models included a propensity score for undergoing transfusion as a variable in the model. The propensity score was developed using the same variables included in the transfusion model described above. Other candidate variables in the in-hospital mortality model included gender, age, postprocedure transfusion, history of smoking, history of hypertension, history of diabetes, history of CHF, history of extra-cardiac vascular disease, history of gastrointestinal bleeding, history of renal failure requiring dialysis, history of COPD, history of cardiac arrest, prior MI, prior PCI, prior CABG, CHF on admission, cardiogenic shock, MI with ventricular tachycardia or fibrillation, left ventricular ejection fraction <50%, emergency PCI, rescue PCI after failed thrombolysis, acute MI, and creatinine $\geqslant$ 1.5 mg/dL. SAS versus 8.2 was used for statistical analysis (Cary, NC).

Results

The average age of anemic patients undergoing PCI within 7 days of an MI was 67.8 years and 57.7% were men. A transfusion was given to 22.3% (n = 1,033) of the population. Transfused patients were more likely to be older, female, have lower preprocedure hemoglobin levels, and have more comorbidities compared with nontransfused patients (Table 1). Transfused patients were also significantly more likely to have cardiogenic shock, MI complicated by ventricular tachycardia or fibrillation, diminished ejection fraction, cardiac arrest, acute MI, or CHF on admission. Patients treated with a transfusion were also twice as likely as nontransfused patients to have creatinine $\geqslant$ 2 mg/dL (18.10% vs. 9.05%, $p < 0.0001$).

Medication use also differed between the transfused and nontransfused anemic patient groups (Table 2). Patients who were not treated with a transfusion were more likely to be given aspirin prior to PCI or have GP IIb/IIIa receptor blockers used at any time during the procedure.

Transfused patients had significantly worse outcomes compared with nontransfused patients (Table 2). Transfused patients were more likely to have an emergency CABG after PCI (3.78% vs. 0.11%, $p < 0.0001$), any CABG after PCI (8.42% vs. 0.47%, $p < 0.0001$), stroke (2.42% vs. 0.84%, $p < 0.0001$), and vascular complication after PCI (16.65% vs. 1.81%, $p < 0.0001$). The unadjusted mortality rate in transfused anemic patients was nearly five times greater than the mortality rate in nontransfused patients (14.52% vs. 3.01%, $p < 0.0001$).

Propensity-Matched Analysis

Demographics, comorbidities, in-hospital characteristics, medication use, and selected outcomes after propensity matching are displayed in Table 3. A total of 598 transfused anemic patients were matched with 598 nontransfused anemic patients. After propensity matching, there were no differences in age, gender, comorbidities, medication use, or in-hospital characteristics between transfused and nontransfused patients (all $p > 0.15$). Vascular complications, emergency CABG, and any CABG following PCI were also matched to account for transfusions treating significant blood losses (all $p > 0.20$).

After propensity matching, transfused patients continued to have a significantly higher in-hospital mortality rate compared with nontransfused patients (12.71% vs. 7.36%, $p = 0.0021$). There was no difference in the rates of postprocedure stroke/transient ischemic attack or reinfarction (Fig. 1).

Multivariate Regression Modeling

As shown in Table 4, independent predictors for receiving a transfusion included nadir hemoglobin less-than or equal to the median, CHF on admission, history of gastrointestinal bleeding or COPD, cardiogenic shock, emergency PCI, and acute MI. The c-statistic for the model was 0.85, indicating excellent model discrimination and the Hosmer-Lemeshow chi square was not significant ($p = 0.98$), indicating excellent fit by deciles.

After adjustment for comorbidities and propensity score, receiving a blood transfusion was identified as an independent predictor of in-hospital death (adjusted OR 2.04, 95% CI 1.43–2.93, Table 5). For this model, the c-statistic was 0.87 and the Hosmer-Lemeshow test p-value was 0.41. After addition to the patient population of patients for whom preprocedure or nadir hemoglobin values were initially missing, and were imputed for the purpose of the analysis, receiving a blood transfusion remained an independent predictor of in-hospital death (adjusted OR 2.07, 95% CI 1.46–2.93, $p < 0.001$).

TABLE 1 Demographics, comorbidities and in-hospital characteristics in anemic patients with myocardial infarction

Variable	Transfused n = 1,033	Not transfused n = 3,590	p-Value
Demographics			
Age (mean [SD])	70.21 (12.20)	67.13 (12.72)	< 0.0001
Female gender	53.34	39.19	< 0.0001
Comorbidities			
Current smoker	20.18	26.18	0.0004
Hypertension	78.61	72.90	0.0002
Diabetes	40.76	36.27	0.0086
Congestive heart failure	26.14	18.33	< 0.0001
Extra-cardiac vascular disease	36.59	26.57	< 0.0001
Gastrointestinal bleeding	13.94	4.60	< 0.0001
COPD	25.65	18.33	< 0.0001
Atrial fibrillation	13.75	11.00	0.0153
Cardiac arrest	3.78	2.70	0.0720
Prior myocardial infarction	38.82	36.69	0.2111
Prior PCI	28.94	29.28	0.8367
Prior CABG	17.04	20.42	0.0160
In-hospital			
Preprocedure hemoglobin (g ≠ dL)	10.47 (1.28)	11.35 (1.04)	< 0.0001
Cardiogenic shock	23.04	5.26	< 0.0001
Myocardial infarction with VT/VF	9.00	4.87	< 0.0001
Ejection fraction <40%	34.75	22.92	< 0.0001
Cardiac arrest	9.29	5.65	< 0.0001
Emergent PCI	51.98	27.30	< 0.0001
Acute myocardial infarction	50.53	32.73	< 0.0001
Congestive heart failure on admittance	39.59	21.36	< 0.0001
Creatinine ≥2.0	18.10	9.05	< 0.0001

Values presented as percentages unless otherwise noted. *Abbreviations*: CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; PCI = percutaneous coronary intervention; SD = standard deviation; VF = ventricular fibrillation; VT = ventricular tachycardia.

Discussion

The results of this analysis suggest that blood transfusion in anemic patients undergoing PCI within 7 days of an MI was associated with a higher rate of in-hospital death. The increase in risk of mortality associated with transfusion was present after adjustment for comorbidities, in-hospital characteristics, and propensity score for transfusion. Furthermore, similar results of increased risk of mortality associated with blood transfusion were found after analysis of propensity-matched groups.

Preprocedure anemia is a highly prevalent occurrence in MI patients undergoing PCI, affecting over a quarter of the study sample in this analysis. Previous studies have verified these results finding 20–30% of the PCI population to be classified as anemic.[1] Given the substantial prevalence of anemia in this population, presumably the use of blood transfusion would also be high. In fact, 22% of patients in this analysis received a post-PCI blood transfusion. Other studies have indicated high rates of blood transfusion, suggesting that 85% of patients who are hospitalized in the intensive care unit for a week receive blood and 16 and 27% of patients in the medical or surgical intensive care unit, respectively, are transfused on any given day.[12] Given these large numbers, the benefits and/or risks associated with blood transfusion warrant consideration.

The value of blood transfusion in critically ill, cardiac surgical patients is widely debated. A growing body of literature suggests that patients may be able to withstand substantially reduced hemoglobin levels without being transfused. Hébert *et al*.[3] compared a liberal transfusion policy (maintaining hemoglobin between 10.0 and 12.0 g/dL) with a conservative transfusion policy (maintaining hemoglobin between 7 and 8 g/dL), with use of blood transfusion if hemoglobin levels fell below the group's threshold level. The authors reported a nonsignificant trend toward reduced 30-day mortality in the conservative transfusion group. In addition, 30-day mortality was also significantly lower in patients younger than 55 years and patients with APACHE II scores of ⩽ 20. Studies of surgical patients have shown similar results. An analysis of relatively ill and elderly patients (mean age of 80 years) undergoing surgical repair for a fractured hip analyzed 30- and 90-day mortality in patients with similar hemoglobin levels who received a

TABLE 2 Medication use and outcomes in anemic patients with myocardial infarction

Variable	Transfused n = 1,033	Not transfused n = 3,590	p-Value
Medication use			
Aspirin prior to procedure	85.96	92.37	< 0.0001
Intravenous heparin prior to procedure	67.28	69.64	0.14
Low-molecular-weight heparin prior to procedure	8.13	7.16	0.29
Ticlopidine/clopidrogrel preprocedure	37.75	40.45	0.12
Glyocoprotein IIb/IIIa inhibitors	69.41	73.48	0.0097
Outcomes			
Any CABG	8.42	0.47	< 0.0001
Emergency CABG	3.78	0.11	< 0.0001
Stroke/transient ischemic attack	2.42	0.84	< 0.0001
Vascular complications	16.65	1.81	< 0.0001
MACE	20.81	5.13	< 0.0001
Death	14.52	3.01	< 0.0001

Values presented as percentages. *Abbreviations*: CABG = coronary artery bypass graft; MACE = major adverse cardiac events is a composite outcome including death, emergency CABG, stroke, and myocardial infarction.

postoperative (within 7 days of surgical repair) transfusion compared with those who did not. Patients with hemoglobin levels as low as 8.0 g/dL who were transfused showed no reduction in 30- or 90-day mortality compared with patients with hemoglobin levels as low as 8.0 g/dL who were not transfused. Analysis below 8.0 g/dL could not be undertaken due to small sample size.[13] These data suggest that the human body may be more resilient than previously believed and that blood transfusion may not be necessary until (and if) severe anemia presents.

Observational studies have also weighed in on the issue. Vincent *et al.*[4] showed blood transfusions to be associated with increased 28-day mortality and reduced organ function in critically ill patients and Rao *et al.*[6] found an association between blood transfusion and increased mortality rates in patients with ACS. Contradicting these studies, a third large observational study found that transfusion was associated with lower 30-day mortality rates in patients with MI.[5]

The cause for the increased risk of death associated with blood transfusion remains unclear. Previous analyses have shown an increased risk of developing acute respiratory distress syndrome in critically ill patients who received packed red blood cell transfusions. Furthermore, a dose–response relationship was found with a proportional increase in risk with increasing number of units transfused.[14] Other studies have shown a sixfold higher rate of nosocomial infections in critical care patients transfused with red blood cells vs. those patients who were not. Again, a dose–response relationship was seen with the odds of developing nosocomial infection increasing by a factor of 1.5 with each unit transfused.[15] Furthermore, case studies have implicated blood transfusions in the development of reversible posterior leukoencephalopathy syndrome and irreversible bilateral occipital lesions consistent with cortical laminar necrosis.[16]

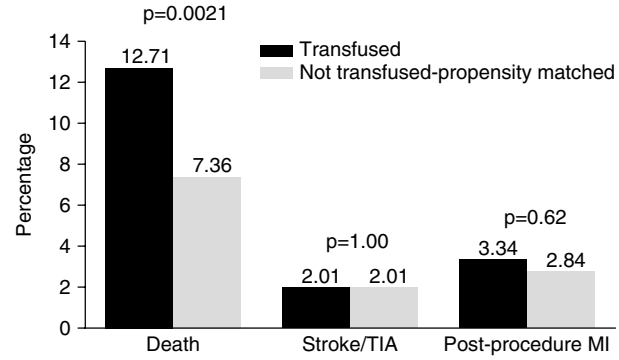

FIG. 1 Outcomes after propensity matching of transfused and nontransfused patients. MI = myocardial infarction, TIA = transient ischemic attack.

Beyond these risks, blood transfusions always carry a small risk of viral transmission, bacterial contamination, or hemolytic reactions.[17]

The mechanism causing some of these adverse reactions seems diffuse and systemic. Blood transfusions may cause a systemic inflammatory response, induce nonspecific immunosuppression, and may cause tissue hypoxemia by occluding microvasculature. Transfusion has also been shown to increase suppressor T lymphocytes and the natural killer cell function, while decreasing monocyte and macrophage activity. Red blood cell transfusion may also cause immune cell allergy and clonal deletion.[12] This immunomodulation may be an underlying factor in the increase in nosocomial infection rates associated with blood transfusion. Some have also suggested that blood-donor antibodies can cause the recipient's neutrophils to react, leading to increased pulmonary microcirculation permeability and to acute lung injury.[17] Thus, the mechanisms underlying adverse

TABLE 3 Demographic and clinical characteristics in anemic patients with myocardial infarction after propensity matching

Variable	Transfused n = 598	Not transfused n = 598	p-Value
Demographics			
Age 60–69	21.91	22.24	0.89
Age 70–79	32.78	33.78	0.71
Age >80	23.58	24.08	0.84
Female gender	54.84	52.51	0.91
Comorbidities			
Current smoker	21.40	21.91	0.83
Hypertension	77.59	79.26	0.48
Diabetes	41.81	41.97	0.91
Congestive heart failure	25.42	27.42	0.43
Extra-cardiac vascular disease	35.45	36.79	0.63
Gastrointestinal bleeding	9.87	11.04	0.51
COPD	21.74	24.58	0.24
Atrial fibrillation	12.88	12.71	0.93
Cardiac arrest	4.01	3.34	0.54
Prior myocardial infarction	40.47	40.30	0.95
Prior PCI	29.93	31.44	0.57
Prior CABG	19.23	20.74	0.52
Renal failure requiring dialysis	6.19	6.52	0.81
In-hospital			
Nadir hemoglobin ≤ median[a]	87.79	89.30	0.41
Cardiogenic shock	14.88	13.88	0.62
Myocardial infarction with VT/VF	6.52	6.02	0.72
Ejection fraction <40%	32.61	30.43	0.42
Cardiac arrest	8.53	6.52	0.18
Emergent PCI	45.48	42.31	0.27
Acute myocardial infarction	45.32	41.81	0.22
Congestive heart failure on admittance	35.12	37.46	0.40
Rescue PCI	7.02	7.69	0.66
Creatinine ≥ 2.0 mg/dL	16.39	17.73	0.54
Creatinine 1.5–2 mg/dL	17.22	17.06	0.94
Aspirin prior to procedure	87.79	88.96	0.53
Heparin prior to procedure	67.22	65.38	0.50
Low-molecular-weight heparin prior to procedure	7.36	8.03	0.66
Ticlopidine/clopidrogrel prior to procedure	36.96	37.29	0.90
Any glycoprotein IIb/IIIa inhibitor	70.40	67.39	0.26
Vascular complication	8.03	6.35	0.26
Emergency CABG	1.34	0.67	0.25
Any CABG	3.68	2.51	0.24

Values presented as percentages. [a]Median nadir hemoglobin = 10.0 g/dL. *Abbreviations*: CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; PCI = percutaneous coronary intervention; VF = ventricular fibrillation; VT = ventricular tachycardia.

outcomes after blood transfusion seem to affect many physiologic systems which are not yet fully understood.

If transfusion of red blood cells carries substantial risks and the body can function at lower hemoglobin levels without increases in adverse outcomes, then reducing the number and frequency of transfusions seems a worthy goal. Guidelines exist to guide physicians and their use of transfusion; however, studies have demonstrated that these guidelines are often not followed.[18–21] Despite these challenges, recent evidence suggests that relatively simple strategies can be effective in changing physician behavior and reducing blood use. Creating simple transfusion guidelines and transfusion use audit procedures with feedback and approval, creating forms that outline criteria for transfusion, and educating the individual provider or group are all strategies that can promote more appropriate use of blood transfusion.[22]

Alternatives to transfusion may show promise and provide increased safety and efficacy. Recombinant human erythropoietin has been shown to increase hemoglobin levels more than traditional blood transfusions when used in critically ill patients, with no difference in adverse outcomes or 28-day mortality rates.[23,24] Interestingly,

TABLE 4 Independent predictors for receiving a postprocedure blood transfusion

Variable	Adjusted odds ratio	95% confidence interval	p-Value
Female gender	1.16	0.98–1.38	0.0871
Age 70–79	1.25	0.99–1.58	0.0566
Age ≥ 80	1.35	1.05–1.75	0.0198
Nadir hemoglobin below the median[a]	16.00	12.39–20.65	< 0.0001
Congestive heart failure on admittance	1.44	1.20–1.74	0.0001
History of gastrointestinal bleeding	2.34	1.76–3.11	< 0.0001
History of COPD	1.35	1.10–1.65	0.0037
History of atrial fibrillation	0.77	0.60–1.00	0.0486
Cardiogenic shock	2.37	1.82–3.10	< 0.0001
MI with VT/VF	1.36	0.96–1.92	0.0883
Emergency PCI	1.75	1.41–2.18	< 0.0001
Acute MI	1.34	1.09–1.66	0.0066
Creatinine 1.5–2 mg/dL	1.21	0.96–1.53	0.1133
Creatinine ≥ 2 mg/dL	1.51	1.18–1.92	0.0009

[a]Nadir hemoglobin median = 10.0 g/dL. *Abbreviations*: COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; VF = ventricular fibrillation; VT = ventricular tachycardia.

TABLE 5 Independent predictors of in-hospital mortality

Variable	Adjusted odds ratio	95% Confidence interval	p-Value
Transfusion	2.02	1.47–2.79	< 0.0001
Propensity score	1.28	1.12–1.46	0.0003
Age ≥ 80	2.12	1.38–3.26	0.0006
Female gender	0.73	0.54–0.99	0.0395
History of cardiac arrest	1.78	1.01–3.13	0.0456
Cardiogenic shock	3.04	2.13–4.34	< 0.0001
MI with VT/VF	1.88	1.25–2.85	0.0027
Ejection fraction <50%	1.58	1.13–2.22	0.0082
Emergency PCI	2.12	1.51–2.96	< 0.0001
Creatinine ≥ 1.5 mg/dL	1.79	1.33–2.41	0.0001

Abbreviations: MI = myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

there was a nonsignificant trend toward lower rates of intensive care unit admissions in the erythropoietin group, suggesting increased safety with this product. Another option may include cell-free hemoglobin solutions that have similar oxygen-carrying capacities as cellular hemoglobin.[25] These alternatives need further study to determine their true risks and benefits.

This study has several limitations. Owing to the structure of the data registry, we were unable to distinguish the type of blood product that was transfused or the quantity transfused. However, our data audits suggest that blood products other than red blood cells were extremely rarely transfused. In addition, the structure of the registry did not allow discrimination between cardiac and noncardiac cause of death. Furthermore, as with any observational study, it is possible that we were unable to adequately control all the variables that may influence the impact of transfusion on mortality. Therefore, in addition to the multivariate analysis, propensity analysis and propensity matching were used to adjust for as many of the differences between the two populations as possible, given the data available. Propensity matching is essentially an analytical technique that creates a case-controlled population with nonstatistically different characteristics. As such, propensity-matching analysis has generally the same major limitation of case-controlled studies: a large portion of the population is excluded, and this portion might have different demographic, in-hospital, and treatment characteristics when compared with the population included in the analysis. Therefore, bias might be introduced into the propensity-matching analyses. However, in our study the results of the propensity-matching analysis agreed with the multivariate analysis (which are of cohort study design) and therefore, the bias involved in the propensity-matching analyses was likely small.

In conclusion, in anemic patients undergoing PCI within 7 days of an MI, transfusion was associated with an increased rate of in-hospital mortality in a propensity-matched and multivariate analysis. A randomized controlled trial is needed to determine the value of transfusion and ideal transfusion criteria.

References

1. McKechnie RS, Smith D, Montoye C, Kline-Rogers E, O'Donnell MJ, et al., Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2): Prognostic implication of anemia on in-hospital outcomes after percutaneous coronary intervention. *Circulation* 2004;110(3):271–277
2. Reinecke H, Trey T, Wellmann J, Heidrich J, Fobker M, et al.: Haemoglobin-related mortality in patients undergoing percutaneous coronary interventions. *Eur Heart J* 2003;24(23):2142–2150

3. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, et al.: A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999;340(6):409–417
4. Vincent JL, Baron JF, Reinhart K, Gattinoni L, Thijs L, et al., ABC (Anemia and Blood Transfusion in Critical Care) Investigators: Anemia and blood transfusion in critically ill patients. *JAMA* 2002;288(12):1499–1507
5. Wu WC, Rathore SS, Wang Y, Radford MJ, Krumholz HM: Blood transfusion in elderly patients with acute myocardial infarction. *N Engl J Med* 2001;345(17):1230–1236
6. Rao SV, Jollis JG, Harrington RA, Granger CB, Newby LK, et al.: Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. *JAMA* 2004; 292(13):1555–1562
7. Kline-Rogers E, Share D, Bondie D, Rogers B, Karavite D, et al., Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2): Development of a multicenter interventional cardiology database: the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2) experience. *J Interv Cardiol* 2002;15(5):387–392
8. Moscucci M, Share D, Kline-Rogers E, O'Donnell M, Maxwell-Eward A, et al., Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2): The Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2) collaborative quality improvement initiative in percutaneous coronary interventions. *J Interv Cardiol* 2002;15(5):381–386
9. The World Health Organization: Nutritional anaemias. Report of a WHO scientific group. *World Health Organ Tech Rep Ser* 1968;405:5–37
10. Gum PA, Thamilarasan M, Watanabe J, Blackstone EH, Lauer MS: Aspirin use and all-cause mortality among patients being evaluated for known or suspected coronary artery disease: a propensity analysis. *JAMA* 2001;286(10):1187–1194
11. Chan AW, Bhatt DL, Chew DP, Quinn MJ, Moliterno DJ, et al.: Early and sustained survival benefit associated with statin therapy at the time of percutaneous coronary intervention. *Circulation* 2002;105(6):691–696
12. Englesbe MJ, Pelletier SJ, Diehl KM, Sung RS, Wahl WL, et al.: Transfusions in surgical patients. *J Am Coll Surg* 2005; 200(2):249–254
13. Carson JL, Duff A, Berlin JA, Lawrence VA, Poses RM, et al.: Perioperative blood transfusion and postoperative mortality. *JAMA* 1998;279(3):199–205
14. Gong MN, Thompson BT, Williams P, Pothier L, Boyce PD, et al.: Clinical predictors of and mortality in acute respiratory distress syndrome: potential role of red cell transfusion. *Crit Care Med* 2005;33(6):1191–1198
15. Taylor RW, Manganaro L, O'Brien J, Trottier SJ, Parkar N, et al.: Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient. *Crit Care Med* 2002;30(10):2249–2254
16. Nagasawa H, Kurita K, Wada M, Kawanami T, Kato T: Blood transfusion-induced irreversible brain damage. *J Neurol* 2005; 252(12):1541–1542
17. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP: Transfusion medicine. First of two parts–blood transfusion. *N Engl J Med* 1999;340(6):438–447
18. Consensus conference: perioperative red blood cell transfusion. *JAMA* 1988;260(18):2700–2703
19. American College of Physicians: Practice strategies for elective red blood cell transfusion. *Ann Intern Med* 1992;116(5):403–406
20. Expert Working Group: Guidelines for red blood cell and plasma transfusion for adults and children. *Can Med Assoc J* 1997;156:S1–S24
21. Moscucci M, Ricciardi M, Eagle KA, Kline E, Bates ER, et al.: Frequency, predictors, and appropriateness of blood transfusion after percutaneous coronary interventions. *Am J Cardiol* 1998;81(6):702–707
22. Tinmouth A, MacDugall L, Fergusson D, Amin M, Graham ID, et al.: Reducing the amount of blood transfused: a systematic review of behavioral interventions to change physicians' transfusion practices. *Arch Intern Med* 2005;165(8):845–852
23. Corwin H, Gettinger A, Pearl R, Fink MP, Levy MM, et al.: EPO Critical Care Trials Group: Efficacy of recombinant human erythropoietin in critically ill patients: a randomized controlled trial. *JAMA* 2002;288(22) 2827–2835
24. Cothren C, Moore EE, Offner PJ, Haenel JB, Johnson JL: Blood substitute and erythropoietin therapy in a severely injured Jehovah's witness. *N Engl J Med* 2002;346(14):1097–1098
25. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP: Transfusion medicine. Second of two parts–blood conservation. *N Engl J Med* 1999;340(7):525–533