Patterns and Outcomes of Red Blood Cell Transfusion in Patients Undergoing Percutaneous Coronary Intervention

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IMPORTANCE Studies have shown variation in the use of red blood cell transfusion among patients with acute coronary syndromes. There are no definitive data for the efficacy of transfusion in improving outcomes, and concerning data exist about possible association with harm. Current transfusion practices in patients undergoing percutaneous coronary intervention (PCI) are not well understood.

OBJECTIVE To determine the current patterns of blood transfusion among patients undergoing PCI and the association of transfusion with adverse cardiac outcomes across hospitals in the United States.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study of all patient visits from the CathPCI Registry from July 2009 to March 2013 that included PCI, excluding those with missing data on bleeding complications or who underwent in-hospital coronary artery bypass graft surgery (N = 2,258,711 visits).

MAIN OUTCOMES AND MEASURES Transfusion rates in the overall population and by hospital (N = 1431) were the primary outcomes. The association of transfusion with myocardial infarction, stroke, and death after accounting for a patient’s propensity for transfusion was also measured.

RESULTS The overall rate of transfusion was 2.14% (95% CI, 2.13%-2.16%) and quarterly transfusion rates slightly declined from July 2009 to March 2013 (from 2.11% [95% CI, 2.03%-2.19%] to 2.04% [95% CI, 1.97%-2.12%]; P < .001). Patients who were more likely to receive transfusion were older (mean, 70.5 vs 64.6 years), were women (56.3% vs 32.5%), and had hypertension (86.4% vs 82.0%), diabetes (44.8% vs 34.6%), advanced renal dysfunction (8.7% vs 2.3%), prior myocardial infarction (33.0% vs 30.2%), or prior heart failure (27.0% vs 11.8%). Overall, 96.3% of sites gave a transfusion to less than 5% of patients and 3.7% of sites gave a transfusion to 5% of patients or more. Variation in hospital risk-standardized rates of transfusion persisted after adjustment, and hospitals showed variability in their transfusion thresholds. Receipt of transfusion was associated with myocardial infarction (42,803 events; 4.5% vs 1.8%; odds ratio [OR], 2.60; 95% CI, 2.57-2.63), stroke (5011 events; 2.0% vs 0.2%; OR, 7.72; 95% CI, 7.47-7.98), and in-hospital death (31,885 events; 12.5% vs 1.2%; OR, 4.63; 95% CI, 4.57-4.69), irrespective of bleeding complications.

CONCLUSIONS AND RELEVANCE Among patients undergoing PCI at US hospitals, there was considerable variation in blood transfusion practices, and receipt of transfusion was associated with increased risk of in-hospital adverse cardiac events. These observational findings may warrant a randomized trial of transfusion strategies for patients undergoing PCI.
Red blood cell transfusion among patients with coronary artery disease is controversial. A growing body of evidence suggests that transfusion in the setting of acute coronary syndromes (ACS) and in hospitalized patients with a history of coronary artery disease may be associated with an increase in risk of myocardial infarction (MI) and death. This is in addition to the other risks described with transfusion of allogeneic blood, such as infection and circulatory overload. However, anemia is a well-known risk factor for exacerbation of myocardial ischemia, and increasing hemoglobin through red blood cell transfusion should increase oxygen delivery and mitigate ischemic outcomes. This paradox between the pathophysiological rationale for transfusion and observational studies demonstrating worse clinical outcomes has led to uncertainty surrounding transfusion practice in these patients. Current guideline statements make cautious recommendations for restricted transfusion strategies in hospitalized patients with a history of coronary artery disease and make no recommendation on transfusion in the setting of ACS citing an absence of definitive evidence.

Given the lack of evidence-based guidelines for transfusion in patients with coronary artery disease, a registry-based analysis showed that there is marked variation in the use of red blood cell transfusion among patients with ACS. Similar to patients with ACS, patients undergoing percutaneous coronary intervention (PCI) receive potent antithrombotic therapies and undergo arteriotomy, placing this subset of patients at particularly high risk of bleeding and transfusion. A single-center study showed that a large proportion of patients undergoing PCI received transfusion for indications outside of published guidelines; however, the transfusion guidelines have been updated to reflect uncertainty regarding transfusion recommendations in patients with coronary artery disease. Moreover, the practice of PCI has evolved to include “bleeding avoidance strategies.” Therefore, the use of red blood cell transfusion may have undergone significant change over time.

Using data from the CathPCI Registry, we sought to describe transfusion practice patterns in a broadly representative population of patients undergoing PCI across the United States. We also sought to evaluate how patient factors are associated with red blood cell transfusion and to determine the association between transfusion and outcomes in the PCI population.

**Methods**

**Study Sample**

The CathPCI Registry is an initiative of the American College of Cardiology Foundation and the Society for Cardiovascular Angiography and Interventions and is the largest ongoing registry of PCI in the United States. Descriptions of the registry have been published previously. Briefly, the registry collects data on patient and hospital characteristics, clinical presentation, procedural characteristics, and in-hospital outcomes for PCI procedures from more than 1400 sites across the United States (approximately 85% of all cardiac catheterization laboratories). Data are entered into National Cardiovascular Data Registry (NCDR)-certified software at participating institutions and exported in a standard format to the American College of Cardiology. The registry has a comprehensive data quality program, including data quality report specifications for data capture and transmission as well as an auditing program. An NCDR committee prospectively defines the variables (available at http://www.ncdr.com).

All patients who underwent cardiac catheterization or PCI from July 2009 to March 2013 were included in the study sample, with the following exceptions: patient visits in which the patient subsequently underwent in-hospital coronary artery bypass graft surgery, patient visits in which a PCI was not performed or that did not represent the first PCI visit during a hospital stay, and procedures with missing data on bleeding events, procedural complications, or discharge status. The study was approved by the institutional review board of Yale University Medical Center and was determined to meet the definition of research not requiring informed consent given that patient information is collected anonymously without unique patient identifiers and only aggregate data are reported.

**Outcomes and Definitions**

The primary outcome was transfusion in the overall population. This outcome was examined with calculation of transfusion rates in the overall population and by hospital (N = 1431), as well as by the occurrence of a bleeding event. These were also calculated quarterly from quarter 3 of 2009 to quarter 1 of 2013. Secondary outcomes included in-hospital MI, congestive heart failure, cardiogenic shock, stroke, and death. The definitions used for transfusion, bleeding events, MI, congestive heart failure, cardiogenic shock, stroke, and death are taken from the CathPCI data collection form, version 4.4, and can be found in the eAppendix in the Supplement.

**Statistical Analysis**

Rates of transfusion were examined in the overall cohort, by hospital site, and in groups of patients with or without documentation of a procedural bleeding complication. We also examined the change in rates over time by quarters from quarter 3 of 2009 to quarter 1 of 2013 using the Cochran-Armitage trend test. Hierarchical logistic regression modeling was used to calculate risk-standardized, site-based rates of transfusion (RSTR). The variables included in the model were age, sex, body mass index, ACS presentation, PCI status, cardiogenic shock, New York Heart Association class IV congestive heart failure (CHF), history of CHF, peripheral vascular disease, chronic lung disease, diabetes, dialysis, previous PCI, and glomerular filtration rate. All of these variables have been previously validated in the CathPCI Registry mortality and bleeding risk models.
For the hospital-level analysis, hospitals were divided into low-, medium-, and high-transfusing groups based on the tertiles of their RSTR. Hospitals with an RSTR at or below the 33rd percentile were considered low transfusing (<1.78% of patients underwent transfusion), hospitals between the 33rd and 66th percentiles were considered medium transfusing (1.78% to <2.79% of patients underwent transfusion), and hospitals above the 66th percentile (≥2.79% of patients underwent transfusion) were considered high transfusing. Transfusion frequencies were then plotted by postprocedure hemoglobin values for each group to determine whether hospital-level transfusion practices were different, specifically by transfusion threshold.

Hospital characteristics were also reported by division into low-, medium-, and high-transfusing hospitals according to their RSTR. Characteristics such as bed number, region, and ownership are reported per number of hospitals. Procedural characteristics such as anticoagulant use and discharge medications are reported per patient visit. The median odds ratios for transfusion among hospitals to quantify the variation of transfusion use among different hospitals and the between-hospital variance were also calculated using PROC GLIMMIX in SAS.

The patient population was divided into cohorts according to whether they had received a transfusion, and baseline characteristics and in-hospital outcomes were compared between these 2 groups. Differences were evaluated using the χ² test for categorical variables and using the t test for continuous variables. Means and standard deviations for continuous variables and frequency rates for categorical variables are reported.

To account for potential confounding in the use of transfusion, inverse probability weighting based on the propensity modeling for transfusion was used in the logistic regression models to determine the association between transfusion and MI, CHF, stroke, and death. Variables included in the propensity model for transfusion were age, sex, race, body mass index, prior MI, prior coronary artery bypass graft/valvular surgery, cardiogenic shock, cardiac arrest, use of intra-aortic balloon pump, prior CHF, peripheral vascular disease, cerebrovascular disease, tobacco use, chronic lung disease, diabetes, hyperlipidemia, family history, dialysis, glomerular filtration rate, New York Heart Association class IV, location of lesion, PCI indication, PCI status, and hospital characteristics such as public vs private ownership, core-based statistical area, number of beds, PCI volume, teaching facility status, and region. Many of these variables have been previously validated in the NCDR mortality risk model. To assess model performance in our sample, we calculated the area under the receiver operating characteristic curve (C statistic). The model showed excellent discrimination, with a C statistic of 0.839. Odds ratios for patient outcomes comparing use of transfusion with no receipt of transfusion are reported with 95% confidence intervals.

To account for the possibility that bleeding events could drive transfusion as well as outcomes, a secondary analysis was performed to determine the association between transfusion and outcomes among patients who did or did not have reported postprocedure bleeding events. To determine the relationship between preprocedure hemoglobin, transfusion, and outcomes, the study sample was stratified by preprocedure hemoglobin levels and the modeling was repeated.

A 2-sided P < .05 was considered significant for all tests. All the statistical calculations were performed at the Yale Center for Outcomes Research and Evaluation with SAS software, version 9.2.0 (SAS Institute Inc).

Results

Study Sample Characteristics

For the purpose of this study, the original sample consisted of 5,274,393 patient visits to the cardiac catheterization laboratory from 1485 sites. Percutaneous coronary intervention occurred during 2,412,974 patient visits. After applying the aforementioned exclusion criteria, 2,258,711 patient visits remained in the study sample (Figure 1) from 1431 hospitals (96% of original sites). There were 48,430 patient visits during which a patient received a postprocedure transfusion. Baseline demographic and procedural characteristics are shown in Table 1. Patients who received transfusion were older, more often female, and more often had comorbidities such as hypertension, diabetes, advanced renal dysfunction, prior MI, and prior CHF. These patients also had a lower estimated glomerular filtration rate, more often presented with ST-segment elevation MI, and less often underwent PCI for elective as opposed to urgent or emergency indications.

Rates of Transfusion

The overall rate of transfusion was 2.14% (95% CI, 2.13%-2.16%). Quarterly transfusion rates from July 2009 to March 2013 slightly declined from 2.11% (95% CI, 2.03%-2.19%) to
2.04% (95% CI, 1.97%-2.12%) of visits (P<.001 for trend). Unadjusted transfusion rates by hospital varied between 0 and 13% (eFigure 1 in the Supplement). The majority of hospitals (96.3%) gave a transfusion to less than 5% of their patients, with 25.5% of hospitals providing transfusion for less than 1% of patients. However, 3.7% of hospitals in the population gave more
than 5% of patients a transfusion. After adjustment, there was still a broad variation in patterns of transfusion across hospitals. As shown in Figure 2, the risk-standardized rates of transfusion across hospitals ranged from 0.3% to 9.3%, with a median of 2.5%.

When stratified by occurrence of a bleeding event, more patients who experienced a bleeding event received transfusion at all postprocedure hemoglobin values compared with patients who did not experience a bleeding event (eFigure 2 in the Supplement). Among patients who did not have a bleeding event, the rates of transfusion increased at postprocedure hemoglobin values of 8 g/dL or lower.

### Hospital Characteristics by Transfusion Rate

When hospitals were divided into low- (<1.78%), medium- (1.78% to <2.79%), and high- (≥2.79%) transfusing hospitals by tertiles of RSTR, transfusion was more frequent at all postprocedure hemoglobin values (≤7 g/dL to ≥12 g/dL) at high-transfusing hospitals compared with medium- and low-transfusing hospitals (Figure 3). High-transfusing hospitals seemed to have a transfusion threshold between 9 g/dL and 10 g/dL, whereas low-transfusing hospitals seemed to have a transfusion threshold between 8 g/dL and 9 g/dL.

High-transfusing hospitals were larger with respect to number of beds and had higher PCI volume compared with the other hospitals (eTable 1 in the Supplement). They also were less likely to be privately owned and less likely to be in rural areas but more likely to be teaching hospitals. High-transfusing hospitals were more likely to be in the New England and Pacific regions, although there was significant variation by region. These hospitals were also less likely to use bivalirudin during procedures and more likely to use GpIIb-IIIa medications but had similar use of radial access site between groups. High-transfusing hospitals prescribed evidenced-based medications on discharge at a similar high frequency compared with lower-transfusing hospitals. The median odds ratio for the likelihood of transfusion by hospital was 1.85 (95% CI, 1.79-1.90) and the between-hospital variation was 0.42 (95% CI, 0.38-0.46), indicating that hospital was responsible for a significant amount of the variation seen in transfusion rates.

### Patient Outcomes

With regard to patient outcomes by transfusion status, patients who underwent transfusion were more likely to have in-hospital MI, stroke, CHF, cardiogenic shock, or death (eTable 2 in the Supplement). After adjustment, receipt of transfusion remained associated with an increased risk for in-hospital MI, stroke, or death individually, and also the composite outcome (Table 2). The analysis was repeated after

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**Figure 2. Distribution of Hospital Risk-Standardized Rates of Transfusion**

Variations in frequency of receipt of transfusion by hospital (N=1431) after adjustment for patient risk factors such as age, sex, body mass index, acute coronary syndromes presentation, percutaneous coronary intervention (PCI) status, cardiogenic shock, New York Heart Association class IV congestive heart failure (CHF), history of CHF, peripheral vascular disease, chronic lung disease, diabetes, dialysis, previous PCI, coronary lesion ≥50%, and glomerular filtration rate.

**Figure 3. Use of Red Blood Cell Transfusion by Postprocedure Hemoglobin Level at High-, Medium-, and Low-Transfusing Hospitals**

Frequency of red blood cell transfusion by postprocedure hemoglobin level when the study sample of hospitals is divided into high-, medium-, and low-transfusing hospitals. Rates of transfusion are higher at high-transfusing sites across all hemoglobin levels. PCI indicates percutaneous coronary intervention; RSTR, risk-standardized transfusion rate.
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Table 2. Association of Transfusion and Outcomes: Adjusted Odds Ratios From Inverse Probability–Weighted Analysisa

<table>
<thead>
<tr>
<th>Visit Outcomes</th>
<th>Overall Population</th>
<th>Patients With Bleeding</th>
<th>Patients Without Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With RBCT, No. (%)</td>
<td>Without RBCT, No. (%)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td></td>
<td>[95% CI]</td>
<td>[95% CI]</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, stroke, or in-hospital death</td>
<td>3152 (18.3) (n = 17 185)</td>
<td>1772 (9.50) (n = 18 650)</td>
<td>1.16 (1.11-1.22)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2202 (4.54) (n = 48 430)</td>
<td>2060 (4.14) (n = 210 281)</td>
<td>2.60 (2.57-2.63)</td>
</tr>
<tr>
<td>Stroke</td>
<td>988 (2.04) (n = 31 245)</td>
<td>722 (3.87) (n = 31 245)</td>
<td>1.35 (1.24-1.46)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>2207 (12.8) (n = 12 3-13)</td>
<td>1007 (5.40) (n = 12 3-13)</td>
<td>1.07 (1.01-1.13)</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; PCI, percutaneous coronary intervention; RBCT, red blood cell transfusion.

* The inverse probability–weighted model included the following variables: age, sex, race, body mass index, prior myocardial infarction, prior coronary artery bypass graft/valvular surgery, cardiogenic shock, cardiac arrest, use of intra-aortic balloon pump, prior congestive heart failure (CHF), peripheral vascular disease, cerebrovascular disease, tobacco use, chronic lung disease, diabetes, hyperlipidemia, family history, dialysis, glomerular filtration rate, New York Heart Association class IV CHF, location of lesion, percutaneous coronary intervention (PCI) indication, PCI status, and hospital characteristics such as public vs private ownership, core-based statistical area, number of beds, PCI volume, teaching facility status, and region.

Table 3. Association of Transfusion and Outcomes by Preprocedure Hemoglobin Level: Adjusted Odds Ratios From Inverse Probability–Weighted Analysis*

<table>
<thead>
<tr>
<th>Myocardial Infarction, Stroke, or In-Hospital Death</th>
<th>Preprocedure Hemoglobin Level, g/dL</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Population</td>
<td>≤10</td>
<td>&gt;10 to ≤13</td>
</tr>
<tr>
<td>With RBCT, No. (%) [95% CI] of PCI visits</td>
<td>2384 (13.3) (12.8-13.8)</td>
<td>3588 (18.1) (17.5-18.6)</td>
</tr>
<tr>
<td>Without RBCT, No. (%) [95% CI] of PCI visits</td>
<td>4425 (5.5-5.9) (3.43-4.12)</td>
<td>23 329 (3.38) (2.68-2.74)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.56 (1.51-1.62)</td>
<td>3.62 (3.57-3.68)</td>
</tr>
<tr>
<td>Patients With Bleeding</td>
<td>581 (17.0) (15.8-18.3)</td>
<td>1459 (17.6) (16.8-18.4)</td>
</tr>
<tr>
<td>Without RBCT, No. (%) [95% CI] of PCI visits</td>
<td>82 (15.4) (12.3-18.5)</td>
<td>580 (11.9) (11.0-12.8)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>0.74 (0.66-0.83)</td>
<td>1.01 (0.93-1.08)</td>
</tr>
<tr>
<td>Patients Without Bleeding</td>
<td>1803 (12.5) (11.9-13.0)</td>
<td>2129 (18.4) (178.7-19.1)</td>
</tr>
<tr>
<td>Without RBCT, No. (%) [95% CI] of PCI visits</td>
<td>4343 (5.62) (5.46-5.79)</td>
<td>21 749 (3.32) (3.27-3.36)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.54 (1.48-1.60)</td>
<td>3.83 (3.77-3.89)</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; PCI, percutaneous coronary intervention; RBCT, red blood cell transfusion.

* The inverse probability–weighted model included the following variables: age, sex, race, body mass index, prior myocardial infarction, prior coronary artery bypass graft/valvular surgery, cardiogenic shock, cardiac arrest, use of intra-aortic balloon pump, prior congestive heart failure (CHF), peripheral vascular disease, cerebrovascular disease, tobacco use, chronic lung disease, diabetes, hyperlipidemia, family history, dialysis, glomerular filtration rate, New York Heart Association class IV CHF, location of lesion, percutaneous coronary intervention (PCI) indication, PCI status, and hospital characteristics such as public vs private ownership, core-based statistical area, number of beds, PCI volume, teaching facility status, and region.

Discussion

There was marked variation in transfusion practice patterns across the United States among patients undergoing PCI. Within this variation there appeared to be patients who underwent transfusion in the absence of clinical bleeding events and patients who underwent transfusion with nearly normal preprocedure hemoglobin values. These patient-level data, as well as our finding that transfusions were more common across all hemoglobin values at some hospitals, suggest that thresholds for transfusion may have been driven more by local prac-
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Conclusions

Considerable variation in blood transfusion practice exists among patients undergoing PCI in the United States, and this variation persists after adjustment for patient differences. Moreover, transfusion thresholds vary widely across hospis.

Limitations

This study has several limitations. First, the data are observational and thus have measured confounding as shown through our bivariable, multivariable, and propensity-modeling analyses, as well as unmeasured confounding that cannot be mitigated. Second, even though the CathPCI Registry captures data from the majority of United States cardiac catheterization laboratories, it does not include all hospitals and thus may not fully represent practice in the United States. Third, we analyzed transfusion patterns at the hospital and patient levels but did not evaluate individual practitioner level variation. It is likely that physicians other than the interventional cardiologist who performed the procedure care for many patients undergoing PCI in the United States, and these physicians may have made postprocedure transfusion decisions. The CathPCI Registry does not contain information on these other practitioners. Fourth, even though hemoglobin level, transfusion, and events were all defined as postprocedure, the absolute temporal relationship between these elements cannot be determined. Thus, the data demonstrate an association between transfusion and adverse in-hospital outcomes, but causality cannot be inferred based on these data.
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