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Determinants of hospital variability in perioperative red blood cell transfusions during coronary artery bypass graft surgery

David C. Fitzgerald, DHA, MPH, CCP,a Annie N. Simpson, PhD,b Robert A. Baker, PhD, CCP,b Xiaoting Wu, PhD,c Min Zhang, PhD,d Michael P. Thompson, PhD,e Gaetano Paone, MD, MHS,e Alphonse Delucia III, MD,a and Donald S. Likosky, PhD,e on behalf of the PERForm Registry and the Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative

ABSTRACT

Objective: To identify to what extent distinguishing patient and procedural characteristics can explain center-level transfusion variation during coronary artery bypass grafting surgery.

Methods: Observational cohort study using the Perfusion Measures and Outcomes Registry from 43 adult cardiac surgical programs from July 1, 2011, to July 1, 2017. Iterative multilevel logistic regression models were constructed using patient demographic characteristics, preoperative risk factors, and intraoperative conservation strategies to progressively explain center-level transfusion variation.

Results: Of the 22,272 adult patients undergoing isolated coronary artery bypass surgery using cardiopulmonary bypass, 7,241 (32.5%) received at least 1 U allogeneic red blood cells (range, 10.9%–59.9%). When compared with patients who were not transfused, patients who received at least 1 U red blood cells were older (68 vs 64 years; P < .001), were women (41.5% vs 15.9%; P < .001), and had a lower body surface area (1.93 m² vs 2.07 m²; P < .001), respectively. Among the models explaining center-level transfusion variability, the intraclass correlation coefficients were 0.07 for model 1 (random intercepts), 0.12 for model 2 (patient factors), 0.14 for model 3 (intraoperative factors), and 0.11 for model 4 (combined). The coefficient of variation for center-level transfusion rates were 0.31, 0.29, 0.40, and 0.30 for models 1 through 4, respectively. The majority of center-level variation could not be explained through models containing both patient and intraoperative factors.

Conclusions: The results suggest that variation in center-level red blood cells transfusion cannot be explained by patient and procedural factors alone. Investigating organizational culture and programmatic infrastructure may be necessary to better understand variation in transfusion practices. (J Thorac Cardiovasc Surg 2020;■:1-10)

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Approximately 85 million allogeneic red blood cell (RBC) units are administered worldwide every year, with cardiac surgery accounting for 15% to 20% of all transfusions. Almost half of all patients undergoing isolated coronary artery bypass grafting (CABG) receive at least 1 U RBC unit during the hospital episode of care. Despite the clinical benefits in treating symptomatic anemia and hemorrhage, exposure to as little as 1 or 2 U RBC has been independently associated with significantly increased postoperative morbidity and mortality following CABG surgery.

Several randomized controlled trials and meta analyses have suggested that a more restrictive strategy for RBC exposure may be noninferior to a liberal transfusion threshold. Current multidisciplinary clinical practice guidelines identify interventions aimed to reduce bleeding and unnecessary blood transfusions in cardiac surgery. Although guidelines may provide practical recommendations for institutional blood conservation programs, their dissemination and direct influence on clinical care may not be fully realized. Wide variation in blood transfusion rates has been reported across institutions even after adjusting for patient risk. Prior work has identified hospital geographic location, academic status, surgical case volume, and procedural mix as risk factors for transfusion. Few studies have empirically tested the independent effect that both pre- and intraoperative factors have on blood transfusion rates before the initiation of cardiopulmonary bypass (CPB). As such, determinants of center-level variation in RBC rates have not been fully explained.

Determinants of center variability in intra- or postoperative RBC transfusion rates were evaluated across adult cardiac surgical programs performing isolated CABG surgery. The primary aim was to identify to what extent distinguishing patient and procedural characteristics that are known before allogeneic RBC transfusions may help explain center-level variation in transfusion rates across adult isolated coronary artery surgical procedures (Video 1).

**MATERIALS AND METHODS**

This study (HUM00151098) was approved by the University of Michigan Institutional Review Board. The Perfusion Measures and Outcomes (PERForm) registry was established in 2010 as a voluntary database. The PERForm registry is structured within the Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative, a cardiac surgeon-led quality collaborative embedded in the Michigan Society of Thoracic and Cardiovascular Surgeons. The PERForm registry complements data from the Society of Thoracic Surgeons by focusing on the care and conduct of cardiovascular perfusion practices. Each record from PERForm is merged with a record from each center’s surgical data.

The study population included adult patients undergoing isolated CABG surgery using CPB support between July 1, 2011, and July 1, 2017. Data were collected from 43 cardiac surgical centers participating in both the Society of Thoracic Surgeons Adult Cardiac Surgery Database and the PERForm registry. There were 33 centers represented in the state of Michigan and 10 participating programs outside of Michigan. Each surgical record was merged with the perfusion record from the PERForm registry. After exclusions (Figure E1), our final dataset included 22,272 patients. The primary outcome was allogeneic RBC transfusions administered during the intraoperative and/or postoperative periods.

Variables that were present before the time of an RBC transfusion decision were considered for analysis, including patient and disease characteristics, equipment selection, laboratory assay results, and intraoperative blood conservation strategies (Table 1).

Median and mode imputation were performed for continuous and categorical covariates with an observed data missingness <10% to ensure that all observations were included during the modeling process. Specifically, missing preoperative risk factor data variables such as diabetes, history of cerebrovascular disease, dialysis status, and prior myocardial infarction were imputed as no disease. Missing data for operative status were considered as elective surgery. Missing data fields, including last preoperative risk factor data variables such as diabetes, history of cerebrovascular disease, dialysis status, and prior myocardial infarction were imputed as no disease. Missing data for operative status were considered as elective surgery. Missing data fields, including last preoperative risk factor data variables such as diabetes, history of cerebrovascular disease, dialysis status, and prior myocardial infarction were imputed as no disease.

Variables with >10% missingness such as...
congestive heart failure and peripheral vascular disease remained by creating missing indicators.

The distribution of demographic variables was reported according to quartile categories of crude transfusion rates. The observed-to-expected ratio for perioperative RBC transfusion was calculated using the observed rates from the data and the expected rates derived from the risk prediction model previously described by Likosky and colleagues. To quantify the degree to which hospitals, patient, and procedural factors influence variation in crude center-level perioperative RBC transfusion rates, a series of mixed effect logistic regression models (models 1-4), similar to the approach described by Xian and colleagues, were constructed (Table 1). Model 1 contained hospital random intercepts and no covariates. Model 2 included the previous model 1 hospital random effect plus patient-related risk factors: patient demographic data, preoperative laboratory serum assay results, and preoperative risk factors. Model 3 contained model 1 plus intraoperative blood conservation techniques and equipment aimed to reduce hemodilution and anemia. Model 4 included all of the previous models (ie, models 1 through 3). Patient and procedural covariates were selected according to the consensus minimal reporting criteria for CPB-related RBC transfusions reported by Likosky and colleagues.20

From each model, the random effect variance was computed and intraclass correlation coefficient (ICC) was calculated using both the simulation method and latent variable method as described by Merlo and colleagues.21 In model 1, with only the hospital random effect, the ICC may be interpreted as the proportion of total observed variance in transfusion that was attributable to the systematic differences between hospitals. In models 2 through 4 with covariate adjustment, the ICC may be interpreted as the proportion of the residual variation after accounting other variables in the model that was attributable to the hospital differences.

Continuous variables were presented as median and interquartile range (25th-75th percentile) and categorical variables were presented as counts and percentages. Pearson χ² and Fisher exact tests were performed for categorical variables, as appropriate, and the Wilcoxon rank-sum test was performed for continuous variables. Statistical analysis was conducted using SAS version 9.4 (SAS Institute, Cary, NC) and R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

**TABLE 1. Multivariable logistic regression models of red blood cell (RBC) transfusion variables**

<table>
<thead>
<tr>
<th>Model</th>
<th>Description</th>
<th>Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hospital random intercepts only</td>
<td>None</td>
</tr>
</tbody>
</table>
| 2     | Model 1 + patient demographic, laboratory assay results, and preoperative risk factors | - Model 1
- Age (y)
- Body surface area (m²)
- Sex (M/F)
- Admission status (elective, urgent, emergent/salvage)
- Preoperative hematocrit (%)
- Serum albumin (g/dL)
- Serum creatinine (mg/dL)
- Platelet count (>10,000)
- Current smoker (y/n)
- Chronic lung disease (y/n)
- Previous myocardial infarction (y/n)
- Congestive heart failure (y/n)
- Cardiogenic shock (y/n)
- Peripheral vascular disease (y/n)
- Cerebrovascular disease (y/n)
- Diabetes mellitus (y/n)
- Dialysis (y/n)
- Hypertension (y/n)
- Anticoagulant medications <48 h (y/n)
- Reoperative status (y/n)
- Number of diseased vessels |
| 3     | Model 1 + perfusion factors (intraoperative blood conservation procedural factors) | - Model 1
- Arterial roller pump use (y/n)
- Acute normovolemic hemodilution (y/n)
- del Nido cardioplegia use (y/n)
- Autotransfusion use (y/n)
- Autologous CPB circuit prime (y/n)
- Indexed net CPB prime (mL/m²) |
| 4     | (hospital random intercepts) + (patient demographic, laboratory assay results, and preoperative risk factors) + (Intraoperative Blood Conservation Procedural Factors) | - Model 1
- Model 2
- Model 3 |

CPB, Cardiopulmonary bypass. *Multivariate logistic regression models consisting of common transfusion-related clinical reporting variables. Each of the models consist of patient, procedural, and combined factors associated with perioperative RBC transfusions.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Perioperative RBC transfusion</th>
<th>( P ) value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (N = 22,272)</td>
<td>No (n = 15,031)</td>
<td>Yes (n = 7241)</td>
</tr>
<tr>
<td>Intraoperative only</td>
<td>1586</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Postoperative transfusion only</td>
<td>3884 (17.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Intraoperative and postoperative</td>
<td>1771</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**Intraoperative CPB equipment**

- **Roller pump**
  - 9914 (44.5)
  - 6771 (45.0)
  - 3143 (43.4) .022

- **Cardioplegia**
  - Non-del Nido CDPG
    - 18,606 (83.5)
    - 12,474 (83.0)
    - 6132 (84.7) <.001

- del Nido only
  - 3250 (14.6)
  - 2311 (15.4)
  - 939 (13.0)

- None
  - 416 (1.9)
  - 246 (1.6)
  - 170 (2.3)

**Demographic characteristics**

- **Age (y)**
  - 65 (58-72)
  - 64 (57-71)
  - 68 (61-75) <.001

- **BSA (m²)**
  - 2.03 (1.87-2.18)
  - 2.07 (1.93-2.21)
  - 1.93 (1.77-2.09) <.001

- **Female**
  - 5398 (24.2)
  - 2391 (15.9)
  - 3007 (41.5) <.001

- **Admission status**
  - Elective
    - 8825 (39.6)
    - 6326 (42.1)
    - 2499 (34.5) <.001

  - Urgent
    - 12,834 (57.6)
    - 8413 (56.0)
    - 4421 (61.1)

  - Emergent/emergent salvage
    - 611 (2.7)
    - 291 (1.9)
    - 320 (4.4)

**Lab values**

- **Preoperative HCT (%)**
  - 40 (36-43)
  - 41 (38-44)
  - 36 (32-39) <.001

- **Total albumin (g/dL)**
  - 3.80 (3.50-4.10)
  - 3.80 (3.60-4.10)
  - 3.70 (3.30-4.00) <.001

- **Last creatinine (mg/dL)**
  - 1.00 (0.80-1.19)
  - 0.97 (0.80-1.10)
  - 1.00 (0.80-1.30) <.001

- **Platelets count (×10,000)**
  - 20.80 (17.30-25.00)
  - 20.70 (17.30-24.60)
  - 21.00 (17.00-26.00) <.001

**Intraoperative blood conservation techniques**

- **First HCT on CPB support**
  - 27.00 (23.00-31.00)
  - 28.00 (25.00-32.00)
  - 23.00 (21.00-27.00) <.001

- **Last HCT before CPB**
  - 35.00 (31.00-39.00)
  - 36.00 (33.00-40.00)
  - 31.00 (27.00-35.00) <.001

- **Anesthesia crystalloid volume indexed to patient weight (mL/m²)**
  - 10.74 (7.53-14.77)
  - 10.32 (7.30-14.10)
  - 11.79 (8.11-16.50) <.001

- **Static prime volume indexed to BSA (mL/m²)**
  - 1000.00 (900.00-1220.00)
  - 1050.00 (900.00-1220.00)
  - 1000.00 (850.00-1250.00) <.001

- **Total prime volume (indexed to BSA) (mL/m²)**
  - 614.10 (506.22-722.91)
  - 604.24 (498.32-704.35)
  - 640.61 (525.15-766.03) <.001

- **Autologous circuit prime**
  - 17,714 (79.5)
  - 12,141 (80.8)
  - 5573 (77.0) <.001

- **Autologous circuit volume (mL)**
  - 500.00 (200.00-625.00)
  - 500.00 (250.00-650.00)
  - 450.00 (350-450) <.001

- **ANH volume**
  - 3176 (14.3)
  - 2591 (17.2)
  - 450 (430-900) <.001

- **ANH volume index to weight**
  - 5.84 (4.6-8.2)
  - 5.84 (4.7-8.77)
  - 5.84 (4.4-6.15) <.001

**Patient risk factors**

- **Current smoker**
  - 5006 (22.5)
  - 3575 (23.8)
  - 1431 (19.8) <.001

- **Previous MI**
  - 12,094 (54.3)
  - 7744 (51.5)
  - 4350 (60.1) <.001

- **Severe/moderate chronic lung disease**
  - 2264 (10.2)
  - 1285 (8.5)
  - 979 (13.5) <.001

- **CHF**
  - 17,058 (76.6)
  - 12,381 (82.4)
  - 4677 (64.6) <.001

- **PVD**
  - 16,633 (74.7)
  - 12,074 (80.3)
  - 4559 (63.0) <.001

- **Diabetes**
  - 10,543 (47.3)
  - 6743 (45.9)
  - 3800 (52.5) <.001

- **Cardiogenic shock**
  - 382 (1.7)
  - 140 (0.9)
  - 242 (3.3) <.001

- **CVD**
  - 4673 (21.0)
  - 2614 (17.4)
  - 2059 (28.4) <.001

- **Preoperative dialysis**
  - 562 (2.5)
  - 112 (0.7)
  - 450 (6.2) <.001

- **Hypertension**
  - 19,970 (89.7)
  - 13,290 (88.4)
  - 6680 (92.3) <.001

(Continued)
RESULTS

Patient demographic and procedural variables were analyzed across by perioperative RBC transfusion status (Table 2). There were 7241 (32.5%) of the 22,272 study participants who received at least 1 U allogeneic RBC. Among those, 3884 (53.6%) patients were transfused in the postoperative period only. Overall, the median age was 65 years (interquartile range, 58-72 years), with men comprising 75.8% of the population. When compared with patients who were not transfused, patients who received at least 1 U RBC were older (68 years vs 64 years; $P<.001$), were women (41.5% vs 33.8%; $P<.001$), had lower body surface area (1.93 m$^2$ vs 2.07 m$^2$; $P<.001$), and were less likely to be electively admitted for surgery (34.5% vs 42.1%), respectively. The transfusion group also had a significantly higher prevalence of preoperative risk factors, including previous preoperative dialysis (6.2% vs 0.7%; $P<.001$) and anticoagulant medication within 48 hours of surgery (50.7% vs 44.0%; $P<.001$). Similar differences between groups were also observed across all perioperative hematocrit values. Patients undergoing transfusion were also significantly less likely to receive blood conservation therapies such as acute normovolemic hemodilution volume and autologous CPB circuit priming. Additionally, the transfusion group received significantly larger indexed amounts of asanguineous crystalloid volume via anesthesia intravenous infusion (11.79 mL/kg vs 10.32 mL/kg; $P<.001$) and total CPB prime volume (640.6 mL/m$^2$ vs 604.2 mL/m$^2$; $P<.001$).

Demographic and procedural variables were also distributed across quartiles of crude center-level perioperative RBC transfusion rates (Table 3). Center-level RBC transfusion rates ranged from 10.9% to 59.9%. The observed-to-expected ratios for RBC transfusion were 0.71 (interquartile range [IQR], 0.60-0.77), 0.89 (IQR, 0.82-0.95), 1.10 (IQR, 1.07-1.24), and 1.28 (IQR, 1.20-1.52), for quartiles 1 to 4, respectively.

The model 1 (hospital intercepts only) random effect variance was 0.256 (Table 4). The ICC was 0.072, implying that 7.2% of the individual variation in transfusion was due to systematic differences between hospitals, whereas 92.8% was due to systematic differences between patients. Model 2 increased the random effect variance (0.45) and ICC (0.12), indicating that the residual variation (unexplained variation) in transfusion after adjusting for patient risk factors due to hospital differences was 12%, and 88% was due to systematic differences between patients. Results from model 3 (ICC, 0.136) indicated that the unexplained variation after adjusting for intraoperative factors due to hospital differences was 13.6%, and 86.4% was due to systematic differences between patients. Nesting of all models together (model 4) resulted in a decrease in the calculated variance (0.420) and ICC (0.113), implying that 11.3% of the individual variation in transfusion after controlling for patient risk and intraoperative factors was due to systematic differences among hospitals, whereas 88.7% of the individual variation in transfusion was due to systematic differences between patients.

A turnip plot (Figure 1) was developed to display the coefficient of variation, defined as the ratio of the standard deviation to the mean hospital center transfusion rate, for each model. A dot was used to represent each hospital. Each hospital was in turn centered symmetrically on the horizontal axis based on its RBC transfusion status. The coefficient of variation for each of the models were 0.33 (observed), and 0.31, 0.29, 0.40, and 0.30 for models 1 through 4, respectively.

DISCUSSION

Previous literature has identified both modifiable and nonmodifiable clinical factors associated with the increased exposure to allogeneic RBC units. Conventional wisdom may suggest that differences in baseline patient risk may be the predominant drivers of differences in center transfusion rates following CABG surgery. With this in mind, the aim of this study was to assess the contributions that pre- and intraoperative factors have in explaining hospital variation in blood transfusion rates. In this large, contemporaneous, multicenter study, the addition of intraoperative factors known at the time of transfusion decision making did not appreciably improve the understanding of determinants of variation in RBC transfusion during CABG surgery (Figure 2).
<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Q1 10.9-23.6</th>
<th>Q2 24.2-31.2</th>
<th>Q3 33.0-39.8</th>
<th>Q4 40.0-59.9</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative RBC transfusion rate (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients (n)</td>
<td>22,272</td>
<td>5807</td>
<td>5178</td>
<td>6005</td>
<td>5282</td>
<td></td>
</tr>
<tr>
<td>Hospitals (n)</td>
<td>43</td>
<td>10</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Surgeons (n)</td>
<td>209</td>
<td>61</td>
<td>40</td>
<td>57</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Perfusionists (n)</td>
<td>294</td>
<td>68</td>
<td>63</td>
<td>74</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>Unique pairs of surgeons and perfusionists</td>
<td>1421</td>
<td>336</td>
<td>314</td>
<td>460</td>
<td>407</td>
<td></td>
</tr>
<tr>
<td>O/E ratio of RBC transfusion</td>
<td>0.98 (0.80-1.23)</td>
<td>0.71 (0.60-0.77)</td>
<td>0.89 (0.82-0.95)</td>
<td>1.10 (1.07-1.24)</td>
<td>1.28 (1.20-1.52)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age (y)</td>
<td>65.0 (58.0-72.0)</td>
<td>65.0 (58-72)</td>
<td>66.0 (59-73)</td>
<td>65.0 (58-72)</td>
<td>65.0 (57.0-72)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>24.2</td>
<td>22</td>
<td>23.3</td>
<td>24.4</td>
<td>27.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>2.0 (1.9-2.2)</td>
<td>2.0 (1.9-2.2)</td>
<td>2.0 (1.9-2.2)</td>
<td>2.0 (1.9-2.2)</td>
<td>2.0 (1.8-2.2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Elective operative status (%)</td>
<td>&lt;.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>39.6</td>
<td>41.7</td>
<td>35.5</td>
<td>43.4</td>
<td>37.1</td>
<td></td>
</tr>
<tr>
<td>Urgent</td>
<td>57.6</td>
<td>55.6</td>
<td>61.4</td>
<td>54.4</td>
<td>59.9</td>
<td></td>
</tr>
<tr>
<td>Emergent/emergent salvage</td>
<td>2.7</td>
<td>2.7</td>
<td>3.1</td>
<td>2.3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>No. of diseased vessels &gt;3</td>
<td>78.4</td>
<td>78.8</td>
<td>78.6</td>
<td>78.1</td>
<td>78.1 .72</td>
<td></td>
</tr>
<tr>
<td>Previous myocardial infarction (%)</td>
<td>54.3</td>
<td>55.1</td>
<td>54</td>
<td>51.9</td>
<td>56.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Reoperative status (%)</td>
<td>2.2</td>
<td>2.3</td>
<td>2.8</td>
<td>1.7</td>
<td>2.3 .0011</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>47.3</td>
<td>47.2</td>
<td>45.1</td>
<td>46.5</td>
<td>50.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
<td>21.0</td>
<td>18.7</td>
<td>23.6</td>
<td>20</td>
<td>22.1 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure (%)</td>
<td>11.2</td>
<td>10.4</td>
<td>10.5</td>
<td>12.4</td>
<td>11.4 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Cardiogenic shock (%)</td>
<td>1.7</td>
<td>1.5</td>
<td>1.8</td>
<td>1.8</td>
<td>1.8 .45</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease (%)</td>
<td>13.2</td>
<td>11.7</td>
<td>13.6</td>
<td>12.2</td>
<td>15.1 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>22.5</td>
<td>20.9</td>
<td>20.3</td>
<td>22.9</td>
<td>25.9 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease (%)</td>
<td>10.2</td>
<td>9.9</td>
<td>9.5</td>
<td>9.1</td>
<td>12.3 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>89.7</td>
<td>88.6</td>
<td>87.9</td>
<td>90.1</td>
<td>92.1 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Dialysis (%)</td>
<td>2.5</td>
<td>2.3</td>
<td>2.2</td>
<td>2.6</td>
<td>3.1 .016</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>55.0 (45.0-60.0)</td>
<td>55.0 (45.0-60.0)</td>
<td>55.0 (47.0-60.0)</td>
<td>55.0 (45.0-60.0)</td>
<td>55.0 (45.0-60)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Preoperative hematocrit (%)</td>
<td>39.9 (36.0-43.0)</td>
<td>40.0 (36.0-43.0)</td>
<td>39.9 (36.0-42.8)</td>
<td>39.7 (35.9-42.9)</td>
<td>39.3 (35.2-42.8)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Platelet count (per µL)</td>
<td>208 (172-251)</td>
<td>209 (173-250)</td>
<td>205 (171-246)</td>
<td>209 (173-253)</td>
<td>209 (171-255)</td>
<td></td>
</tr>
<tr>
<td>Anticoagulant medications &lt;48 h (%)</td>
<td>46.2</td>
<td>41.6</td>
<td>43.3</td>
<td>49.4</td>
<td>50.5 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.0 (0.8-1.2)</td>
<td>1.0 (0.8-1.1)</td>
<td>1.0 (0.8-1.2)</td>
<td>1.0 (0.8-1.2)</td>
<td>1.0 (0.8-1.2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.8 (3.5-4.1)</td>
<td>3.8 (3.6-4.1)</td>
<td>3.8 (3.4-4.1)</td>
<td>3.8 (3.4-4.0)</td>
<td>3.8 (3.5-4.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Arterial roller pump use (%)</td>
<td>44.5</td>
<td>35.5</td>
<td>51.1</td>
<td>78.9</td>
<td>8.7 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Del Nido cardioplegia use (%)</td>
<td>14.6</td>
<td>14.2</td>
<td>23.9</td>
<td>14.9</td>
<td>5.5 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Autotransfusion use (%)</td>
<td>85.2</td>
<td>94.44</td>
<td>59.77</td>
<td>90.56</td>
<td>93.92 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Acute normovolemic hemodilution (y/n)</td>
<td>14.3</td>
<td>17.3</td>
<td>16.1</td>
<td>13.5</td>
<td>9.9 &lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Acute normovolemic hemodilution (mL) (among available data)</td>
<td>450 (430-900)</td>
<td>900 (450-900)</td>
<td>500 (450-900)</td>
<td>450 (400-450)</td>
<td>350 (350-450)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

(Continued)
A turnip plot may be used to illustrate the dispersion of hospital transfusion variation around the mean rates. Only small differences in variation were observed across each of the covariate-adjusted models. When all of the covariates were taken account (model 4), the coefficient of variation decreased.

The ICC and random effects variance were used to test the relatedness of transfusions between hospitals. Even after adjusting for many of the often cited patient and procedural transfusion-related risk, there was little conformity in transfusion rates among hospitals. Guidelines for interpreting the ICC reported by Koo and Li recommend that values <0.5 may be indicative of poor reliability. The results indicate that the clinical factors believed to be key determinants in transfusion decisions did not explain the variability in RBC transfusions among hospitals. Additional investigation into nonclinical factors (eg, provider transfusion triggers, organizational culture, and blood management protocols) may improve the understanding of center-level differences.

In an observational cohort of 102,470 patients from 798 clinical sites undergoing isolated CABG surgery, Bennett-Guerrero and colleagues reported significant variation in hospital risk-adjusted transfusion rates according to geographic location (P = .007), academic status (P = .03), and hospital volume (P < .001). Although these factors only attributed for 11.1% of the observed variance, procedural case mix accounted for only 20% of the total variation. Likosky and colleagues examined regional-specific discretionary (1-2 U) RBC transfusions for isolated CABG procedures across 5 regional cardiac surgical quality collaboratives. The analysis included 11,200 patients across the 56 participating centers who received 0, 1, or 2 U RBCs during the index admission. Significant variation in RBC units and volume was observed across regions and remained so after pre- and intraoperative risks (9.1% to 31.7%; P < .001).

Organizational culture, broadly defined as the basic assumptions and values that guide organizations, may be associated with variance in clinical practice. Using multilevel mixed-effect logistic and linear regression models, Jin and colleagues examined variation in blood transfusion practices among 5744 isolated CABG procedures performed by 42 surgeons at 12 hospitals within the same health system. Observed variances in RBC transfusions at the hospital level (0.82) were more than twice as high as surgeons practicing at the same hospital (0.35), suggesting an association between organizational culture and transfusion practice through factors such as team familiarity, quality improvement and data sharing, and standardized clinical practices. Likosky and colleagues compared perioperative RBC transfusion rates

---

**TABLE 3. Continued**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Perioperative RBC transfusion rate (%)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10.9-59.9</td>
<td>10.9-23.6</td>
<td>24.2-31.2</td>
</tr>
<tr>
<td>Acute normovolemic hemodilution (mL) (among available data) indexed to weight</td>
<td>5.8 (4.6-8.2)</td>
<td>7.7 (5.8-10.4)</td>
<td>6.3 (5.0-9.3)</td>
</tr>
<tr>
<td>Autologous blood CPB prime†,‡</td>
<td>79.5</td>
<td>89.2</td>
<td>59.7</td>
</tr>
<tr>
<td>Autologous blood prime†,‡</td>
<td>550 (400-700)</td>
<td>600 (400-650)</td>
<td>500 (400-600)</td>
</tr>
<tr>
<td>Static CPB prime indexed to body surface area (mL/m²)</td>
<td>1000 (900-1220)</td>
<td>1200 (900-1215)</td>
<td>1000 (900-1200)</td>
</tr>
<tr>
<td>Net prime volume indexed to body surface area (mL/m²)</td>
<td>371.9 (258.5-514.3)</td>
<td>373.7 (262.4-505.1)</td>
<td>434.8 (286.7-640.1)</td>
</tr>
<tr>
<td>Last Pre-CPB Hematocrit (%)</td>
<td>35.0 (31.0-39.0)</td>
<td>35 (31-38)</td>
<td>36 (32-39)</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as median (interquartile range) and categorical variables are expressed as %. RBC, Red blood cell; O/E, observed/expected; CPB, cardiopulmonary bypass. *Significance set at P < .05. †Mandatory reporting measures based on reference. ‡Retrograde autologous prime.

**TABLE 4. Random effect variance and intraclass correlation coefficient (ICC) model results**

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random effects variance</td>
<td>0.256</td>
<td>0.453</td>
<td>0.519</td>
<td>0.420</td>
</tr>
<tr>
<td>ICC coefficient with latent variable approach</td>
<td>0.072</td>
<td>0.12</td>
<td>0.136</td>
<td>0.113</td>
</tr>
<tr>
<td>ICC coefficient with simulation approach</td>
<td>0.052</td>
<td>0.062</td>
<td>0.062</td>
<td>0.064</td>
</tr>
</tbody>
</table>

After covariate adjustment in models 2 through 4, the intraclass correlation coefficient (ICC) represents the proportion of the residual variation after accounting for other variables in the model attributable to the hospital differences. As covariates are added, the unexplained variance does not appreciably change the models. ICC, Intraclass correlation coefficient. *Model 1: Hospital intercepts only; model 2: model 1 + patient demographic, laboratory assay results, and preoperative risk factors; model 3: model 1 + intraoperative blood conservation procedural factors; model 4: model 1 + model 2 + model 3.
for both CABG and percutaneous coronary intervention (PCI) at 33 Michigan cardiac surgical programs.31 A total of 16,568 CABG and 94,634 PCI patients were included for analysis. There was wide variation in transfusion rates observed across centers for both CABG (26.5%–71.3%) and PCI (1.6%–6.0%). Although perhaps somewhat surprising, the investigators found that an institution’s CABG transfusion rate significantly correlated with the PCI rate.31 These findings suggest that factors beyond patient-level risk may help explain center-level differences in transfusion practices. A number of studies have evaluated the association between clinical providers and RBC transfusions. A single-center analysis of 4823 patients by Cote and colleagues23 found that differing practice patterns among cardiac surgeons and anesthesiologists were independent predictors of perioperative transfusion.23 Significant differences in perioperative transfusion rates were reported among surgeons.

The authors conducted an observational study of 22,272 patients undergoing coronary artery bypass grafting across 43 centers. Iterative modeling approaches were used to evaluate the contribution of patient and intraoperative factors on explain hospital-level transfusion rates. The majority of center-level variation could not be explained through the patient and intraoperative factors.
(32.4%-51.5%; *P* < 0.0001), anesthesiologists (34.4%-51.9%; *P* < 0.0001), by year of hospital admission (28.2% in 2004 and 48.8% in 2008; *P* < 0.0001). Differences in transfusion rates among practitioners were found after adjustment for baseline and intraoperative covariates.23 Previous surveys conducted among critical care practitioners reported significant individual variation in acceptable hemoglobin concentrations before transfusion.18,33,34 Although differences in transfusion triggers may be attributed to patient-related clinical factors, physicians may weigh these clinical characteristics differently in the absence of formal institutional protocols. Clinical transfusion triggers may also be influenced by environmental factors such as computer decision support, motivation to adopt guidelines and support from colleagues.34

Despite the reported benefits of team familiarity on clinical effectiveness and surgical teamwork, its association with blood transfusion behaviors has not been previously described. Shared work experiences and familiarity among team members have been reported to contribute to improved anticipation, coordination and productivity.38 Conversely, clinicians that experience a high level of dispersion across larger and unfamiliar teams may lack the bonds and interpersonal relationships for effective collaboration. Poor communication between unfamiliar team members may lead to avoidable transfusions because team members may not compensate for this lack of familiarity with increased communication.39 Decisions among intraoperative care members may be improved with teamwork and experience.40,41 Although the number of unique staffing pairs among surgeons and perfusionists were calculated (Table 3), this study did not capture all potentially relevant team members (eg, anesthesia personnel, critical care/intensive care unit team members). Capture of these care providers may have provided a more reliable estimate of explanatory transfusion variation within and across centers. Other modifying factors include increased staff turnover, variances in surgical case volume, and staff education in blood management.

Although single and multicenter studies have reported reductions in potentially discretionary transfusions through programmatic guideline development, education and feedback/audit activities, these activities have not been considered mandatory research reporting criteria.20 Findings presented in this study highlight the importance of identifying and comparing programmatic differences in blood management. Such variables may include the presence of transfusion triggers, protocols, institutional blood management committees, and a surgical champion with an interest in promoting blood conservation. Variability in practice may exist in circumstances when multiple clinicians have been empowered to make transfusion decisions. Differences in clinical opinion combined with multiple triggers may not support standardized transfusion algorithms. The single-center experience of Cote and colleagues describes a joint process on intraoperative transfusion decisions that collectively involve the surgeon, anesthesiologist, and perfusionist. However, once the patient has been admitted to the postoperative care arena, the surgeon may be the dominant decision maker.

There were several limitations to this study. First, as in any observational cohort study, the influence of unmeasured confounding (eg, preoperative transfusion and provider transfusion trigger) cannot be ruled out. Nonetheless, the authors adjusted for commonly reported risk factors associated with the risk of transfusion.18 Additionally, the analysis was restricted to variables that were known before the initiation of CPB support and before a transfusion decision was made. Second, there may also be potential collinearity among the model covariates that could influence the regression coefficient. For example, the intraoperative procedural model included net CPB prime volume, defined as the difference between CPB static prime volume and autologous blood prime volume. As such, the autologous CPB prime volume was removed from the model as a separate covariate. All attempts were made to omit any of the independent variables that demonstrated strong correlation. Last, these findings may only be generalizable to the institutions participating in the PERFOrm registry.

**CONCLUSIONS**
Variation in perioperative RBC transfusion rates across hospitals could not be explained by conventional patient and procedural factors present at the time of a transfusion decision. Further investigation should focus on the role of other potentially important determinants of hospital variability in transfusion practices. For instance, although professional societies have published blood management guidelines, existing registries do not track many important variables (eg, transfusion triggers). Further efforts aimed at ensuring optimal transfusion decisions will likely require advancements in clinical registries and team-based blood management protocols.

**Conflict of Interest Statement**
The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

**References**
Perioperative Management

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Key Words: coronary artery bypass, cardiac surgical procedures, erythrocyte transfusions, perioperative care, blood loss/surgical, bypass/cardiopulmonary

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Isolated coronary artery bypass grafting (CABG)  
N = 22,487 patients  
(July 2011-July 2017)

Isolated CABG for red blood cell transfusion prediction  
N = 22,444

Exclude patients with duplicate record ID and participant ID  
N = 43 patients

Exclude patients with unplanned cardiopulmonary bypass or refuse transfusion  
N = 172 patients

Isolated CABG  
N = 22,272 patients for analysis

**FIGURE E1.** Selection criteria for study population inclusion.
Determinants of hospital variability in perioperative red blood cell transfusions during coronary artery bypass graft surgery

David C. Fitzgerald, DHA, MPH, CCP, Annie N. Simpson, PhD, Robert A. Baker, PhD, CCP, Xiaoting Wu, PhD, Min Zhang, PhD, Michael P. Thompson, PhD, Gaetano Paone, MD, MHS, Alphonse Delucia III, MD, and Donald S. Likosky, PhD, on behalf of the PERForm Registry and the Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative, Charleston, SC; Adelaide, Australia; and Ann Arbor, Detroit, and Kalamazoo, Mich

Investigating the organizational culture and infrastructure of cardiac surgical programs may be necessary to explain center-level variation in RBC transfusion practices.