Increased Mortality, Postoperative Morbidity, and Cost After Red Blood Cell Transfusion in Patients Having Cardiac Surgery

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Background—Red blood cell transfusion can both benefit and harm. To inform decisions about transfusion, we aimed to quantify associations of transfusion with clinical outcomes and cost in patients having cardiac surgery.

Methods and Results—Clinical, hematology, and blood transfusion databases were linked with the UK population register. Additional hematocrit information was obtained from intensive care unit charts. Composite infection (respiratory or wound infection or septicemia) and ischemic outcomes (myocardial infarction, stroke, renal impairment, or failure) were prespecified as coprimary end points. Secondary outcomes were resource use, cost, and survival. Associations were estimated by regression modeling with adjustment for potential confounding. All adult patients having cardiac surgery between April 1, 1996, and December 31, 2003, with key exposure and outcome data were included (98%). Adjusted odds ratios for composite infection (737 of 8516) and ischemic outcomes (832 of 8518) for transfused versus nontransfused patients were 3.38 (95% confidence interval [CI], 2.60 to 4.40) and 3.35 (95% CI, 2.68 to 4.35), respectively. Transfusion was associated with increased relative cost of admission (any transfusion, 1.42 times [95% CI, 1.37 to 1.46], varying from 1.11 for 1 unit to 3.35 for 9 units). At any time after their operations, transfused patients were less likely to have been discharged from hospital (hazard ratio [HR], 0.63; 95% CI, 0.60 to 0.67) and were more likely to have died (0 to 30 days: HR, 6.69; 95% CI, 3.66 to 15.1; 31 days to 1 year: HR, 2.59; 95% CI, 1.68 to 4.17; >1 year: HR, 1.32; 95% CI, 1.08 to 1.64).

Conclusions—Red blood cell transfusion in patients having cardiac surgery is strongly associated with both infection and ischemic postoperative morbidity, hospital stay, increased early and late mortality, and hospital costs. (Circulation. 2007;116:2544-2552.)

Key Words: infection ■ myocardial infarction ■ stroke ■ surgery ■ blood transfusions

Transfusion of allogenic red blood cells (RBCs) is increasingly recognized as a risk factor for adverse outcome after cardiac surgery.1,2 Unnecessary transfusions are likely to be associated with unnecessary morbidity and additional indirect hospitalization costs. Direct costs also are considerable; adult cardiac surgery accounts for a significant proportion of all RBC transfusions in the United Kingdom and the United States.3,4

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The evidence base on which RBCs are transfused is poor. A low hematocrit in the absence of hemorrhagic shock remains the most common indication in the critically ill.5–7 However, the hematocrit level at which the benefits of transfusion outweigh the risks in anemic cardiac surgery patients is unclear. Consequently, the hematocrit threshold at which patients are transfused varies widely both within and between institutions, with 25% to 95% of cardiac surgery patients receiving RBC transfusions in surveys.6,8

We analyzed the association between RBC transfusion, nadir hematocrit, clinical outcomes, and hospital costs in a large cohort of patients having cardiac surgery to inform the design of a subsequent randomized controlled trial and potentially to promote collective equipoise among surgeons and cardiac intensivists.

Methods

Study Design
This retrospective cohort study linked data from several routinely collected data sources. The research objectives and the analyses
to address them were planned before the analyses were carried out, and the protocol was approved by a UK National Health Service (NHS) Research Ethics Committee (06/Q2002/50). Because of the dangers of selective outcome reporting and other biases that can arise in the analysis of observational data, we distinguish aspects of the study that were prespecified from those that were not.

**Study Population**

The Bristol Royal Infirmary established a database of adult cardiac surgery patients in April 1996 (Patient Analysis and Tracking Systems [PATS], Dendrite Clinical Systems, London, UK). A standard set of perioperative and postoperative data are collected prospectively by the anesthetist, surgeon, and intensive care unit (ICU), high-dependency unit (HDU), and ward nurses. All adult patients (\(\geq 16\) years) in this database up to December 31, 2003, whose data could be linked (see below) were included.

**Data Sources**

Three databases were linked: (1) the PATS database, (2) the hematology database of blood test results processed through the main laboratory of the hospital (providing longitudinal hematocrits during a patient’s hospital stay), and (3) the blood bank database of blood products issued and used. The PATS database also is linked with the UK population register through the NHS Strategic Tracing Service to audit long-term survival.

Because hematocrit is the most important indicator for transfusion, we aimed to stratify analyses by the nadir hematocrit during a patient’s postoperative course. Hematocrit is measured hourly by ICU staff, not in the main laboratory. Therefore, all available ICU charts for the study period were checked manually to obtain the nadir hematocrit during the first 12 postoperative hours.

**Definitions of Exposures of Interest and Potential Confounding Factors**

Units of RBC transfused were documented from the blood bank database. Any RBC transfusion versus none was the a priori exposure variable for RBC transfusion. Confounding factors included in the analysis plan as the tendency for these patients to be transfused more frequently that were not.

An additional prespecified subgroup analysis investigated whether the effect of transfusion changed after November 30, 1999, because the UK National Blood Service carried out universal leukodepletion after this date.

**Statistical Analysis**

Specific high-risk subgroups were identified in the analysis plan, namely older age, female gender, valvular or other operations, preoperative creatinine >150 mmol/L, presence of lung disease (chronic obstructive airways disease or asthma), diabetes mellitus, and incompletion of revascularization. We did not anticipate effect modification but specified testing of interactions with these factors because of evidence and opinion suggesting that high risk and elderly patients warrant transfusion at more liberal hematocrit thresholds as well as the tendency for these patients to be transfused more frequently. An additional prespecified subgroup analysis investigated whether the effect of transfusion changed after November 30, 1999, because the UK National Blood Service carried out universal leukodepletion after this date.

**Definitions of Outcomes of Interest**

Two coprimary outcomes were prespecified. A composite infection outcome was defined as respiratory infection or wound infection or sepsis. This outcome was intended to reflect the potential harm from unnecessary RBC transfusion resulting from immunosuppression. A composite ischemic outcome was prespecified as myocardial infarction, permanent or transient stroke, or renal complication (creatinine >200 mmol/L or requirement for hemodialysis, excluding patients on dialysis before their operations). This outcome was intended to reflect the potential harm from not giving an RBC transfusion when transfusion would have been beneficial. We hypothesized that the risk of experiencing the ischemic outcome would outweigh the risk of an infection when the nadir hematocrit was very low.

We used NHS reference costs for 2005 for ICU, HDU, and postoperative stay and the costs of blood products (in October 2006, provided by the UK National Blood Service) to estimate the relative increase in hospital costs for patients who were transfused compared with those who were not.

Finally, we investigated the effect of transfusion on ICU/HDU and hospital stay (time to discharge) and survival after surgery using the NHS Strategic Tracing Service. These outcomes were not prespecified. No other outcomes were analyzed.

**Study Population**

A total of 8724 patients were recorded in the PATS database during the study period; 63 who had only thoracic or vascular...
procedures were excluded. Forty patients had missing hematocrit data, and another 23 patients could not be linked with the blood bank database. The remaining 8598 were all successfully linked with the NHS Strategic Tracing Service. Infection and ischemic outcomes could not be derived for 82 and 80 (neither for 53) of these patients, leaving 8516 and 8518 patients in analyses of the respective outcomes (Appendix A, flow diagram, in the online-only Data Supplement). All 8598 patients were included in analyses of length of ICU/HDU and postoperative hospital stay and survival. Table 1 shows the patients’ characteristics.

Some patients (221 of 8598, 2.6%) died in hospital; most had data that allowed the infection (79%), ischemic (86%), and survival outcomes (100%) to be derived, and they were included. (About half of the patients with missing information on infection and ischemic outcomes died in hospital; 53% of patients who died in hospital and who had missing information about infection and ischemic outcomes died on the day of operation or the following day.) Patients who died in hospital were more likely to have been transfused than those who survived to discharge (96% versus 56%). Similar percentages of patients who died in hospital and who had missing infection or ischemic outcomes were transfused (44 of 48 [92%] and 28 of 32 [88%], respectively).

Infections and Ischemic Events

Frequencies of infection and ischemic outcomes were higher for patients who were transfused than for those who were not (Table 2). Interactions of hematocrit stratum and RBC transfusion, adjusted for propensity score, were not significant for either outcome (Appendix B in the online-only Data Supplement). Adjusted odds ratio estimates were 3.38 (95% CI, 2.60 to 4.40) and 3.35 (95% CI, 2.68 to 4.35; Figure 1) for the associations of transfusion with infection and ischemic outcomes, respectively.

In prespecified subgroup analyses, interactions of any RBC transfusion with prognostic factors were not statistically significant except for type of operation (infection and ischemic outcomes) and age (infection only; Figure 1). No interaction was present of transfusion and operation date after 30%, November 30, 1999, when all blood in the United Kingdom action was present of transfusion and operation date after ische-

Table 1. Characteristics of Patients

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Not Transfused (N=3689), n (%)</th>
<th>Transfused (N=4909), n (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolated on-pump CABG</td>
<td>1506 (40.8)</td>
<td>2454 (50.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Isolated off-pump CABG</td>
<td>1436 (38.9)</td>
<td>655 (13.3)</td>
<td>...</td>
</tr>
<tr>
<td>Valve replacement</td>
<td>430 (11.6)</td>
<td>865 (17.6)</td>
<td>...</td>
</tr>
<tr>
<td>Valve replacement+CABG</td>
<td>89 (2.4)</td>
<td>535 (10.9)</td>
<td>...</td>
</tr>
<tr>
<td>Other*</td>
<td>228 (6.2)</td>
<td>400 (8.2)</td>
<td>...</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥16 and &lt;50</td>
<td>460 (12.5)</td>
<td>370 (7.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>≥50 and &lt;60</td>
<td>1036 (28.1)</td>
<td>782 (15.9)</td>
<td>...</td>
</tr>
<tr>
<td>≥60 and &lt;70</td>
<td>1418 (38.4)</td>
<td>1,825 (37.2)</td>
<td>...</td>
</tr>
<tr>
<td>≥70</td>
<td>775 (21.0)</td>
<td>1932 (39.4)</td>
<td>...</td>
</tr>
<tr>
<td>Male gender</td>
<td>3186 (86.4)</td>
<td>3232 (65.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CCS class &gt;2</td>
<td>1777 (48.2)</td>
<td>2454 (50.0)</td>
<td>0.09</td>
</tr>
<tr>
<td>NYHA class &gt;3</td>
<td>159 (4.3)</td>
<td>500 (10.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ejection fraction &lt;30%</td>
<td>149 (4.0)</td>
<td>335 (6.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MI in the last month</td>
<td>146 (4.0)</td>
<td>275 (5.6)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>127 (3.4)</td>
<td>534 (10.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>95 (2.6)</td>
<td>171 (3.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>Creatinine &gt;150 μmol/L</td>
<td>98 (2.7)</td>
<td>525 (10.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Asthma/COAD</td>
<td>325 (8.8)</td>
<td>543 (11.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Peripheral vascular disease/DVT</td>
<td>229 (6.2)</td>
<td>385 (7.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>138 (3.7)</td>
<td>304 (6.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left main stem stenosis &gt;50%</td>
<td>391 (10.6)</td>
<td>555 (11.3)</td>
<td>0.30</td>
</tr>
<tr>
<td>Preoperative intravenous nitrates/heparin</td>
<td>245 (6.6)</td>
<td>399 (8.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1992 (54.0)</td>
<td>2623 (53.4)</td>
<td>0.60</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>520 (14.1)</td>
<td>731 (14.9)</td>
<td>0.30</td>
</tr>
<tr>
<td>Triple vessel disease</td>
<td>1619 (49.3)</td>
<td>2680 (54.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>1043 (28.3)</td>
<td>1748 (35.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>2121 (57.5)</td>
<td>2653 (54.0)</td>
<td>...</td>
</tr>
<tr>
<td>Current smoker</td>
<td>525 (14.2)</td>
<td>508 (10.4)</td>
<td>...</td>
</tr>
<tr>
<td>Operative priority</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>1918 (52.0)</td>
<td>2018 (41.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urgent</td>
<td>1738 (47.1)</td>
<td>2635 (53.7)</td>
<td>...</td>
</tr>
<tr>
<td>Emergency/salvage</td>
<td>33 (0.9)</td>
<td>256 (5.2)</td>
<td>...</td>
</tr>
<tr>
<td>Parsonnet score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–9</td>
<td>2680 (72.7)</td>
<td>2372 (48.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>10–19</td>
<td>873 (23.7)</td>
<td>1691 (34.5)</td>
<td>...</td>
</tr>
<tr>
<td>≥20</td>
<td>136 (3.7)</td>
<td>846 (17.2)</td>
<td>...</td>
</tr>
</tbody>
</table>

CABG indicates coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; NYHA, New York Heart Association; MI, myocardial infarction; COAD, chronic obstructive airways disease; and DVT, deep vein thrombosis.

*Other operations included repair of congenital anomalies and cardiac operations combined with vascular or thoracic procedures but excluded isolated thoracic or vascular procedures (eg, aorta or carotid endarterectomy).
Table 2. Frequencies of Composite Infection and Ischemic Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Not Transfused</th>
<th>Transfused</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>n</td>
</tr>
<tr>
<td>Infection*</td>
<td>3674</td>
<td>.</td>
</tr>
<tr>
<td>Nadir hematocrit &lt;21</td>
<td>52</td>
<td>1</td>
</tr>
<tr>
<td>Nadir hematocrit ≥21 and &lt;24</td>
<td>390</td>
<td>16</td>
</tr>
<tr>
<td>Nadir hematocrit ≥24 and &lt;27</td>
<td>1176</td>
<td>42</td>
</tr>
<tr>
<td>Nadir hematocrit ≥27</td>
<td>2056</td>
<td>82</td>
</tr>
<tr>
<td>Ischemia†</td>
<td>3670</td>
<td>.</td>
</tr>
<tr>
<td>Nadir hematocrit &lt;21</td>
<td>52</td>
<td>1</td>
</tr>
<tr>
<td>Nadir hematocrit ≥21 and &lt;24</td>
<td>390</td>
<td>13</td>
</tr>
<tr>
<td>Nadir hematocrit ≥24 and &lt;27</td>
<td>1175</td>
<td>40</td>
</tr>
<tr>
<td>Nadir hematocrit ≥27</td>
<td>2053</td>
<td>72</td>
</tr>
</tbody>
</table>

N indicates denominator hematocrit stratum/total; n, number experiencing the outcome.

*737 of 8516 (8.7%) had this outcome (missing for 82): 381 (4.5%) had a respiratory infection; 220 (2.6%) had a wound infection; 136 (1.6%) had both. Eight of 14 patients with sepsis also had a respiratory infection.

†832 of 8518 (9.8%) had this outcome (missing for 80): 543 (6.4%) had a respiratory infection; 220 (2.6%) had a stroke.

The corresponding proportions were 64% and 66% when patients with a nadir hematocrit <21 were excluded (assuming that transfusions below this criterion were clinically necessary).

Proportions of infections and ischemic outcomes in the study population attributable to transfusion (assuming that the observed associations are causal) were 80% and 81%, respectively. The corresponding proportions were 64% and 66% when patients with a nadir hematocrit <21 were excluded (assuming that transfusions below this criterion were clinically necessary).

Effect of RBC Transfusion on the Cost of Admission

Costs of admission in UK pounds were calculated for each patient using the following unit costs: £1172, £914, and

![Table 2. Frequencies of Composite Infection and Ischemic Outcomes](image-url)
£376 per day of ICU, HDU, and ward stay, respectively, and £130.50, £214, and £31.50 per unit of RBCs, platelets, and fresh frozen plasma. Costs were transformed into natural logarithms to normalize their distribution. The effect of RBC transfusion was estimated from a linear regression model that included RBC units, hematocrit stratum, the interaction of these 2 exposures, propensity score, and the factors added in further models described above. Figure 2 shows how the relative increase in cost varied with RBC units transfused and nadir hematocrit stratum. Table 3 shows the increase in relative cost overall and for increasing units of RBCs transfused.

Length of ICU and Postoperative Hospital Stay
Figure 3 shows Kaplan-Meier curves for the cumulative probability of discharge from ICU/HDU and hospital with increasing postoperative time. After adjustment, transfused patients were ≈30% less likely to have been discharged from ICU/HDU (hazard ratio, 0.69; 95% CI, 0.65 to 0.72; \( P<0.0001 \)) and ≈35% less likely to have been discharged from hospital (hazard ratio, 0.63; 95% CI, 0.60 to 0.67; \( P<0.0001 \)) at any postoperative time. The proportional-hazards assumption was satisfied in both analyses.

All-Cause Mortality
Figure 4 shows Kaplan-Meier curves for all-cause mortality up to 7 years after surgery (median duration of follow-up, 4.25 years). The proportional-hazards assumption was violated because most deaths within 30 days after surgery occurred among transfused patients. The analysis was rerun with follow-up time divided into 3 epochs: 0 to 30 days (=20% of deaths), 31 days to 1 year (=20% of deaths), and >1 year (=60% of deaths); each epoch considered only participants under observation during that epoch. For each epoch, survivors were censored at the end of follow-up or the end of the epoch, whichever occurred first. This improved the model fit (\( \chi^2, 29.4; df, 2; P<0.0001 \)). Adjusted hazard ratios for the 3 epochs were 6.69 (95% CI, 3.66 to 15.1; \( P<0.0001 \)), 2.59 (95% CI, 1.68 to 4.18; \( P<0.0001 \)), and 1.32 (95% CI, 1.08 to 1.64; \( P=0.003 \)), respectively.

Discussion
The study has 5 main findings. First, RBC transfusion was strongly associated with infection, and a strong dose-response relationship was present. We did not find any evidence that
the likelihood of infection was reduced by leukodepletion of red cells.

Second, RBC transfusion also was strongly associated with the composite ischemic outcome. Again, a strong dose-response relationship was present. This finding is counter to our original conception in which we reasoned that ischemia-related morbidity would be more likely to occur in patients who would have benefited from transfusion but who did not receive one.

Third, these associations of transfusion with early complications were highly consistent. When comparing any with no transfusion, no effect modification by nadir hematocrit could be discerned, and the associations were apparent in all prespecified “high-risk” subgroups.

Fourth, the increased morbidity associated with transfusion translated into longer ICU/HDU and total postoperative hospital stays and increased admission costs. The impact of these associations could be considerable; if causal, avoiding transfusion would have prevented well over 50% of all infections and ischemic events in our hospital and would have reduced the nonoperative costs of an admission by ≈40%.

Fifth, transfusion affects mortality. The hazard of death in the first 30 days was almost 6 times higher for transfused patients than for those who were not transfused. Transfused patients continued to have a substantially increased hazard of death through the first postoperative year and possibly thereafter.

**Study Limitations and Strengths**

It is important to consider whether these observational findings could have arisen because of confounding. Transfused patients were sicker before their operations and may have had poorer outcomes for this reason rather than because they were transfused. Four observations argue against this. First, prognostic factors were well balanced

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**Figure 3.** Kaplan–Meier “survival” curve showing the cumulative proportion of patients discharged from ICU/HDU and from hospital over time according to whether patients had had an RBC transfusion. Patients who died in hospital were censored at death.

**Figure 4.** Kaplan–Meier survival curve showing the cumulative proportion of patients who died over time according to whether patients had had an RBC transfusion. Vertical dotted lines separate the epochs of follow-up time for which hazard ratios were estimated (ie, 0 to 30 days, 31 days to 1 year, and after 1 year).
Findings in the Context of the Literature

Our findings with respect to the effect of RBC transfusion on the composite infection outcome and use of hospital resources are consistent with previous research, and we do not consider these further. However, the effects of RBC transfusion on the composite ischemic outcome merit discussion.

RBC transfusion is intended primarily to maintain or restore tissue oxygenation. Cardiac surgery can be associated with severe bleeding, with some patients at risk of hemorrhagic shock. In such cases, transfusion is life-saving. The majority of patients in the cohort were transfused, but most were clearly not in hemorrhagic shock. The finding that transfusion is associated with an increased likelihood of the composite ischemic outcome suggests that many transfusions are at best ineffective because causality between transfusion and ischemia is not demonstrated. At worst, RBC transfusion may cause tissue ischemia and organ dysfunction.

Some previous studies support a causal association between RBC transfusion and tissue ischemia, counter to our original conception. RBC transfusion in critically ill septic patients has been observed to reduce intra gastric pH, an index of mesenteric ischemia. Transfusion of stored RBCs also has been shown to induce tissue hypoxia in rodents. Increased red cell aggregability and rigidity, the diminished microvascular autoregulatory abilities of stored red cells, and the accumulation of potentially toxic microparticles, lipophosphatidylcholines, or proinflammatory cytokines in the storage supernatant may all contribute to tissue hypoxia and organ dysfunction in transfused patients. Alternatively, systemic inflammation, a feature of the response to transfusion of nonleukodepleted red cells, is implicated in atherosclerotic plaque rupture, stroke, and acute coronary syndromes. It has been proposed that leukodepletion reduces the deleterious effects of transfusion. However, we did not observe this, in keeping with some previous randomized trials in which the benefits of leukodepletion were found to be small or nonexistent. Whether transfusion of leukodepleted red cells results in systemic inflammation has not been investigated. However, many of the pathological cellular changes and accumulation of toxic species in the supernatant seen during storage occur in both leukodepleted and nonleukodepleted cells.

Setting a hematocrit level as the trigger for RBC transfusion, with more liberal thresholds for elderly and high-risk patients, is not supported by this study. The reason is that hematocrit levels in isolation, unless very low, are poor indicators of tissue hypoxia. Tissue hypoxia occurs in healthy adults at hemoglobins as low as 5 to 6 g/dL (hematocrits of 15 to 18). This level of anemia is considerably lower than commonly tolerated by physicians when managing their cardiac surgery patients (typically hematocrits of 24 to 26). More restrictive transfusion thresholds (eg, hematocrit of 21) have been shown to be beneficial in critically ill noncardiac surgical patients in a randomized trial. In the present study, no apparent benefit was derived from RBC transfusion at hematocrits as low as 21. Therefore, this may represent a practical “restrictive” threshold for a randomized trial.

Low cardiac output is a key determinant of tissue oxygenation after cardiac surgery. In such cases, more objective measures of tissue oxygenation are required. Using clinical organ dysfunction or evidence of global tissue hypoxia as indicators for transfusion is neither practical nor desirable. Noninvasive measurement of regional tissue oxygenation is possible using near-infrared spectroscopy, and future refinement of this technology has the potential to guide transfusion therapy.
Conclusions
RBC transfusion appears to be harmful for almost all cardiac surgery patients and wastes a scarce commodity and other health service resources. It is difficult to identify patients in whom transfusion is truly necessary on the basis of hematocrit, age, or comorbidity. This study reinforces the need for prospective evaluation of restrictive transfusion triggers and objective clinical indicators for RBC transfusion in cardiac surgical patients.

Acknowledgments
We thank Dr Radek Capoun, Michael Stear, and Jan Wild for their work in extracting data from ICU charts and entering the data into a computer database. We also thank Dr Alan Cohen for comments on the manuscript.

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Disclosures
None.

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**CLINICAL PERSPECTIVE**

This single-center, observational retrospective study investigated associations between red blood cell transfusion and infectious and ischemic adverse outcomes in >8500 cardiac surgery patients who had operations over an 8-year period. As reported previously, transfusion was strongly associated with infection. More important, however, were 3 new findings. First, transfusion was strongly associated (both large in magnitude and dose-related) with a composite ischemic outcome (stroke, myocardial infarction, and renal failure); this finding is inconsistent with the widely held belief that red cell transfusion improves tissue oxygenation. Second, this effect was constant across diverse risk groups and perioperative nadir hemoglobin levels. Third, transfusion (blood products and associated morbidity) increased overall hospitalization costs by >40% on average. These findings highlight the need for additional research on potential pathophysiological mechanisms of transfusion. Despite many reports of the potential harms of red blood cell transfusion, we know little about how transfusion affects immune function or tissue oxygenation or how to make stored allogeneic blood products safer. The study also demonstrates our poor understanding of the indications for red blood cell transfusion. Conventionally, decisions to transfuse are based on hemoglobin thresholds tailored to the patient’s age and comorbidity. However, in our study, these factors did not influence the observed risks from transfusion. Finally, we hope that demonstrating the impact of red blood cell transfusion on hospitalization costs will provide the impetus for governments to fund research to address these gaps in knowledge.

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