Blood Transfusion in Cardiac Surgery
A Silent Epidemic Revisited

James D. Rawn, MD

Mr Corazon is a 78-year-old man with insulin-dependent diabetes mellitus and an ejection fraction of 40% who is postoperative day 2 from coronary artery bypass grafting. He has been extubated and feels good, but he remains on a low-dose epinephrine infusion to support his blood pressure. His cardiac index is 2.2 L/m², and he has a mixed venous oxygen saturation of 59%. He has low filling pressures and marginal urine output. His hematocrit is 24%. His surgeon and his cardiologist confer and agree to transfuse him with 1 unit of red blood cells. They explain to him that he needs the blood transfusion and that the major risk of transfusion is the very low risk of viral infection. After the transfusion, his mixed venous oxygen saturation and urine output improve, and his epinephrine infusion is weaned off. He is transferred out of the intensive care unit the following day.

The rationale for transfusing Mr Corazon is understandable. Historically, patients were thought to benefit from transfusions that boosted their hematocrit to ≥30%, particularly if they were older and sicker. Transfused blood is an excellent volume expander and remains in the intravascular space better than other resuscitation fluids. Transfused patients often “look better.” It is possible that Mr Corazon’s transfusion allowed his hemodynamics to improve sufficiently to wean him more quickly from his inotropic support. We might even expect that his recovery has been accelerated and his length of stay reduced.

How should we evaluate this decision making in light of the available evidence? The article by Murphy et al in the current issue of Circulation found no benefit from transfusion for hematocrits as low as 21% (hemoglobin of 7 g/dL), and the risk of death within 30 days of surgery was almost 6 times greater for patients who received blood. In addition, transfused patients were more likely to experience increased infections and ischemic complications (myocardial infarction, renal compromise, and stroke). This study joins a decade of observational studies demonstrating an association between red blood cell transfusion and adverse outcomes in cardiac surgery.1-5 In a dose-dependent and often durable manner, red blood cell transfusion in cardiac surgery patients has been linked as an independent variable to an increase in infectious complications, myocardial infarction, stroke, renal failure, prolonged ventilation, atrial fibrillation, hospital length of stay, and mortality. Although the immediate impact on survival is significantly greater, transfusion with as little as 1 unit of red blood cells has been associated with decreased 10-year survival after coronary artery bypass grafting.6 It has been difficult to find evidence of benefit.

The studies linking transfusion to cardiac surgery outcomes are retrospective; despite careful risk adjustment, it is possible that these associations reflect a tendency among clinicians to transfuse the most critically ill patients or miss another important confounder. One cautionary tale involves a study by the Northern New England Cardiovascular Disease Study Group that initially stimulated an increase in blood transfusion when it was reported that the lowest hematocrit on bypass was correlated with increased mortality and postoperative heart failure.7 Subsequent analysis has suggested that although anemia is a marker for poor outcomes, the tendency for anemic patients to be transfused explains much of the association; moreover, blood transfusions were associated with postoperative requirements for mechanical and inotropic support regardless of the degree of anemia.8

The Transfusion Requirements in Critical Care trial is important because it is a prospective randomized trial that supports a causal link between blood transfusion and adverse outcomes in critically ill patients. When patients were randomized to liberal (transfusion threshold <10 g/dL) or restrictive (transfusion threshold <7 g/dL) transfusion groups, cardiac and pulmonary complications increased significantly and a trend existed toward increased mortality in the liberal transfusion group. When younger (<55 years of age) or less critically ill (Acute Physiology, Age, Chronic Health Evaluation [APACHE] score <20) patients were considered, a statistically significant increase in mortality was present in patients who were more liberally transfused.9

The historic rationale for blood transfusion includes the purported benefit of improved oxygen delivery. The Transfusion Requirements in Critical Care (TRICC) trial investigators raised concern about the applicability of restrictive transfusion triggers in patients with acute coronary syndromes. A subsequent subgroup analysis of patients with cardiovascular disease showed a trend toward increased survival in the liberal transfusion group, but transfusion also resulted in a statistically significant increase in pulmonary edema and multiorgan system dysfunction.10 Wu et al11 published an analysis based on Medicare administrative data that showed an improvement in survival for patients >65 years of age treated for acute myocardial infarction if they received blood transfusions when their admission hematocrit...
was <30. Subsequent studies based on clinical data suggested that blood transfusion was a risk factor for death and myocardial infarction in patients with acute coronary syndromes.\textsuperscript{12} Rao et al\textsuperscript{13} found this association to be significant for patients who received blood for hematocrits >25%.

The present study found that ischemic complications (myocardial infarction, neurogenic and renal injury) were not decreased with blood transfusion regardless of the patient’s nadir hematocrit or comorbidities. The lack of benefit from blood transfusions in decreasing these complications might be explained because hemoglobin levels rarely limit oxygen delivery given the transfusion triggers that predominate in cardiac surgery.\textsuperscript{14} Possible mechanisms for the contribution of transfusion to ischemic complications include proinflammatory effects and storage defects. Stored red blood cells are 2,3-DPG deficient and consequently less adept at unloading oxygen and less deformable, possibly leading to sludging and capillary occlusion.

The association of blood transfusion with infection confirms previous reports. The mechanism is presumably the result of immunosuppressive effects. Blood was used to decrease the incidence of rejection in the early days of kidney transplantation, and transfusion has been associated with cancer recurrence and death in patients with malignancy. In an effort to conserve a limited and expensive resource and to minimize the injury caused by transfusion therapy, the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists have joined forces and, with impressive effort, have produced a clinical practice guideline. Their guideline emphasizes that the benefits of transfusion have not been adequately demonstrated and that existing evidence is an imperfect guide to transfusion decisions. They suggest a transfusion trigger of hemoglobin <7 g/dL in postoperative cardiac surgery patients (class IIa recommendation). In addition, they suggest (class IIb recommendation) that it is “not unreasonable to transfuse red cells in certain patients with critical noncardiac end-organ ischemia (eg, central nervous system and gut) whose hemoglobin levels are as high as 10 g/dL, but more evidence to support this recommendation is required.” The present study suggests that more evidence may be hard to find.


References


Key Words: Editorials, blood cells, transfusion, infection, kidney, surgery
Blood Transfusion in Cardiac Surgery: A Silent Epidemic Revisited
James D. Rawn

Circulation. 2007;116:2523-2524
doi: 10.1161/CIRCULATIONAHA.107.739094
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/116/22/2523

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/