

postburn hospital stay. The increasing evidence derived from retrospective studies that the indication and threshold for blood product administrations has to be redefined leads us to call for a large prospective clinical trial. The prospective trial should determine whether surgical techniques can effectively decrease blood loss during the operation, determine the indications for blood transfusion, and whether the amount and timing of transfusions determine the outcome of severely burned patients.

In summary, burned patients who require large amounts of blood products are at high risk to develop infectious complications and to die when compared with patients requiring low amounts of blood products. We suggest that the next step would be to initiate a large prospective clinical trial to determine the threshold for blood transfusions and possibly new methods to limit blood loss during surgery. This prospective randomized study should address these issues and answer these questions before recommendations can be made to change clinical practice.

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REFERENCES

1. Palmieri TL, Caruso DM, Foster KN, et al: Effect of blood transfusion on outcome after major burn injury: A multicenter study. *Crit Care Med* 2006; 34:1602-1607
2. Corwin HL, Gettinger A, Pearl RG, et al: The CRIT Study: Anemia and blood transfusion in the critically ill. Current clinical practice in the United States. *Crit Care Med* 2004; 32: 39-52
3. Napolitano LM, Corwin HL: Efficacy of red blood cell transfusion in the critically ill. *Crit Care Clin* 2004; 20:255-268
4. Alvarez G, Hebert PC, Szick S: Debate: Transfusing to normal haemoglobin levels will not improve outcome. *Crit Care* 2001; 5:56-63
5. Spiess BD: Transfusion of blood products affects outcome in cardiac surgery. *Semin Cardiothorac Vasc Anesth* 2004; 8:267-281
6. Palmieri TL, Greenhalgh DG: Blood transfusion in burns: What do we do? *J Burn Care Rehabil* 2004; 25:71-75
7. Jeschke MG, Chinkes DL, Finnerty CC, et al: Blood transfusions are associated with increased risk for the development of sepsis in severely burned pediatric patients. *Crit Care Med* 2006 (in review)
8. Hart DW, Wolf SE, Beauford RB, et al: Determinants of blood loss during primary burn excision. *Surgery* 2001; 130:396-402
9. Pirenne J, Kitade H, Kawai M, et al: Regulatory cells, TH1/TH2 unbalance, and antibody-induced chronic rejection in operational tolerance induced by donor-specific blood transfusion. *Transplantation* 2005; 79(3 Suppl):S25-S27
10. Hart DW, Wolf SE, Chinkes DL, et al: Effects of early excision and aggressive enteral feeding on hypermetabolism, catabolism, and sepsis after severe burn. *J Trauma* 2003; 54:755-764
11. Jeschke MG, Barrow RE, Herndon DN: Extended hypermetabolic response of the liver in severely burned pediatric patients. *Arch Surg* 2004; 139:641-647
12. Jeschke MG, Barrow RE, Mlcak RP, et al: Endogenous anabolic hormones and hypermetabolism: Effect of trauma and gender differences. *Ann Surg* 2005; 241:759-768
13. Tracey KJ: Tumor necrosis factor (cachectin) in the biology of septic shock syndrome. *Circ Shock* 1991; 35:123-128
14. Tracey KJ, Lowry SF, Cerami A: Cachectin/TNF mediates the pathophysiological effects of bacterial endotoxin/lipopolysaccharide (LPS). *Prog Clin Biol Res* 1988; 272:77-88

Blood product transfusion in association with coronary artery bypass grafting: Proceed with caution*

A total of 400,000 coronary artery bypass grafting (CABG) procedures are performed each year in the United States, many on productive citizens in midlife. Improving the safety of this procedure is important. In this issue of *Critical Care Medicine*, Dr. Koch and colleagues (1) report on their study in which they quantified the incremental risk associated with the transfusion of blood products on mortality and morbidity after CABG surgery. They also investigated patient- and pro-

cedure-related variables associated with the need for packed red blood cell (RBC) transfusion.

Blood transfusion and outcome after cardiac surgery have been studied extensively (2-8), and patient outcome seemed worse when blood transfusion was instituted in the perioperative period. Some of these studies were limited by small patient populations and others by combinations of cardiac procedures (e.g., CABG and valve surgery) that may have confounded the results. Some did not evaluate dose-dependent effects of RBC transfusion or patient outcome after transfusion of blood products other than RBCs. This present study addresses those issues.

Almost half of the patients (48.6%) of Dr. Koch and colleagues (1) underwent blood product transfusion. Transfusion of RBCs was associated with unit-by-unit increased risk for in-hospital mortality and morbidity, even after controlling for risk

factors previously associated with adverse outcome after CABG. Higher rates of transfusion were seen in the elderly, patients with lower body mass indexes, low preoperative hematocrit, or those undergoing reoperation. Unexpectedly, platelet transfusion was associated with lower postoperative morbidity (9). Also contrary to previous findings, transfusion of fresh frozen plasma led to increased in-hospital mortality.

The greatest strength of this study is prospective. Perioperative patient data and information from the original blood component utilization forms were collected from a large homogeneous patient population. Analysis of transfusion blood products other than RBCs on outcome was also important, as there is a paucity of such information in the cardiac surgery literature. However, the design and analysis generated questions regarding

*See also p. 1608.

Key Words: blood transfusion; coronary artery bypass graft; outcome; risk factors; hematocrit; anemia
Dr. Poston received a grant from Bayer Pharmaceuticals. Drs. Malone and Hess do not have any financial interests to disclose.

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DOI: 10.1097/01.CCM.0000219373.66120.01

confounding variables. Some of these concerns are outlined below.

Dr. Koch and colleagues (1) state that "patient-related disease characteristics, laboratory values and operative variables, . . . were variably associated with individual postoperative morbidities and mortality," but the specific variables were not listed. Although the authors controlled for traditional risk factors, they did not specify whether they controlled for physiologic variables (e.g., acidosis) that have been evaluated as confounding variables in other recent transfusion studies (10). They tried to account for these variables statistically by utilizing a balancing score, but concede that RBC transfusions might be a surrogate marker for sicker patients.

More detailed discrimination of the time of blood transfusion in relation to the onset of adverse outcomes would provide support for their conclusions. It is difficult to blame a blood transfusion for an adverse outcome that was diagnosed before the transfusion. Of the 20,513 units of RBCs transfused, the authors stated that 11,177 (54%) were given postoperatively in the intensive care unit. However, the majority of complications in cardiac surgery relate to events in the operating room or on the first postoperative night. Moreover, clinicians frequently transfuse cardiac surgery patients after the diagnosis of a complication. Review of those given transfusions beyond the initial 12- to 24-hr risk period for procedural complications might identify patients who fail to show a temporal relationship consistent with their conclusions that the transfused blood caused the complication. Identifying and excluding such patients from their data set would strengthen the suggestion of causality.

Specific patient and procedural questions came to mind while reviewing this article. How many of the patients in the study required a transfusion for bleeding? Might the local policy of avoiding aprotinin, the most effective measure for prophylaxis against bleeding, have led to more bleeding and the need for more blood products (11)? The investigators reported that most of the patients who underwent transfusion received only 1 or 2 units of RBCs, making bleeding a less likely indication for transfusion in those patients. What were the indications for transfusion?

Fresh frozen plasma was associated with reduced odds for postoperative mortality. Was this because fresh frozen plasma led to a cessation of bleeding in these patients? This would seem unlikely according to the results of a recent meta-analysis of randomized clinical studies that showed minimal efficacy of fresh frozen plasma for this purpose (12–14). Perhaps the (nonprotocol) decision to give fresh frozen plasma signified a conscious effort by the clinician to avoid having to give cell-based transfusions (i.e., RBCs or platelets). The Cleveland Clinic Health System advertises "bloodless CABG surgery" for appropriate candidates (www.fairviewhospital.org/bloodless). This implies that they might have a fairly large cohort of low-risk patients with severe anemia after CABG. Comparing the outcome of this group vs. a matched cohort of low-risk patients who were transfused would strengthen their findings considerably.

Despite its flaws, this study is important to the critical care literature. It provides data regarding a therapy, presently under great scrutiny, on a challenging component of the ICU patient population. The correlation between blood use and poor outcome in CABG surgery is strong; therefore, decisions to utilize transfusion must be made carefully. We can save lives by being frugal in our use of blood. We can save lives by improving CABG surgery. We can save lives by improving the quality of blood products. We all have work to do.

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REFERENCES

1. Koch CG, Li L, Duncan AI, et al: Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. *Crit Care Med* 2006; 34:1608–1616

2. Zacharias A, Habib R: Factors predisposing to median sternotomy complications: Deep vs. superficial infection. *Chest* 1996; 110:1173–1178
3. Fransen E, Maessen J, Dentener M, et al: Impact of blood transfusions on inflammatory mediator release in patients undergoing cardiac surgery. *Chest* 1999; 116:1233–1239
4. Haynes SL, Wong JC, Torella F, et al: The influence of homologous blood transfusion on immunity and clinical outcome in aortic surgery. *Eur J Vasc Endovasc Surg* 2001; 22:244–250
5. Engoren M, Habib RH, Zacharias A, et al: Effect of blood transfusion on long-term survival after cardiac operation. *Ann Thorac Surg* 2002; 74:1180–1186
6. Leal-Noval SR, Marquez-Vacaro JA, Garcia-Curiel A, et al: Nosocomial pneumonia in patients undergoing heart surgery. *Crit Care Med* 2000; 28:935–940
7. Leal-Noval SR, Rincon-Ferrari MD, Garcia-Curiel A, et al: Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. *Chest* 2001; 119:1461–1468
8. Kuduvali M, Oo AY, Newall N, et al: Effect of peri-operative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery. *Eur J Cardiothorac Surg* 2005; 27:592–598
9. Spiess BD: Transfusion of blood products affects outcome in cardiac surgery. *Semin Cardiothorac Vasc Anesth* 2004; 8:267–281
10. Malone DL, Dunne J, Tracy JK, et al: Blood transfusion, independent of shock severity, is associated with worse outcome in trauma. *J Trauma* 2003; 54:898–905
11. Parolari A, Antona C, Gerometta P, et al: The effect of "high dose" aprotinin and other factors on bleeding and revisions for bleeding in adult coronary and valve operations: An analysis of 2190 patients during a five-year period (1987–1991). *Eur J Cardiothorac Surg* 1995; 9:77–82
12. Casbard AC, Williamson LM, Murphy MF, et al: The role of prophylactic fresh frozen plasma in decreasing blood loss and correcting coagulopathy in cardiac surgery: A systematic review. *Anaesthesia* 2004; 59: 550–558
13. Hebert PC, Wells G, Blajchman MA, et al: A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care: Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999; 340: 409–417
14. Corwin HL, Gettinger A, Pearl RG, et al: Anemia and blood transfusion in the critically ill: Current clinical practice in the United States. The CRIT study. *Crit Care Med* 2004; 32:39–52