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Intraoperative Red Blood Cell Transfusion During Coronary Artery Bypass Graft Surgery Increases the Risk of Postoperative Low-Output Heart Failure

Stephen D. Surgenor, MD, MS; Gordon R. DeFoe, CCP; Mary P. Fillinger, MD; Donald S. Likosky, PhD; Robert C. Groom, CCP, MS; Cantwell Clark, MD, MS; Robert E. Helm, MD; Robert S. Kramer, MD; Bruce J. Leavitt, MD; John D. Klemperer, MD; Charles F. Krumholz, CCP; Benjamin M. Westbrook, MD; Dean J. Galatis, MD; Carmine Frumiento, MD, MS; Cathy S. Ross, MS; Elaine M. Olmstead, BA; Gerald T. O'Connor, PhD, DSc

Background—Hemodilutional anemia during cardiopulmonary bypass (CPB) is associated with increased mortality during coronary artery bypass graft (CABG) surgery. The impact of intraoperative red blood cell (RBC) transfusion to treat anemia during surgery is less understood. We examined the relationship between anemia during CPB, RBC transfusion, and risk of low-output heart failure (LOF).

Methods and Results—Data were collected on 8004 isolated CABG patients in northern New England between 1996 and 2004. Patients were excluded if they experienced postoperative bleeding or received ≥3 units of transfused RBCs. LOF was defined as need for intraoperative or postoperative intra-aortic balloon pump, return to CPB, or ≥2 inotropes at 48 hours. Having a lower nadir HCT was also associated with an increased risk of developing LOF (adjusted odds ratio, 0.90; 95% CI, 0.82 to 0.92; $P=0.016$), and that risk was further increased when patients received RBC transfusion. When adjusted for nadir hematocrit, exposure to RBC transfusion was a significant, independent predictor of LOF (adjusted odds ratio, 1.27; 95% CI, 1.00 to 1.61; $P=0.047$).

Conclusions—In this study, we observed that exposure to both hemodilutional anemia and RBC transfusion during surgery are associated with increased risk of LOF, defined as placement of an intraoperative or postoperative intra-aortic balloon pump, return to CPB after initial separation, or treatment with ≥2 inotropes at 48 hours postoperatively, after CABG. The risk of LOF is greater among patients exposed to intraoperative RBCs versus anemia alone. **(*Circulation*. 2006; 114[suppl I]:I-43–I-48.)**

Key Words: cardiopulmonary bypass ■ blood cells ■ anemia ■ heart failure ■ mortality

Hemodilutional anemia during cardiopulmonary bypass (CPB) has been associated with increased risk of renal failure, stroke, and mortality during coronary artery bypass graft (CABG) surgery.[1–5] Plausible explanations for these observations include injury related to anemia or the intraoperative red blood cell (RBC) transfusion used to treat the anemia. First, anemia may reduce the oxygen supply available to the tissues to adequately meet demand, leading to ischemic tissue injury. Studies have shown that severe perioperative anemia among patients refusing transfusions for religious reasons is associated with increased risk of mortality, particularly with coexisting cardiac disease.[6] Nonetheless, hemodilutional anemia is "intuitively reasonable" according to a standard reference text of cardiac surgery and remains a standard practice during CPB management.[7] Second, low hematocrit during CPB may be a marker for treatment with RBC transfusions. RBC transfusions are complex biologic products that initiate a systemic inflammatory response, induce nonspecific immunosuppression, and perhaps occlude local microvasculature causing local tissue hypoxemia.[8–10]

Nevertheless, a surgical tradition of aggressive transfusion practice is commonplace despite guidelines to the contrary from the National Institutes of Health, American College of Physicians, American Society of Anesthesiologists, and Canadian Medical Association.[11–15] Determining which of these explanations is the predominant driver of adverse outcomes is paramount to advancing our knowledge regarding the role of tolerating hemodilutional ane-

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mia versus treatment with RBC transfusion during the management of CPB.

In 2001, our Northern New England Cardiovascular Disease Study Group (NNECDSG) published a study examining the effect of low nadir hematocrit (nHCT) on CPB. We concluded that low hematocrit on CPB was associated with an increased risk of in-hospital mortality. Not included in this article was the intraoperative management of low nHCT. This study builds on our previous study. We conducted a prospective cohort study to identify the relative importance of anemia during CPB and RBC transfusion to the risk of low-output heart failure (LOF) among patients undergoing CABG.

Methods

The NNECDSG is a voluntary research consortium from 8 medical centers in Vermont, New Hampshire, and Maine. The intent of the group is to foster continuous improvement in the quality of care of patients with cardiovascular disease. A registry including all of the CABG procedures performed in the region has been maintained since 1987. The medical centers have received internal review board approval for participation in this registry. Patient consent is obtained at each medical center. We had full access to the data and take responsibility for its integrity. We have all read and agree to the article as written.

This prospective observational study used data from consecutive isolated CABG procedures performed from July 1996 through July 2004 at all 8 of the member centers. During this period, complete data were available for 8709 isolated CABG patients. Patients undergoing valve surgery or another surgical procedure concurrent with CABG were excluded. Also excluded were patients who were re-explored for bleeding after CABG (N=175), and who received ≥3 units of RBCs (N=530). After exclusions, there were 8004 patients.

Definitions for patient and disease risk factors have been published previously elsewhere. Those examined were: age, gender, body surface area, preoperative hematocrit and white blood cell count, coexisting diseases (vascular disease [peripheral vascular disease]), diabetes, chronic obstructive pulmonary disease, congestive heart failure, dialysis, and/or preoperative creatinine ≥2), previous CABG surgery, preoperative ejection fraction, left main coronary artery stenosis, number of diseased coronary arteries, myocardial infarction (MI) within 7 days, and priority at surgery (elective, urgent or emergency).[16]

Lowest nHCT was defined as the lowest hematocrit value during CPB. For this analysis, nHCT values were grouped by quartiles using the following cut points: ≤20, 21 to 22, 23 to 24, and ≥25. All of the intraoperative RBC transfusions were collected, including units used in the CPB prime and those given at any other time in the operating room. The use of any RBC transfusion (1 or 2 units) was compared with no RBCs used. During the study period, the use of central venous catheter, pulmonary artery catheter, transesophageal echocardiogram, and the decisions to transfuse during the intraoperative period were at the discretion of the surgeon and anesthesiologist. The primary outcome of LOF was defined as needing one of the following: intraoperative intra-aortic balloon pump (IABP), return to CPB after initial separation, or ≥2 inotropes at 48 hours postoperatively.

Standard statistical methods, that is, χ^2 tests for categorical variables, were used to assess the statistical significance of observed differences in patient and disease characteristics by patient subgroup. Multivariable logistic regression was used to determine the independent effects of nHCT and use of transfused RBCs while adjusting for potential confounding risk factors. Covariates used in this analysis were selected based on the findings of others in modeling risk of adverse outcomes after CABG surgery, as well as on previous work by the NNECDSG.[14] All of the analyses were performed using Stata release 8.0 software.[17]

Results

Patients with a nHCT ≤20% made up 16.4% of the study population (N =1,315). The distribution of patients was: 18.3% with nHCT 21 to 22; 22.4% with nHCT 23 to 24; and 42.9% with nHCT ≥25. Patients in the lower nHCT groups were much more likely to receive intraoperative RBC transfusion than patients with higher hematocrit values. The proportion of patients receiving RBC transfusion by nHCT group were: 62.7% for nHCT ≤20; 32.6% for nHCT 21 to 22; 16.4% for nHCT 23 to 24; and 6.1% for nHCT ≥25. In each hematocrit quartile, patients were managed with and without RBC transfusion. Among all 8004 patients, there were 644 cases of LOF (8.1%).

Patient and disease characteristics for each of the hematocrit quartiles stratified by exposure to RBC transfusion are presented in Table 1. Patients who were treated with RBC transfusion were more likely to be older, female, have a smaller body surface area, a lower preoperative hematocrit, and a higher preoperative white blood cell count. Also, they were more likely to have coexisting diseases (congestive heart failure, diabetes mellitus, peripheral vascular disease, or recent MI) and were more frequently urgent or emergent at the time of surgery.

The relationship of the crude rate of LOF with nHCT and intraoperative RBC transfusion are presented in Figure 1. Lower nHCT values are associated with higher rates of LOF. The risk of LOF for patients whose nHCT is ≤22 (11.0%) is nearly double that of patients with an nHCT of ≥25 (5.9%), a relative risk of 1.85 (95% CI, 1.56 to 2.19). Exposure to RBC transfusion, even in small quantities, also increases the risk of LOF. The risk of LOF for patients exposed to 1 or 2 transfused RBC units (12.4%) is nearly double the risk for those who were not exposed (6.8%), a relative risk of 1.82 (95% CI, 1.56 to 2.13).

Figure 2 shows unadjusted rates of LOF for patients managed with or without RBC transfusion stratified by nHCT group. For patients who were not exposed to intraoperative RBC transfusion, the risk of LOF doubled across the quartiles of nHCT. Among patients who were exposed to RBC transfusion, there was a consistent risk of LOF of ≈12%, regardless of the severity of the hemodilutional anemia during CPB. In each hematocrit quartile, the risk of LOF was greatest among the patients exposed to intraoperative RBCs.

Multivariable logistic regression was used to determine the independent effects of nHCT and use of transfused RBCs on the risk of LOF while adjusting for potential confounding risk factors. nHCT is represented in the model by the 4-category hematocrit variable described earlier so that an estimation of trend across categories could be determined (Table 2). After adjustment for patient and disease characteristics, both nHCT and intraoperative RBC transfusion were independent predictors of LOF. Each quartile of nHCT was associated with a 10% increase in the risk of LOF (adjusted odds ratio, 0.90; 95% CI, 0.82 to 0.98; P trend=0.016). For example, patients with an nHCT 23% to 24% had a 10% higher risk of LOF than patients with an nHCT ≥25%. Intraoperative exposure to 1 or 2 units of allogeneic stored RBCs was associated with a 27% increase in risk of LOF compared with exposure to no intraoperative RBC transfusion (adjusted odds ratio, 1.27; 95% CI, 1.00 to 1.61; P=0.047).

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TABLE 1. Patient and Disease Characteristics by nHCT and Intraoperative Blood Use

	HCT ≤20		HCT 21 to 22		HCT 23 to 24		HCT ≥25		
Variable	No RBCs	1 to 2 Units RBCs	No RBCs	1 to 2 Units RBCs	No RBCs	1 to 2 Units RBCs	No RBCs	1 to 2 Units RBCs	*P* Value
No. of procedures	491	824	985	476	1501	294	3225	208	
Age (years), % by group									
<60	27.8	16.2	26.8	12.9	30.0	10.9	43.6	15.9	<0.001
60 to 69	33.5	31.5	34.7	27.9	34.2	28.9	32.5	24.0	
70 to 79	32.9	41.6	33.1	46.0	30.9	42.5	21.0	45.2	
≥80	5.9	10.7	5.4	13.3	4.9	17.7	2.9	14.9	
Sex, % female	35.0	62.6	24.6	54.1	14.9	57.1	5.2	51.0	<0.001
Body surface area (m^2), % yes									
<1.70	11.2	24.5	7.0	20.6	4.3	23.9	2.1	27.9	<0.001
1.70 to 1.99	52.6	52.1	48.8	50.0	42.0	54.3	26.4	51.9	
≥2.00	36.3	23.4	44.2	29.5	53.7	21.8	71.5	20.2	
Preoperative HCT									
<35	18.7	37.2	14.4	38.1	8.9	52.7	3.7	49.2	<0.001
35 to 40	48.3	46.0	46.3	43.0	38.5	36.3	24.6	40.4	
>40	33.1	16.8	39.3	18.9	52.6	11.0	71.7	10.4	
Preoperative WBC									
≤7	37.5	39.6	37.6	39.1	41.6	34.4	37.6	40.2	<0.001
8 to 12	57.5	51.3	55.9	50.4	53.4	57.0	57.3	53.9	
>12	5.1	9.1	6.6	10.4	5.1	8.6	5.1	5.9	
Comorbid disease									
Vascular disease, % yes	18.5	25.2	18.2	28.2	17.0	33.0	15.0	27.4	<0.001
Diabetes, % yes	35.4	39.7	34.2	41.2	32.1	39.5	29.4	44.7	<0.001
COPD, % yes	9.8	11.9	9.5	14.5	8.4	11.6	8.0	13.9	<0.001
CHF, % yes	13.2	17.7	10.6	23.3	9.2	25.5	9.2	28.9	<0.001
Dialysis or creatinine ≥2, % yes	2.7	6.1	3.2	6.5	2.1	8.2	1.4	5.8	<0.001
Ejection fraction, %									
<40	14.5	14.1	13.7	19.9	12.4	16.7	14.4	22.0	0.011
40 to 49	14.3	15.2	18.3	15.8	15.7	16.3	14.6	14.7	
50 to 59	25.7	23.1	24.3	21.5	26.2	25.4	26.7	21.5	
≥60	45.6	47.7	43.7	42.8	45.6	41.7	44.3	41.8	
Coronary artery disease									
Prior CABG	5.7	6.3	4.7	7.6	4.3	6.1	3.0	3.4	<0.001
Left main stenosis =50, % yes	27.7	30.7	28.3	30.9	28.1	30.6	25.8	32.2	0.028
No. diseased vessels, %									
1	16.7	12.7	13.3	9.2	11.4	12.1	12.7	14.7	<0.001
2	38.0	34.4	36.4	37.8	41.4	35.6	41.6	40.2	
3	45.4	52.8	50.3	53.1	47.2	52.3	45.6	45.1	
Recent MI (≤7 days), % yes	10.2	11.7	9.8	14.7	9.7	22.1	10.8	30.3	<0.001
Priority at surgery, %									
Elective	24.4	21.1	29.4	21.4	32.2	17.0	35.3	14.4	<0.001
Urgent	70.9	72.5	68.0	74.6	65.1	79.6	62.4	84.1	
Emergency	4.7	6.4	2.5	4.0	2.7	3.4	2.3	1.4	

P values for χ^2 tests.

Discussion

This study clearly demonstrated that management of hemodilutional anemia during surgery with RBC transfusion is associated with increased risk of LOF (defined as placement of an intraoperative or postoperative IABP, return to CPB after initial separation, or treatment with ≥2 inotropes at 48 hours postoperatively) irrespective of the extent of anemia. These observations were possible because in each quartile of

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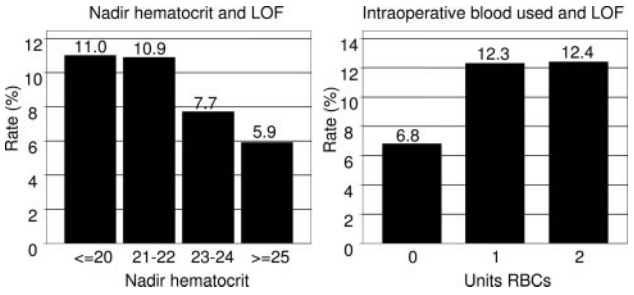

Figure 1. nHCT, intraoperative blood use, and LOF.

nHCT, there were patients managed with and without RBC transfusion. Patients who were exposed to RBC transfusion were more likely to be older, female, have smaller body surface area, lower preoperative hematocrit, or coexisting diseases. After adjustment for baseline characteristics, the administration of RBC transfusion was associated with a 27% increased risk of LOF. In addition, hemodilutional anemia was an independent predictor of LOF. The risk of LOF increased by 10% for each lower quartile of nHCT.

We intentionally included only patients exposed to small amounts of intraoperative allogeneic RBC transfusions (1 or 2 U) in this analysis. This restriction maximized the likelihood that this analysis reflects the management of routine perioperative anemia and minimized the potential bias of including patients treated with RBC transfusion as the management of active hemorrhage or severe anemia. The significant adverse impact of RBC transfusions on the risk of developing LOF that we observed in this study is, therefore, more likely related to exposure to RBC transfusion.

We selected LOF as the primary outcome for this analysis, first because differences in rates of fatal LOF explain 80% of the variation in surgeon-specific CABG mortality rates in northern New England.[18] Second, LOF events occur immediately after CPB. Because of this temporal relationship, LOF is ideally suited to examine the outcome of the intraoperative management, whereas in-hospital CABG mortality can also be related to postoperative complications unrelated to intraoperative management. Finally, LOF is an outcome that has a higher incidence (10%) than mortality (2.5%) in our region. We defined LOF based on treatments used to support failing myocardium: IABP, return to CPB after initial separation,

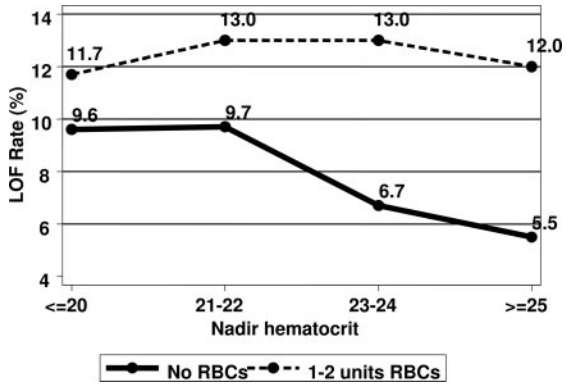

Figure 2. Crude risk of LOF by nHCT stratified by RBC transfusion during CPB.

TABLE 2. Multivariate Logistic Model

Variable	Odds Ratio	95% CI	*P* Value
Age, y			
60 to 69	1.01	(0.81 to 1.27)	0.901
70 to 79	1.12	(0.9 to 1.41)	0.314
≥80	0.87	(0.59 to 1.27)	0.463
Sex	1.29	(1.02 to 1.62)	0.030
Body surface area, m^2			
31 to 36	0.89	(0.64 to 1.23)	0.479
≥37	0.86	(0.71 to 1.05)	0.136
Preoperative HCT			
<35	1.05	(0.8 to 1.36)	0.738
35 to 40	0.96	(0.78 to 1.18)	0.701
Missing	0.64	(0.37 to 1.12)	0.121
Preoperative WBC			
≥12	1.62	(1.21 to 2.15)	0.001
Missing	1.74	(1.04 to 2.89)	0.034
Comorbidities			
Vascular disease	1.09	(0.88 to 1.34)	0.420
Diabetes	1.02	(0.85 to 1.23)	0.807
COPD	1.03	(0.79 to 1.35)	0.837
CHF	1.30	(1.03 to 1.64)	0.027
Renal failure or creatine ≥2	1.59	(1.08 to 2.32)	0.018
Ejection fraction			
<40	2.66	(2.07 to 3.41)	<0.001
40 to 49	1.36	(1.04 to 1.78)	0.026
50 to 59	1.23	(0.96 to 1.56)	0.096
Missing	0.85	(0.59 to 1.22)	0.386
Coronary artery disease			
Left main stenosis ≥50%	1.05	(0.86 to 1.27)	0.629
Prior CABG	3.28	(2.46 to 4.36)	<0.001
3 vessel disease	1.14	(0.95 to 1.36)	0.170
Vessel disease missing	2.67	(1.62 to 4.39)	<0.001
MI within 7 days	1.08	(0.84 to 1.38)	0.545
Priority at surgery			
Emergency	7.07	(4.96 to 10.07)	<0.001
Urgent	1.52	(1.21 to 1.89)	<0.001
nHCT group	0.90	(0.82 to 0.98)	0.016
Intraoperative RBCs	1.27	(1.00 to 1.61)	0.047

and ≥2 inotropes at 48 hours postoperatively as described previously.[19] We chose not to use hemodynamic data, such as cardiac output or filling pressures, because a patient supported with IABP, on 2 inotropic drugs, after failing 2 attempts to successfully separate from bypass, might have an acceptable measured cardiac output and filling pressures but is clearly doing poorly compared with a patient with acceptable measured cardiac output and filling pressures on no such support after first attempt to separate from CPB.

Any observational study is subject to confounding. We have identified all of the patients and disease characteristics that are collected in the NNECDSG database that our previous experience has taught us were important to patient

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outcomes.[13,14] It is possible that other confounding variables do exist that could be pertinent to this analysis. A prospective, randomized trial of intraoperative RBC transfusions during cardiac surgery would contribute to confirmation of this and other observations regarding the management of hemodilutional anemia during CPB.[1–5]

How is it possible that RBC transfusion, which has been historically thought of as an effective strategy to mitigate the risks of anemia, could adversely impact patients by increasing the risk of requiring IABP, return to CPB after initial separation, or need for postoperative inotropes for prolonged periods? The first possible mechanism is that stored allogeneic units of RBCS may alter the immune system of the recipient.[20] Although this immunomodulation may be relevant to infection outcomes, it is less likely to be the main issue for LOF, an outcome that occurs temporally soon after RBC transfusion. The second possible mechanism is that RBC transfusions can initiate the systemic inflammatory response during CPB, manifesting as hypotension and hypoxemia, which could lead to increased need for inotropes and IABP or difficulty separating from CPB.[21] The third possible mechanism is related to the blood product storage lesion. Stored allogeneic RBCs have an increased affinity for oxygen and limited oxygen delivery capacity because of depletion of 2,3-diphosphglycerate. It can take up to 24 hours for 2,3-diphosphglycerate levels to return to normal, a process that may be slower in patients with acute conditions, such as acidosis.[22] The fourth possible mechanism is morphological changes that result from storage of RBC units. Normal RBCs are quite flexible and able to transit the lung capillary bed in 1 ms.[23] Changes to the shape and skeletal integrity of stored RBCs may decrease their ability to deform, making capillary sludging and even capillary obstruction more likely.[24,25]

An increasing awareness of these possible mechanisms should heighten the debate over transfusions in cardiac surgery when considered in combination with evidence in favor of restrictive transfusion strategies among critically ill patients.[26] Reducing the amount of white blood cells and plasma debris in stored units of RBCs has been suggested as a method to reduce adverse events related to RBC transfusions. Meta-analysis does support that leukoreduction can reduce postoperative infection rates, but complete elimination was not observed.[27] During this study, we did not collect data on whether the RBC units given were leukoreduced. We can comment that NNECDSG centers did increase their use of leukoreduced RBCs during this time, but even at the completion of this study it is not universally practiced.

Another observational study concluded that higher hematocrit at time of intensive care unit admission after CABG surgery was associated with an increased rate of MI and the need for IABP for left ventricular dysfunction.[28] At first glance, this observation seemed at odds with the results of other analyses regarding hemodilutional anemia during CPB and increased risk of mortality and morbidity. The current observation is that high hematocrits are a consequence of intraoperative RBC transfusion and are associated with increased risk of LOF. Low hematocrits during CPB are associated with the likelihood of RBC transfusion exposure, which will tend to increase the initial postoperative hematocrit.

Our findings reflect the current intraoperative management and treatment of anemia within northern New England. Accordingly, the decision to transfuse was not a purely random event as would be the case in the setting of a randomized trial. Patients included in this study may either have been given RBCs preemptively as part of the CPB prime (ie, nHCT was anticipated to be low) or as treatment of observed low hematocrit while on CPB. However, it is important to recall that there is significant variation in the use of RBC transfusion across institutions and individual surgeons.[29] The decision to transfuse was not always linked to the patient's condition (eg, use of a "transfusion trigger" or consideration of other patient physiological parameters), and some RBC transfusions may be unwarranted. Our study attempted to explore these unwarranted transfusions by focusing on patients who received just 1 or 2 unit transfusions.

These observations suggest that we should rethink the use of RBC transfusions in the setting of CABG surgery by minimizing hemodilutional anemia during CPB with other strategies, such as preoperative erythropoietin and iron; use of autologous transfusion; conservation of intravenous fluids (preoperative and intraoperative); avoidance of blood loss; reduction of the CPB prime volume; use of a transfusion threshold based on patients' physiological needs, such as oxygen debt, rather than treating a number; ultrafiltration during CPB; patient warming systems to achieve normothermic core temperature at completion of procedure; avoidance of operation within 5 to 7 days of clopidogrel administration; and point-of-care coagulation testing to reduce delays in diagnosing reversible causes of hemorrhage. The adoption of these strategies is at different stages across the 8 centers in the NNECDSG.

Conclusions

In this prospective regional observational study of 8004 CABG patients, we demonstrated that the management of hemodilutional anemia during surgery with RBC transfusion is associated with an increased risk of LOF irrespective of the extent of anemia.

Disclosures

None.

References

1. Defoe GR, Ross CS, Olmstead EA, Surgenor SD, Fillinger MP, Groom RC, Forest RJ, Pieroni JW, Warren CS, Bogosian ME, Krumholz CF, Clark C, Clough RA, Weldner PW, Lahey SJ, Leavitt BJ, Marrin CA, Charlesworth DC, Marshall P, O'Connor GT. Lowest hematocrit on bypass and adverse outcomes associated with coronary artery bypass grafting. *Ann Thorac Surgery*. 2001;71:769–776.
2. Fang WC, Helm RE, Krieger KH, Rosengart TK, DuBois WJ, Sason C, Lesser ML, Isom OW, Gold JP. Impact of minimum hematocrit during cardiopulmonary bypass on mortality in patients undergoing coronary artery surgery. *Circulation.* 1997;96:II194–II199.
3. Swaminathan M, Phillips-Bute BG, Conlon PJ, Smith PK, Newman MF, Stafford-Smith M. The association of lowest hematocrit during cardiopulmonary bypass with acute renal injury after coronary aftery bypass surgery. *Ann Thorac Surgery*. 2003;76:784–792.
4. Habib RH, Zacharias A, Schwann TA, Riordan CJ, Engoren M, Durham SJ, Shah A. Role of hemodilutional anemia and transfusion in renal injury

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after coronary revascularization: implications on operative outcome. *CCM*. 2005;33:1749–1756.
5. Karkouti K, Djaiani G, Borger M, Beattie WS, Fedorko L, Wijeysundera D, Ivanov J, Karski J. Low hematocrit during cardiopulmonary bypass is associated with increased risk of perioperative stroke in cardiac surgery. *Ann Thorac Surg*. 2005;80:1381–1387.
6. Carson JL, Duff A, Poses PM, Berlin JA, Spence RK, Trout R, Noveck H, Strom BL. Effect of anemia and cardiovascular disease on surgical mortality and morbidity. *Lancet*. 1996;348:1055.
7. Kirklin J. *Cardiac Surgery*. New York, NY: Churchill Livingstone; 1993.
8. Blumberg, N. Deleterious clinical effects of transfusion immunomodulation: proven beyond a reasonable doubt. *Transfusions*. 2005;45: 33S–40S.
9. Lacelle PL. Alteration of deformability of the erythrocyte membrane in stored blood. *Transfusion*. 1996;9:229–237.
10. Simchon S, Jan KM, Chien S. Influence on reduced red cell deformability on regional blood flow. *Am J Physiol*. 1987;253:H898–H903.
11. Practice strategies for elective red blood cell transfusions. Am College of Physicians. *Ann Intern Med.* 1992;116:403–406.
12. Consensus conference. Perioperative red blood cell transfusion. *JAMA*. 1988;260:2700–2703.
13. Innes, G. Guidelines for red blood cells and plasma transfusion for adults and children: an emergency physician's overview of the 1997 Canadian blood transfusion guidelines. Part 1: red blood cell transfusion. Canadian Medical Association Expert Working Group. *J Emerg Med*. 1998;16: 129–131.
14. Practice Guidelines for Blood Component Therapy: A Report by the American Society of Anesthesiologists Task Force on Blood Component Therapy. *Anesthesiology*. 1996;84:732–747.
15. Englesbe MJ, Pelletier SJ, Diehl KM, Sung RS, Wahl WL, Punch J, Bartlett RH. Transfusions in Surgical Patients. *J Am Coll Surg*. 2005; 200:249–254.
16. Clough RA, Leavitt BJ, Morton JR, Plume SK, Hernandez F, Nugent W, Lahey SJ, Ross CS, O'Connor GT. The effect of comorbid illness on mortality outcomes in cardiac surgery. *Arch Surg*. 2002;137:428–433.
17. *STATA Statistical Software Release 8.0*. College Station, TX: STATA Corp; 2004.
18. O'Connor GT, Birkmeyer JD, Dacey LJ, Quinton HB, Marrin CA, Birkmeyer NJ, Morton JR, Leavitt BJ, Maloney CT, Hernandez F, Clough RA, Nugent WC, Olmstead EM, Charlesworth DC, Plume SK. Results of a regional study of modes of death associated with coronary artery bypass surgery. *Ann Thorac Surg*. 1998;66:1323–1328.
19. Surgenor SD, O'Connor GT, Lahey SJ, Quinn R, Charlesworth DC, Dacey LJ, Clough RA, Leavitt BJ, Defoe GR, Fillinger M, Nugent WC. Predicting the risk of death from heart failure after coronary artery bypass graft surgery. *Anesth Analg*. 2001;92:596–601.
20. Blumberg, N. Deleterious clinical effects of transfusion immunomodulation: proven beyond a reasonable doubt. *Transfusions*. 2005;45: 33S–40S.
21. Fransen E, Maessen J, Dentener M, Senden N, Buurman W. Impact of blood transfusions on inflammatory mediator release in patients undergoing cardiac surgery. *Chest*. 1999;116:1233–1239.
22. Valeri CR, Hirsch NM. Restoration in vivo of erythrocyte adenosine triphosphate, 2,3 diphosphoglycerate, potassium ion, and sodium ion concentrations following transfusion of adenine-citrate-dextrose stored human red blood cells. *J Lab Clin Med*. 1969;73:722–733.
23. Hamasaki N, Yamamoto M. Red blood cell function and blood storage. *Vox Sang*. 2000;79:191–197.
24. Lacelle PL. Alteration of deformability of the erythrocyte membrane in stored blood. *Transfusion*. 1969;9:229–237.
25. Simchon S, Jan KM, Chien S. Influence on reduced red cell deformability on regional blood flow. *Am J Physiol*. 1987;253:H898–H903.
26. Hebert PC, Wells G, Blajchman MA, Blajchman MA, Marshall J, Martin C, Pagliarello G., Tweeddale M, Schweitzer I, Yetisir E. A multicenter, randomized, controlled trial of transfusion requirements in critical care. *N Engl J Med.* 1999;409–417.
27. Fergusson D, Khanna MP, Tinmouth A, Hebert PC. Transfusion of leukoreduced red blood cells may decrease post-operative infections: two meta-analyses of randomized controlled trials. *Can J Anaesth*. 2004;54: 417–424.
28. Spiess BD, Ley C, Body SC, Siegel LC, Stover EP, Maddi R, D'Ambra M, Jain U, Liu F, Herskowitz A, Mangano DT, Levin J. Hematocrit value on intensive care unit entry influences the frequency of Q wave myocardial infarction after coronary artery bypass grafting. *J Cardiovasc Surg*. 1998;116:460–467.
29. Surgenor DM, Churchill WH, Wallace EL, Rizzo RJ, Chapman RH, McGurk S, Bertholf, MF, Goodnough LT, Kao KJ, Koerner TA, Olson JD, Woodson RD. Determinants of red cell, platelet, plasma and cryoprecipitate transfusions during coronary artery bypass graft surgery: the Collaborative Hospital Transfusion Study. *Transfusion*. 1996;36: 521–532.

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