Transfusion of 1 and 2 Units of Red Blood Cells Is Associated With Increased Morbidity and Mortality

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Background. **This study examined the relationship between transfusion of 1 or 2 units of red blood cells (RBCs) and the risk of morbidity and mortality after isolated on-pump coronary artery bypass grafting (CABG).**

Methods. **A total of 22,785 consecutive patients underwent isolated on-pump CABG between January 1, 2008, and December 31, 2011 in Michigan. We excluded 5,950 patients who received three or more RBC units. Twenty-one preoperative variables significantly associated with transfusion by univariate analysis were included in a logistic regression model predicting transfusion, and propensity scores were calculated. Transfusion and the propensity score covariate were included in additional logistic regression models predicting mortality and each of 11 postoperative outcomes.**

Results. **Operative mortality for the study cohort of 16,835 patients was 0.8% overall, 0.5% for the 10,884 patients with no transfusion, and 1.3% for the 5,951 patients who received transfusion of 1 or 2 units (odds ratio 2.44; confidence interval 1.74 to 3.42; $p < 0.0001$). The association between transfusion and mortality lessened after propensity adjustment but remained highly significant (odds ratio 1.86; confidence interval 1.21 to 2.87; $p = 0.005$). Of the 11 postoperative outcomes studied, all but sternal wound infection and need for dialysis were also significantly associated with transfusion.**

Conclusions. **Transfusion of as little as 1 or 2 units of RBCs is common and is significantly associated with increased morbidity and mortality after on-pump CABG. The relationship persists after adjustment for preoperative risk factors. These results suggest that aggressive attempts at blood conservation and avoidance of even small amounts of RBC transfusion may improve outcomes after CABG.**

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Red blood cell (RBC) transfusions are associated with morbidity and with short-term and long-term mortality after coronary artery bypass grafting (CABG) [1–6]. In addition, transfusion rates have been shown to vary widely, from less than 10% at some institutions to greater than 90% at others [7, 8]. Although RBCs may certainly have life-preserving value, the impact of smaller quantities in a nonemergent setting has not been well documented. It can be argued that these small-volume transfusions are more discretionary and therefore potentially avoidable. This observational cohort study was undertaken to explore the frequency and impact of small, potentially unnecessary RBC transfusions on operative mortality and morbidity in the setting of isolated on-pump CABG.

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Material and Methods

Patient Population

The Michigan Society of Thoracic and Cardiovascular Surgeons Quality Collaborative (MSTCVS-QC) is a multidisciplinary group consisting of all 33 hospitals that perform cardiac surgical procedures on adults in the state of Michigan [9]. All programs use the Society of Thoracic Surgeons (STS) data collection form and submit data on a quarterly basis to both the STS database and the MSTCVS-QC data warehouse. Data audits are conducted annually to ensure data integrity. For consistency, all audit visits are conducted by a core group of trained quality collaborative nurses. The last annual audit revealed 97% accuracy with 100% documentation of 30-day follow-up.

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Between January 2008 and December 2011, a total of 22,785 patients underwent isolated on-pump CABG in the state of Michigan (Fig 1). Of these, 5,950 were excluded subsequent to receiving 3 or more units of packed RBCs during their index admission, leaving a final dataset of 16,835 patients for analysis.

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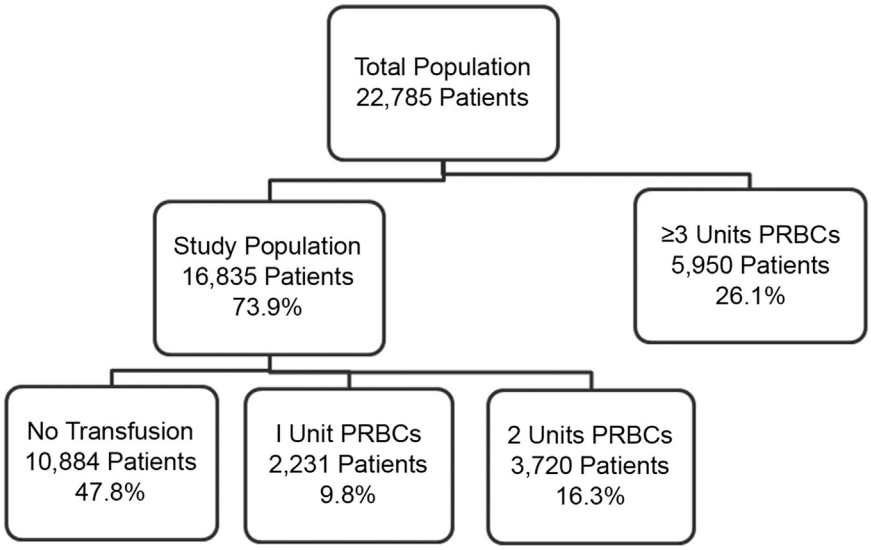

Fig 1. Patient groups. (PRBCs = packed red blood cells.)

The primary exposure for this study was the delivery of 0, 1, or 2 units of RBCs. The primary outcome was operative (in-hospital or 30-day) mortality. We also explored the association between transfusion and 11 postoperative outcomes: sternal wound infection, stroke, renal failure, new-onset dialysis, atrial fibrillation, reoperation for bleeding, initial ventilator time >8 hours, prolonged ventilation time >24 hours, total intensive care unit stay >24 hours, postoperative length of stay >7 days, and discharge to home.

Statistical Analyses

Standard statistical tests were used to estimate the association between the number (and delivery or not) of RBC transfusions and patient, process, and outcome measures. These tests include χ^2 tests for categorical data and Wilcoxon rank-sum tests for continuous data. We reported odds ratios (OR) and 95% confidence intervals (CI).

The following preoperative characteristics that had statistically significant associations with either blood transfusion or operative mortality were included in a logistic regression model predicting blood transfusion: age, sex, height, weight, race, preoperative creatinine level, preoperative hematocrit level, diabetes, renal failure receiving dialysis, hypertension, chronic lung disease, peripheral arterial disease, cerebrovascular disease, cigarette smoking, history of myocardial infarction, procedure status (elective, urgent, emergent), use of intravenous nitrates, adenosine diphosphate inhibitors within 5 days, number of diseased coronary arteries, and preoperative left ventricular ejection fraction. Propensity scores were calculated with the use of the model. Blood transfusion and the propensity score covariate were then included in another logistic regression model predicting operative mortality. The adjusted association between blood transfusion and operative mortality was reported in the form of an odds ratio and a 95% confidence interval. This process was repeated for the other 11 postoperative outcomes. Unadjusted associations were calculated with the use of simple logistic regression models, with blood transfusion as a single predictor for each outcomes; rates were compared with χ^2 tests. In addition to the propensity-adjusted analyses, multivariable logistic regression models were also fit for each of the outcomes, including mortality. Statistical analyses were performed with SAS 9.2 software. The tests were considered significant at $p \leq 0.05$.

Results

The preoperative characteristics for the study cohort by transfusion status are presented in Table 1. Patients receiving transfusions were older and sicker, had smaller body size and lower preoperative hematocrit, and were more likely to have undergone urgent or emergent procedures.

Of the total population of 22,685 patients, 52.2% (11,901) received transfusions, and half of these (5,951) received either 1 or 2 units of RBCs. The mortality for the study cohort of 16,835 patients was 0.8%. Those who received transfusions had a mortality rate of 1.3% versus 0.5% for those with no transfusion (OR 2.44; CI 1.74 to 3.42; $p < 0.001$). The relationship lessened somewhat when adjusted for the propensity score covariate but remained significant (OR 1.86; CI 1.21 to 2.87; $p = 0.005$). Univariate and multivariate analyses of preoperative demographics and of transfusion status for predicting mortality are shown in Table 2. The relationship between transfusion and mortality obtained from the multivariable logistic model was similar to that of the propensity analysis (OR 1.90; CI 1.23 to 2.91; $p = 0.003$).

Transfusion of either 1 or 2 units of red cells was each independently associated with mortality (1 unit vs no transfusion: OR 1.91; CI 1.18 to 3.10; $p = 0.009$; 2 units vs

Table 1. Univariate Analyses of 0- to 2-Unit Blood Transfusions Using Preoperative Characteristics (n = 16,835)

Characteristic	Response	No Transfusion (n = 10,884)	1- to 2-Unit Transfusion (n = 5,951)	*p* Value
Patient age		62.32 ± 9.97	66.26 ± 10.35	<0.001
Sex (% female)		1,414 (13.9%)	2,190 (36.8%)	<0.001
Weight (kg)		95.25 ± 19.49	86.32 ± 19.58	<0.001
Height (cm)		174.6 ± 9.33	169.7 ± 10.87	<0.001
Body surface area		2.14 ± 0.24	2.01 ± 0.26	<0.001
Race (% black)		606 (5.6%)	553 (9.3%)	<0.001
Last creatinine level		1.03 ± 0.52	1.13 ± 0.84	<0.001
Last preoperative hematocrit		40.90 ± 4.30	37.56 ± 4.73	<0.001
Diabetes (% yes)		4,090 (37.6%)	2,569 (43.2%)	<0.001
Diabetes (% insulin control)	Insulin	1,271 (37.1%)	1,002 (44.9%)	<0.001
Dyslipidemia	No	1,395 (12.8%)	749 (12.6%)	0.67
	Yes	9,489 (87.2%)	5,201 (87.4%)	
Renal failure–dialysis	No	10,801 (99.3%)	5,822 (97.8%)	<0.001
	Yes	75 (0.7%)	128 (2.2%)	
Hypertension	No	1,594 (14.6%)	675 (11.3%)	<0.001
	Yes	9,290 (85.4%)	5,274 (88.7%)	
Chronic lung disease	No	8,657 (79.5%)	4,519 (75.9%)	<0.001
	Yes	2,227 (20.5%)	1,431 (24.1%)	
Chronic lung disease	Moderate	504 (60.7%)	329 (55.2%)	0.037
	Severe	326 (39.3%)	267 (44.8%)	
Peripheral arterial disease	No	9,575 (88.0%)	4,874 (81.9%)	<0.001
	Yes	1,309 (12.0%)	1,077 (18.1%)	
Cerebrovascular disease	No	9,747 (89.6%)	4,971 (83.5%)	<0.001
	Yes	1,137 (10.4%)	979 (16.5%)	
Cigarette smoker	No	7,476 (68.7%)	4,265 (71.7%)	<0.001
	Yes	3,408 (31.3%)	1,686 (28.3%)	
Prior cerebrovascular accident	No	620 (54.6%)	551 (56.3%)	0.416
	Yes	516 (45.4%)	427 (43.7%)	
Previous PCI	No	7,860 (72.2%)	4,287 (72.0%)	0.806
	Yes	3,024 (27.8%)	1,664 (28.0%)	
Myocardial infarction	No	5,818 (53.5%)	2,937 (49.4%)	<0.001
	Yes	5,066 (46.5%)	3,014 (50.6%)	
Prior heart failure	No	1,193 (93.5%)	539 (89.1%)	<0.001
	Yes	83 (6.5%)	66 (10.9%)	
Classification: NYHA	Class III	290 (58.4%)	355 (55.6%)	0.361
	Class IV	207 (41.6%)	283 (44.4%)	
Operative status	Elective	4,234 (38.9%)	1,963 (33.0%)	<0.001
	Emergent	260 (2.4%)	206 (3.5%)	
	Urgent	6,387 (58.7%)	3,777 (63.5%)	
β-Blockers	No	1,217 (11.2%)	711 (11.9%)	0.136
	Yes	9,667 (88.8%)	5,240 (88.1%)	
ACE or ARB inhibitors	No	5,870 (61.1%)	2,975 (55.6%)	<0.001
	Yes	3,737 (38.9%)	2,371 (44.4%)	
IV nitrates	No	9,322 (85.6%)	4,998 (84.0%)	0.004
	Yes	1,562 (14.4%)	953 (16.0%)	
Aspirin	No	1,601 (14.7%)	921 (15.5%)	0.183
	Yes	9,283 (85.3%)	5,030 (84.5%)	
Lipid-lowering agents	No	2,183 (20.1%)	1,188 (20.0%)	0.884
	Yes	8,701 (79.9%)	4,763 (80.0%)	
ADP inhibitors within 5 days	No	10,018 (92.1%)	5,238 (88.0%)	<0.001
	Yes	863 (7.9%)	711 (12.0%)	

(*Continued*)

Table 1. Continued

Characteristic	Response	No Transfusion (n = 10,884)	1- to 2-Unit Transfusion (n = 5,951)	*p* Value
No. of diseased vessels	One	357 (3.3%)	158 (2.7%)	<0.001
	Two	2,354 (21.7%)	1,146 (19.3%)	
	Three	8,155 (75.1%)	4,635 (78.0%)	
Left main disease ≥50%	No	7,331 (67.4%)	3,920 (65.9%)	0.051
	Yes	3,553 (32.6%)	2,031 (34.1%)	
Ejection fraction		52.35 ± 11.22	51.40 ± 12.54	0.002
Ejection fraction (<40%)	<40%	1,230 (11.4%)	928 (15.8%)	<0.001
	≥40	9,537 (88.6%)	4,931 (84.2%)	
Previous CABG	No	3,028 (92.8%)	1,681 (89.8%)	<0.001
	Yes	236 (7.2%)	191 (10.2%)	

ACE = angiotensin converting enzyme; ADP = adenosine diphosphate; ARB = angiotensin receptor blocker; CABG = coronary artery bypass grafting; IV = intravenous; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.

no transfusion: OR 2.75; CI 1.90 to 3.98; $p = <0.001$). We did not find a dose-response relationship between number of transfusions and risk of death (2 units vs 1 unit: OR 1.44; CI 0.88 to 2.35; $p = 0.144$).

The univariate, multivariate regression, and propensity-adjusted effects of transfusion across several morbid outcomes are represented in Table 3. In both crude and adjusted analyses, transfusions increased the

Table 2. Univariate and Multivariate Logistic Models Predicting Mortality

		Univariate Models n = 16,835[a]		Multivariate Model n = 14,644	
Preoperative Characteristic	Response	OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Blood transfusion	1 or 2 vs none	2.44 (1.74 to 3.42)	<0.001	1.90 (1.23 to 2.91)	0.003
Patient age		1.05 (1.03 to 1.07)	<0.001	1.05 (1.03 to 1.08)	<0.001
Sex	Male vs female	0.59 (0.41 to 0.85)	0.005	0.57 (0.32 to 1.04)	0.067
Weight (kg)		1.00 (0.99 to 1.01)	0.561	1.01 (1.00 to 1.02)	0.157
Height (cm)		0.99 (0.97 to 1.00)	0.050	1.00 (0.98 to 1.03)	0.853
Race	White vs black	0.71 (0.40 to 1.25)	0.236	1.15 (0.52 to 2.55)	0.729
Last creatinine level		1.32 (1.18 to 1.47)	<0.001	1.14 (0.88 to 1.48)	0.323
Last preoperative hematocrit		0.96 (0.93 to 1.00)	0.029	1.02 (0.98 to 1.06)	0.405
Diabetes	Yes vs no	0.96 (0.68 to 1.36)	0.835	0.79 (0.52 to 1.21)	0.283
Renal failure–dialysis	Yes vs no	4.53 (2.09 to 9.82)	<0.001	1.30 (0.26 to 6.55)	0.749
Hypertension	Yes vs no	1.03 (0.63 to 1.69)	0.908	0.91 (0.50 to 1.68)	0.770
Chronic lung disease	Yes vs no	1.77 (1.24 to 2.53)	0.002	1.81 (1.20 to 2.75)	0.005
Peripheral arterial disease	Yes vs no	2.43 (1.67 to 3.54)	<0.001	2.15 (1.38 to 3.35)	<0.001
Cerebrovascular disease	Yes vs no	1.80 (1.18 to 2.73)	0.006	1.41 (0.88 to 2.27)	0.152
Cigarette smoker	Yes vs no	0.88 (0.61 to 1.29)	0.519	0.75 (0.45 to 1.25)	0.265
Myocardial infarction	Yes vs no	2.09 (1.46 to 2.97)	<0.001	1.51 (0.99 to 2.32)	0.057
Operative status	Emergent vs elective	3.00 (1.50 to 5.99)	0.002	1.85 (0.73 to 4.65)	0.194
	Urgent vs elective	1.08 (0.75 to 1.56)	0.664	0.85 (0.54 to 1.34)	0.485
ACE or ARB inhibitors	Yes vs no	0.83 (0.57 to 1.22)	0.344	0.84 (0.56 to 1.25)	0.392
IV nitrates	Yes vs no	1.89 (1.28 to 2.79)	0.001	1.75 (1.06 to 2.91)	0.029
ADP inhibitors within 5 days	Yes vs no	1.10 (0.63 to 1.92)	0.727	0.58 (0.27 to 1.28)	0.180
No. of diseased vessels	Three vs one	2.27 (0.56 to 9.19)	0.253	2.61 (0.36 to18.97)	0.343
	Two vs one	1.70 (0.40 to 7.22)	0.474	2.03 (0.27 to15.37)	0.495
Ejection fraction		0.97 (0.96 to 0.98)	<0.001	0.98 (0.96 to 0.99)	0.006

[a] Because of missing data, n ranges from 16,835 to 14,953.

ACE = angiotensin converting enzyme; ADP = adenosine diphosphate; ARB = angiotensin receptor blocker; CI = confidence interval; IV = intravenous; OR = odds ratio.

Table 3. Univariate and Multivariate Logistic Regression-Adjusted and Propensity-Adjusted Associations Between Blood Transfusion (0 vs 1 or 2) and Postoperative Outcomes

	Univariate Comparison			Multivariate Logistic Regression		Propensity-Adjusted	
Outcome	No blood n = 10,884	1–2 Units n = 5,951	*p* Value	OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Operative mortality	59 (0.5%)	78 (1.3%)	<0.001	1.90 (1.23 to 2.91)	0.003	1.86 (1.21 to 2.87)	0.005
Deep sternal infection	39 (0.4%)	30 (0.5%)	0.157	0.85 (0.48 to 1.51)	0.588	0.91 (0.51 to 1.62)	0.758
Permanent stroke	70 (0.6%)	89 (1.5%)	<0.001	1.71 (1.18 to 2.48)	0.005	1.73 (1.18 to 2.52)	0.005
Renal failure	111 (1.0%)	147 (2.5%)	<0.001	2.56 (1.90 to 3.44)	<0.001	2.63 (1.95 to 3.55)	<0.001
Atrial fibrillation	2,238 (20.6%)	1,416 (23.8%)	<0.001	1.21 (1.10 to 1.32)	<0.001	1.21 (1.11 to 1.33)	<0.001
Initial ventilator time (>8 h)	3,918 (36.1%)	3,129 (53.0%)	<0.001	1.71 (1.58 to 1.85)	<0.001	1.65 (1.53 to 1.78)	<0.001
Prolonged ventilation	447 (4.1%)	579 (9.7%)	<0.001	2.45 (2.09 to 2.88)	<0.001	2.34 (2.00 to 2.74)	<0.001
Reoperation for bleeding	17 (0.2%)	28 (0.5%)	0.002	6.78 (3.36 to 13.68)	<0.001	6.24 (3.12 to 12.49)	<0.001
Need for dialysis	24 (0.2%)	28 (0.5%)	0.005	1.61 (0.83 to 3.12)	0.161	1.50 (0.76 to 2.93)	0.241
Total ICU time (>24 h)	5,679 (59.1%)	3,771 (70.6%)	<0.001	1.43 (1.32 to 1.55)	<0.001	1.42 (1.31 to 1.53)	<0.001
Postoperative LOS (>7 days)	1,439 (13.2%)	1,683 (28.3%)	<0.001	2.24 (2.03 to 2.47)	<0.001	2.16 (1.96 to 2.38)	<0.001
Discharge home	10,172 (93.8%)	5,025 (85.2%)	<0.001	0.63 (0.55 to 0.72)	<0.001	0.64 (0.57 to 0.73)	<0.001

ICU = intensive care unit; LOS = length of stay.

risk of most morbid outcomes, exclusive of deep sternal wound infections and need for dialysis.

Comment

In this large multicenter study, we found that small quantities of RBC (ie, 1 and 2 units) were administered to 26% of the total population, accounting for half of all patients receiving transfusion. The patients who received transfusion were older and sicker, and transfusion status was associated with a greater risk of operative mortality and all of the postoperative outcomes studied except for sternal wound infection and the need for dialysis.

A growing literature suggests that 1- and 2-unit transfusions are common and that even these small quantities are associated with worse outcomes after cardiac operations. This is important because transfusion at this level seems more likely to be discretionary and hence avoidable, and it has little in the way of scientific evidence to support it. In a report from Koch and associates [4], RBC transfusion was related to increased rates of essentially every postoperative comorbid event, including renal failure, infections, cardiac and neurologic events, prolonged ventilation, and operative mortality [4]. The relationship was dose dependent, and patients receiving even 1 unit of RBCs had a 77% increased adjusted odds of mortality compared with those not receiving transfusions. Approximately 26% of their patients received 1 or 2 units of RBCs, which is comparable with the rate found in our population. Murphy and colleagues [3] reported similar associations between transfusion and worsening outcomes, along with increased costs of care. The 13.6% of patients who received a single unit of RBCs in their study had a 46% increase in infectious outcomes, a 63% increase in ischemic outcomes, and an 11% relative increase in costs. Those receiving 2 units of packed cells (14.5% of patients) had a 136% increase in infections, a 130% increase in ischemic events, and a 21% increase in costs.

In an analysis of more than 9,000 patients undergoing CABG, valve procedures, or combined procedures, Surgenor and colleagues [10] found that exposure to 1 or 2 units of RBCs was associated with a 67% increased risk of early death. Patients receiving transfusions also had a 16% increase in the risk of late mortality. Jakobsen and associates [11] reported an increase of greater than 10% in long-term mortality for low-risk patients receiving as little as 1 to 2 units of RBCs. Transfusions of 1 and 2 units accounted for 55% of the population receiving transfusion in their study, similar to the 50% rate in this study.

Blood conservation clinical practice guidelines from the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists, first reported in 2007 and updated in 2011, extensively review the indications for transfusion and provide many recommendations that can enhance the appropriateness of care and contribute to decreased use of blood [12, 13]. Yet, institutional transfusion rates remain highly variable, with no evidence to suggest that higher transfusion rates provide any benefit [8]. A common rationale for RBC transfusion is to increase oxygen delivery to organ tissues sensitive to ischemia in

patients with hematocrit or hemoglobin levels below a predetermined and usually arbitrarily set lower limit. However, well-described changes in RBC morphology, and the significant depletion of 2, 3-DPG and nitric oxide levels that occurs during storage, are known to profoundly limit the capacity of these RBCs to carry and deliver oxygen to the tissues, and thus call into question the benefit of many of these transfusions [14–17].

Further confounding the risk-reward algorithm of transfusion, what might be considered the optimal or at least a safe target for a minimal hemoglobin level has yet to be clearly established, but it is very likely lower than what has generally been accepted to date. Several reports have documented a significant association between various nadir levels of intraoperative and postoperative hematocrit and increased morbidity and mortality. Complicating the quest for consensus, however, has been a lack of consistency in study design and data availability; some have been adjusted for various patient and procedural demographics, transfusion status, or both, and some have not [1, 17–20].

Transfusion in the setting of anemia may in fact worsen rather than improve outcomes. Surgenor and colleagues [21] reported an increase in the risk of low-output heart failure after CABG associated with various nadir levels of hematocrit, which was even greater among patients exposed to intraoperative RBCs than in those with anemia alone. Others have demonstrated a significant dose-dependent association between lowest hematocrit during bypass and postoperative renal injury, which was worsened at each hematocrit level when RBC transfusions were administered [22, 23]. Karkouti and associates [24] found "an independent, direct relationship between degree of hemodilution during cardiopulmonary bypass and perioperative stroke," but cautioned that "limiting hemodilution during bypass by red cell transfusion may do more harm than good."

Yun and colleagues [25] have reported a two-fold increase in mortality in patients under the age of 80 receiving transfusions of 1 to 2 units of RBCs when undergoing a variety of nonemergent cardiac procedures, but these authors were surprised to find no significant increase in risk for those over age 80. They considered the possibility that transfusion may have somehow positively compensated for the greater incidence of chronic anemia found in the elderly cohort, but nonetheless they continue to advocate "thoughtful restrictive transfusion practices" in this population.

In an attempt to focus the breadth of this study, we have limited our analysis to a specific volume of transfusion (1vs 2 units). To account for differences between study cohorts, we used both propensity score analysis and multivariate logistic regression. The results from both techniques were similar, namely, that RBC transfusion remains associated with worse outcomes even after adjustment for differences in patient demographics. In this regard, our work mirrors that of other published studies.

The limitations of this analysis remain similar to those of any retrospective database-generated observational study. We acknowledge that there may be some risk of a type II error as we explore the impact of transfusions on some rarer morbid outcomes, including deep sternal wound infection and need for dialysis. Nevertheless, in no instances did transfusion appear to be protective across 11 commonly reported morbid outcomes, and we know of no evidence that convincingly suggests that any outcomes are improved after cardiac operations for patients who receive transfusions.

We have no information regarding the age of the blood transfused or of various institutional or physician preferences for transfusion or of other care process variables that may significantly affect outcome. Importantly, we have no data regarding the hematocrit level—particularly the intraoperative or on-bypass nadir hematocrit—or the clinical circumstances that prompted transfusion: a shortcoming that has been the Achilles heel of research in this area. Despite the use of increasingly sophisticated statistical methods that aim to make clinically dissimilar patient populations comparable, it remains difficult to fully account for the associated patient-related factors and other potential unmeasured confounders that likely affect these relationships. Is it really the hematocrit level, or is it the transfusion, or is it the patient, or the procedure, or the physician, or most likely some combination of all of these that ultimately most affects outcome? Simply stated, the complex interaction between patient demographics, nadir hematocrit, transfusion status, and patient outcomes remains incompletely understood and in need of further study.

In conclusion, we found that transfusion of as little as 1 or 2 units of RBCs is common and is significantly associated with increased morbidity and mortality after on-pump CABG. The relationship persists after adjustment for patient characteristics and risk. We thus assert that the perioperative transfusion of RBCs is associated with worse outcomes, but we must also admit that this hypothesis-generating statement cannot and should not be construed as a declaration of cause and effect. Nonetheless, we do not hesitate to suggest that aggressive attempts at blood conservation are warranted, and avoidance of even small amounts of RBC transfusion may improve outcomes after CABG.

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DISCUSSION

DR JEFF CARROW (New Brunswick, NJ): What variables were included in your regression model? What did you adjust for? And did you have the pretransfusion hemoglobin?

DR PAONE: We did. As I noted in the presentation, there were 35 common preoperative demographic variables compared; and of those, 21 were significantly associated with transfusion and they included preoperative hematocrit, age, sex, height, weight, body surface area, preoperative creatinine. I do not remember the others specifically, but there was a total of 21, and they were included in the regression.

DR CARROW: What about the pretransfusion hemoglobin?

DR PAONE: No, we do not have information on the pretransfusion hemoglobin. The only hemoglobin that's in the database at the moment is the preoperative level, essentially either on admission, or that recorded as the last one before the data get entered. I will say that the state collaborative now has a perfusion registry, which I believe 17 of the 33 programs are presently contributing data to. We are collecting a large amount of perfusion-related data in the operating room, particularly prebypass, nadir bypass, postbypass, and pretransfer hematocrits, and we hope to be able to break down and look at these issues more closely.

DR ROBERT EMERY (Minneapolis, MN): Congratulations on continuing your work. Your article in the *Journal of Thoracic and Cardiovascular Surgery* in January 2012 was a great report. This is wonderful work, and it provides more evidence so we can make real decisions based on data in pushing forward blood conservation as a quality measure for open heart operations.

DR PAONE: Thank you.

DR VINCENT CONTI (Galveston, TX): Very good analysis. One of the questions I have is it seems like patients who have had any significant preoperative length of stay and who have had a cardiac catheterization before their operation have a much higher incidence of needing this 1-unit or 2-unit transfusion. Did you analyze whether there was a relationship between length of preoperative stay and cardiac catheterization at that admission before operation as a variable that could have contributed to this borderline need for a blood transfusion?

DR PAONE: It's a very good point. The answer to your question is no. The database analysis basically starts on arrival to the cardiac surgery service. But I do think that you're exactly right. In large part depending on whether they've been catheterizeded and how much blood they've lost during the catheterization will certainly affect what we record as their preoperative hematocrit, and that can certainly influence particularly, I suspect, 1-unit and 2-unit transfusions.

DR GLENN WHITMAN (Baltimore, MD): But, excuse me, there was no difference in these groups regarding preoperative hematocrit; is that correct?

DR PAONE: No, there was a difference between those receiving transfusions and those not receiving transfusions in preoperative hematocrit, and that was included in their regression. With the propensity score, we made them similar. But if you look at the crude analysis, absolutely, patients who received transfusions will have lower hematocrits than those who did not.

DR WHITMAN: But then in the propensity analysis they were kept the same?

DR PAONE: Yes, that should have been corrected in the regression. That's true, yes.

DR ANTHONY ACINAPURA (Brooklyn, NY): Do you have in your data the indications for transfusion on the patients who received blood?

DR PAONE: No. And I mentioned that. That's one of the limitations of our study from our database. We do not have the indication for transfusion.

DR WHITMAN: Do you think that there is a consensus in the state regarding indications for transfusion?

DR PAONE: I'm not quite sure I'd call it a consensus. No, I'm pretty sure there isn't. We're working toward that. Yesterday's paper was with regard to working toward a consensus.

DR ALEX ZAPOLANSKI (Ridgewood, NJ): You mentioned these are all on-pump cases, right? I presume that there are some off-pump surgical procedures done in Michigan. Do you have the data for that subgroup of patients? Do you plan to match them to this? I mean, avoiding hemodilution is the best way to conserve blood, right?

DR PAONE: We specifically looked at on-pump here because I think that the indications, particularly for 1 or 2 units, and especially in the operating room, may well be different between on-pump and off-pump. Michigan actually does a relatively small amount of off-pump CABG—about 9% of our cases are off-pump—and we have looked at that. In general, the incidence of transfusion during our off-pump cases is about 10% lower than for on-pump. We had been in the low 50% or so range for on-pump and low to mid 40% range for off-pump. So certainly we do see less transfusion with off-pump cases as well.

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