HEMATOCRIT VALUE ON INTENSIVE CARE UNIT ENTRY INFLUENCES THE FREQUENCY OF Q-WAVE MYOCARDIAL INFARCTION AFTER CORONARY ARTERY BYPASS GRAFTING

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Objectives: No data exist regarding "the best" hematocrit value after coronary artery bypass graft surgery. Transfusion practice varies, because neither an optimal hematocrit value nor a uniform transfusion trigger criterion has been determined. **Methods:** To investigate the optimal hematocrit value, we studied 2202 patients undergoing coronary bypass. The hematocrit value on entry into the intensive care unit (IHCT) was categorized into three groups: high ($\geq 34\%$), medium (25% to 33%), and low ($\leq 24\%$). Characteristics and adverse events (outcomes) were compared, and the effect of IHCT on the risk of myocardial infarction was determined by logistic regression. **Results:** High IHCT ($\geq 34\%$) was associated with an increased rate of myocardial infarction (8.3% vs 5.5% vs 3.6%; $p \leq 0.03$, high, medium vs low) and with more severe left ventricular dysfunction (11.7% vs 7.4% and 5.7%; $p = 0.006$, high, medium vs low). Mortality rate increased with higher IHCT when all the high-risk subgroups were combined (8.6% vs 4.5% vs 3.2%; $p < 0.001$, high, medium vs low). By multivariate analysis, IHCT remained the most significant predictor of adverse outcomes (relative risk high vs low 2.22, 95% confidence interval: 1.04 to 4.76). No characteristic, event, medication, or transfusion therapy confounded the relationship between IHCT and outcome. **Conclusion:** High IHCT is associated with a higher rate of myocardial infarction and is an independent predictor of infarction. On the basis of the risk of myocardial infarction, there is no rationale for transfusion to an arbitrary level after coronary artery bypass grafting. (*J Thorac Cardiovasc Surg* 1998;116:460-7)

No data exist regarding the "best" hematocrit (HCT) value after cardiopulmonary bypass. Clinicians have assumed that anemia increases the risk of myocardial ischemia after coronary artery bypass graft (CABG) operations. Several recent studies have suggested that there might not be an association between anemia and morbidity after CABG.^{1,2} Therefore no safe lower limit of HCT has been established, yet the risks of transfusion are well

delineated.³ A wide variability exists in blood use for CABG operations.^{4,5} The difference in transfusion practice is probably a reflection of the lack of adequate data regarding morbidity and mortality risks for HCT levels after CABG. Any new data regarding relative outcome risks and HCT may have an impact on national blood use and costs (15% to 20% of blood is used in cardiopulmonary bypass).⁶⁻⁸

In the patient undergoing CABG, the highest risk

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See Appendixes 1 and 2 for list of *McSPI* investigators and central analysis group members.

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Table I. Distribution of preoperative and intraoperative characteristics of patients in the three IHCT groups

	HCT $\leq$ 24% (n = 248)	HCT 25%-33% (n = 1544)	HCT $\geq$ 34% (n = 410)	
Characteristic	% (n)	% (n)	% (n)	p Value
Age (yr; mean, SD)	64.3 $\pm$ 10.2	64.8 $\pm$ 10.1	63.7 $\pm$ 11.1	0.13
BSA (m ² ; mean, SD)	1.86 $\pm$ 0.20	1.93 $\pm$ 0.21	1.93 $\pm$ 0.24	<0.001*
Female gender	26 (65)	23 (356)	25 (104)	0.40
History of smoking	62 (150)	67 (1,014)	70 (285)	0.06
History of COPD	170 (42)	18.9 (293)	19.5 (80)	0.47
History of anemia	10 (25)	7 (107)	5 (19)	0.03
History of unstable angina	45 (109)	45 (695)	48 (193)	0.69
History of MI	52 (127)	54 (820)	54 (218)	0.78
History of CHF	32 (80)	32 (484)	30 (120)	0.71
Prior CABG	9 (23)	12 (185)	16 (64)	0.04†
History of thrombolysis‡	4 (11)	6 (92)	4 (15)	0.15
History of aspirin use§	67 (165)	64 (991)	59 (243)	0.11
Emergency surgery	19 (47)	22 (333)	23 (96)	0.40
Valve or other surgery	18 (44)	15 (235)	14 (58)	0.46
Bypass time (min; mean, SD)	113 $\pm$ 49	113 $\pm$ 46	111 $\pm$ 48	0.63
Crossclamp time (min; mean, SD)	65 $\pm$ 32	66 $\pm$ 32	64 $\pm$ 30	0.72
No. of grafts (mean, SD)	3.25 $\pm$ 1.2	3.23 $\pm$ 1.1	3.09 $\pm$ 1.1	0.05*
History of diabetes	24.6 (61)	25.7 (397)	25.3 (103)	0.81
History of renal disease	6.9 (17)	5.5 (85)	4.2 (17)	0.10
Recent MI ($\leq$ 31 days)	16.3 (40)	16.7 (254)	18.1 (73)	0.42
History of peripheral vascular disease	20.6 (53)	23.4 (340)	22.6 (92)	0.93
Canadian Heart Assoc classification IV	25.0 (55)	26.7 (350)	28.0 (97)	0.74
Canadian Heart Assoc classification V	7.3 (16)	7.4 (97)	5.2 (18)	0.53
Canadian Heart Assoc classification VI	5.0 (11)	5.5 (72)	4.9 (17)	0.93

IHCT, Hematocrit value on entry into the intensive care unit; SD, standard deviation; BSA, body surface area; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; CHF, congestive heart failure; CABG, coronary artery bypass grafting. Calculated percents take into account any missing data.

* $p \leq 0.05$ between low HCT and either medium or high HCT.

† $p \leq 0.05$ between low HCT and high HCT group.

‡History of thrombolysis within 24 hours before CABG.

§History of aspirin use within 7 days before CABG.

period for adverse myocardial ischemic events is in the immediate perioperative period.^{9, 10} Recent data have shown that the period within 1 to 2 hours after protamine administration is associated with the largest number of electrocardiographic changes of ischemia.¹⁰ The HCT during these first several hours after CABG represents the sum total of preoperative HCT, hemodilution, blood loss, fluid administration, transfusion therapy, and the transfusion philosophy (transfusion HCT trigger). A representative HCT of that time interval is the HCT on entry to the intensive care unit (IHCT). In a large-scale multicenter study, the relationship between IHCT and adverse clinical outcomes was examined in an effort to answer the question: Is there a "best" IHCT after CABG?

Methods

Patients. The Multicenter Study of Perioperative Ischemia (McSPI) Cardiac Surgery Database was a prospective observational study of 2417 patients in the United States undergoing elective CABG operations with or without other concurrent cardiac procedures. The study

was designed to assess the frequency of adverse postoperative outcomes and to determine the presence of preoperative patient characteristics.¹¹ Between 100 and 108 patients were enrolled at each of 24 centers from September 1991 to September 1993 with the use of a standardized questionnaire that has been previously well described.¹³ The volume of intraoperative crystalloid and colloid was measured, as was the use of transfusion (red blood cells [RBCs], platelets, fresh frozen plasma, or cryoprecipitate) during and after the operation. Blood loss was assessed by chest tube drainage.

Postbypass morbidity was defined as (1) low cardiac index (<1.5 L/min $\cdot$ m²) or hypotension (arterial systolic pressure < 80 mm Hg for ≥ 10 minutes), or the administration of three or more inotropic agents; (2) the presence of myocardial ischemia by ST segment deviation or the use of intravenous nitroglycerin; (3) hypertension (systolic blood pressure > 180 mm Hg for ≥ 10 minutes), or tachycardia (heart rate > 100 beats/min for at least 10 minutes).

Adverse events. Adverse postoperative events included Q-wave myocardial infarction (MI), death, renal failure (necessitating hemodialysis), adverse central nervous system outcome (stroke, transient ischemic attack, or stupor/coma at discharge), or severe left ventricular dysfunction necessitating the use of an intraaortic balloon pump. To

Fig. 1. Level (mean $\pm$ standard deviation) of HCT on admission, on entry to the ICU, and at discharge according to IHCT group. Note that the three subgroups were similar at hospital entry and discharge. L, Low HCT ($\leq 24\%$); M, medium HCT (25% to 33%); H, high HCT ($\geq 34\%$).

determine the presence of a new Q-wave MI, one preoperative and two postoperative 12-lead electrocardiograms (one collected on postoperative days 0 to 3 and one on days 4 to 10) were analyzed according to Minnesota Code criteria by three electrocardiographers at a central core facility (Ischemia Research and Education Foundation [IREF], San Francisco, Calif.), who were blinded to patients' identities and clinical courses.¹²

HCT. HCT values were recorded at hospital admission, on arrival in the intensive care unit (ICU), and at discharge. The minimum and maximum postoperative values were also noted. The changes in HCT from admission to ICU entry and from ICU entry to discharge were calculated for each patient. Previous studies either considered an HCT of 25% as a lower limit or were vague regarding a transfusion trigger. Experimental data suggest that HCT exceeding 33% may be associated with decreased tissue oxygen delivery.¹³ We thus defined three groups of patients on the basis of IHCT: low ($\leq 24\%$), medium (25% to 33%), and high HCT ($\geq 34\%$).

Association of IHCT and intraoperative and postoperative variables. To identify any differences among patients with low, normal, and high IHCT values, we examined preoperative and intraoperative characteristics in each IHCT group. Because IHCT was thought to be a consequence of many intraoperative factors, operative events including blood and fluid loss, postbypass morbidity, and the use of transfusion were carefully examined for the three IHCT groups. Rates of adverse postoperative outcomes were compared across IHCT groups. In addition, these outcomes were examined in subgroups of patients at high risk for adverse events (patients with unstable angina, emergency CABG, reoperation, or a combination of these factors).^{9, 14-17} All associations were examined by means of the χ^2 test for categorical variables and either general linear modeling or the Kruskal-Wallis test for continuous variables.¹⁸ All tests were two-tailed.

Multivariate analysis. We limited multivariate analyses to Q-wave MI, because this was the only outcome with a blinded diagnosis. First, we examined the effect of IHCT on risk of MI after adjustment for single variables. We

also examined the effect of site on the relationship between IHCT and MI. Because no variable appeared to confound the relationship between IHCT and MI, we constructed a stepwise logistic regression model using variables previously reported in the literature (age, sex, history of MI, smoking, and reoperation CABG).¹⁴⁻¹⁷ The entry and stay α level were both set at 0.2 in this analysis (variable will remain if $p \leq 0.2$ and will be removed if $p > 0.2$). All IHCT levels were forced to remain in the model at all times. The Hosmer-Lemeshow test measuring goodness-of-fit was used to validate the final stepwise logistic regression model.¹⁹

Results

Patients. Interpretable electrocardiographic and HCT values were available for a total of 2202 patients. The demographic, preoperative, and intraoperative characteristics of the three IHCT groups are presented in Table I. Patients' ages ranged from 28 to 95 years (mean $\pm$ standard deviation: 64.6 ± 10.3 years), with 32% older than 70 years of age. CABG was performed on an emergency basis in nearly 25% of cases, and approximately 16% of patients underwent an additional cardiac procedure, primarily valve repair or replacement.

HCT. Overall, mean HCT at hospital discharge was 25% lower than at admission (discharge HCT = $30.8\% \pm 4.2\%$, range = 20.1% to 51.8%; admission HCT = $39.8\% \pm 4.8\%$, range = 28.0% to 54.4%). The IHCT had a mean of $29.7\% \pm 4.7\%$ and a range of 13.0% to 47.0%. "Medium" IHCT (25% to 33%) was found in 70% ($n = 1544$) of patients, "low" ($\leq 24\%$) in 11% ($n = 248$), and "high" ($> 34\%$) in 19% ($n = 410$). Patients having a high IHCT were likely to have had higher HCT values at both hospital admission and discharge than patients with either low or medium HCT values (Fig. 1). IHCT decreased an average of 16 points from baseline hospital admission values in patients with low IHCT, versus 10 and 6 points in patients with medium and high IHCTs, respectively.

Association between HCT and preoperative variables. Demographic characteristics and medical history for the three IHCT groups are presented in Table I. Patients undergoing reoperation were more likely to have a high IHCT, and patients with a history of anemia, a low IHCT (Table I). Patients in the low IHCT group had a smaller body surface area and a lower mean weight (high IHCT: 81.2 ± 17.8 kg; medium IHCT: 80.7 ± 15.6 kg; low IHCT: 75.9 ± 13.7 kg; $p < 0.001$, high vs low). Other preoperative clinical characteristics were similar among the three groups.

Table II. Volumes of fluid administered, percent of patients given an intraoperative and/or postoperative transfusion, and amount of chest tube drainage in the three IHCT groups

IHCT	Intraoperative			Intensive care unit			Day of operation
	Crystalloid or colloid (ml)	Packed RBCs and whole blood	Platelets	Packed RBCs and whole blood	Platelets	FFP and cryoprecipitate	
	(mean, SD; median)	% (n)	% (n)	% (n)	% (n)	% (n)	
HCT $\leq$ 24% (n = 248)	3084 $\pm$ 1476 (2715)	50.0 (124)	23.0 (57)	20.2 (50)	66.9 (166)	23.0 (57)	774 $\pm$ 534 (620)
HCT 25%-33% (n = 1544)	2995 $\pm$ 1550 (2800)	51.6 (797)	15.9 (246)	12.0 (185)	48.0 (741)	14.3 (221)	673 $\pm$ 556 (542)
HCT $\geq$ 34% (n = 410)	2654 $\pm$ 1699 (2500)	49.5 (203)	14.4 (59)	10.5 (43)	32.2 (132)	13.4 (55)	638 $\pm$ 541 (545)
p Value	0.01	0.71	0.01	0.001	<0.001	0.001	0.008

IHCT, Hematocrit value on entry into the intensive care unit; RBCs, red blood cells; FFP, fresh frozen plasma.

Table III. Rates of adverse ischemic outcome in the whole study population sample and in high-risk subgroups stratified by IHCT group

	Whole study population			p Value	Unstable angina			p Value	Emergency CABG			p Value	Redo CABG			p Value
	$\leq$ 24%	25%-33%	$\geq$ 34%		$\leq$ 24%	25%-33%	$\geq$ 34%		$\leq$ 24%	25%-33%	$\geq$ 34%		$\leq$ 24%	25%-33%	$\geq$ 34%	
	No.	No.	No.		No.	No.	No.		No.	No.	No.		No.	No.	No.	
No.	248	1544	410		109	695	193		47	333	96		23	185	64	
Q-wave MI; % (n)	3.6 (9)	5.5 (85)	8.3 (34)	.03	5.5 (6)	6.6 (46)	10.4 (20)	.16	4.3 (2)	5.1 (17)	7.3 (7)	.66	4.4 (1)	6.5 (12)	14.1 (9)	.13
Severe LV dysfunc- tion; % (n)	5.7 (14)	7.4 (114)	11.7 (48)	.006	6.4 (7)	9.8 (68)	17.1 (33)	.004	12.8 (6)	15.6 (53)	18.8 (18)	.63	21.7 (5)	21.6 (40)	32.8 (21)	.19
All cause mortality; % (n)	5.2 (13)	2.6 (40)	5.6 (23)	0.003	3.7 (4)	3.3 (23)	10.4 (20)	<.001	6.4 (3)	3.6 (12)	10.4 (10)	.03	13.0 (3)	5.9 (11)	14.1 (9)	.09

IHCT, Hematocrit value on entry into the intensive care unit; CABG, coronary artery bypass grafting; MI, myocardial infarction; LV, left ventricular.

Association between HCT and transfusion variables. Differences in HCT level from admission to ICU entry were not explained by intraoperative RBC transfusion (Table II). The percentage of patients who received either platelets or fresh frozen plasma was higher in the low IHCT group. Among those who did receive hemostatic products, the median number of units used was not different (8 units of platelets per recipient for all IHCT groups, $p = 0.55$) (fresh frozen plasma low IHCT = 4 units; median IHCT = 2 units; high IHCT = 2 units, $p = 0.15$). Intraoperative crystalloid and colloid administration showed a statistically significant difference (Table II), with the low IHCT group receiving more, but the difference between the low and high IHCT groups of 430 ml is clinically insignificant. Mean chest tube drainage (Table II) was greatest in the low IHCT groups but, again, was not of clinical significance (136 ml difference between low IHCT

and high IHCT). However, a higher proportion of patients with low IHCT had chest tube drainages exceeding 1500 ml on the day of the operation (high IHCT = 3.4%; median IHCT = 5.0%; low IHCT = 8.5%, $p = 0.02$).

Intraoperative hypertension occurred more often in the low IHCT group, but no differences occurred in postoperative hemodynamics, catecholamine therapy, or vasodilators.

Postoperatively, patients with low IHCT were most likely to receive RBC transfusion. Patients who received non-RBC transfusion in the operating room were more likely to receive a transfusion in the ICU. The proportion of patients returning to the operating room for hemorrhage did not differ between groups (low: 3%; medium: 3%; high: 1%; $p = 0.23$).

Association of IHCT with adverse outcome. Postoperative adverse events differed between the IHCT

Table IV. Effect of IHCT group on risk of MI after adjustment for single variables

Adjusted variable	IHCT $\leq 24\%$; odds ratio	IHCT 25%-33%; odds ratio (95% CI)	IHCT $\geq 34\%$; odds ratio (95% CI)
None	1.00	1.55 (0.77-3.12)	2.40 (1.13-5.10)
Prior history of MI	1.00	1.52 (0.74-3.03)	2.40 (1.13-5.10)
Recent MI	1.00	1.52 (0.75-3.06)	2.42 (1.14-5.13)
Gender	1.00	1.56 (0.77-3.14)	2.41 (1.13-5.11)
History of unstable angina	1.00	1.71 (0.82-3.58)	2.69 (1.23-5.93)
History of angina	1.00	1.71 (0.82-3.57)	2.67 (1.21-5.87)
History of CHF	1.00	1.53 (0.76-3.08)	2.45 (1.16-5.21)
New York Heart Classification >3	1.00	1.55 (0.77-3.11)	2.40 (1.13-5.09)
History of smoking	1.00	1.51 (0.75-3.05)	2.24 (1.05-4.76)
Prior PTCA	1.00	1.54 (0.76-3.10)	2.38 (1.12-5.04)
History of diabetes	1.00	1.55 (0.77-3.12)	2.41 (1.13-5.11)
Age	1.00	1.53 (0.76-3.09)	2.44 (1.15-5.17)
Age >70 yr	1.00	1.53 (0.76-3.09)	2.43 (1.15-5.17)
Reoperation CABG	1.00	1.53 (0.76-3.08)	2.34 (1.10-4.97)
≥ 3 Vessels bypassed	1.00	1.55 (0.77-3.12)	2.40 (1.12-5.09)
Left main disease	1.00	1.55 (0.77-3.12)	2.41 (1.13-5.11)
Low ejection fraction ($\leq 30\%$)	1.00	1.49 (0.70-3.15)	2.12 (0.93-4.80)
CPB time	1.00	1.56 (0.77-3.13)	2.42 (1.14-5.13)
CPB time ≥ 120 min	1.00	1.56 (0.77-3.14)	2.41 (1.14-5.12)

IHCT, Hematocrit value on entry into the intensive care unit; MI, Q-wave myocardial infarction; CHF, congestive heart failure; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass. Note: No difference in odds ratios testing different covariates as compared with the model using none.

groups (Table III). Rates of Q-wave MI and severe left ventricular failure were lowest in patients with low IHCT and significantly higher in those with high IHCT ($p = 0.03$). Rates of postoperative central nervous system dysfunction and renal failure did not differ between groups: central nervous system dysfunction: high IHCT = 4.4%, medium = 3.5%, low = 4.4% ($p = 0.59$); renal failure: high IHCT = 6.6%, medium = 5.4%, low = 7.7% ($p = 0.29$). In the whole sample, mortality rates were similar in the low and high IHCT groups. However, high-risk patients tended toward increased all-cause mortality in the high IHCT group (high = 8.6%, medium = 3.2%, low = 4.5%, $p < 0.001$). In patients with a history of unstable angina, high IHCT was associated with a threefold increase in mortality.

Fig. 2 demonstrates the rates of individual and combined ischemic adverse outcomes in patients stratified by IHCT. In every category of adverse outcome other than death, patients with high IHCT had a greater risk. No other measures of HCT (admission, lowest and highest postoperative, or discharge values) were associated with any adverse outcomes.

Confounding by intraoperative events. To determine whether high IHCT was a surrogate marker for intraoperative morbidity, and thus directly associated with outcome (e.g., patients who were in

more clinically unstable condition after bypass may have been more likely to receive a transfusion and thus fall into the high IHCT group and, as well, have more adverse ischemic outcomes), we examined the association between IHCT, postbypass morbidity, adverse ischemic outcome, and the use of RBC transfusion therapy. As expected, patients who had a low cardiac index (<1.5 L/min), hypotension, or who received three or more inotropic drugs during the immediate postbypass period were more likely to have an adverse outcome. However, the frequencies of these clinical variables were equally distributed between the IHCT groups (Table I) and they were not independent predictors.

Multivariate analyses. Institution did not confound the relationship between level of IHCT and risk of MI. Logistic regression models of Q-wave MI risk in each IHCT group with covariates showed that none demonstrated different odds ratios (Table IV). Our final stepwise regression model (Table V) showed that IHCT was the most important predictor of Q-wave MI. Patients with high IHCT were more than twice as likely to have a Q-wave MI as patients with low IHCT ($p = 0.04$) and 1.4 times more likely than patients with a medium IHCT ($p = 0.31$). In additional models including intraoperative variables such as (1) RBC transfusion requirements (2) postbypass signs of hemodynamic instability (e.g., hypo-

Table V. Final stepwise logistic regression model odds ratios (OR) and 95% confidence intervals (CI) for prediction of postoperative Q-wave MI

Variables in model	OR (95% CI)	p Value
IHCT group		
≤24%	1	
24%-33%	1.44 (0.71-2.92)	0.31
≥34%	2.22 (1.04-4.76)	0.04
Age (yr)		
<60	1.00	
60-70	1.33 (0.83-2.14)	0.24
>70	1.61 (0.98-2.64)	0.06
Sex		
Male	1.00	
Female	1.38 (0.90-2.11)	0.14
History of MI		
No	1.00	
Yes	1.88 (1.27-2.8)	0.002
History of smoking		
No	1.00	
Yes	1.65 (1.06-2.6)	0.03
Reoperation		
CABG		
No	1.00	
Yes	1.35 (0.83-2.21)	0.23

OR, Odds ratio; CI, confidence intervals; MI, myocardial infarction; IHCT, hematocrit value on entry into the intensive care unit; CABG, coronary artery bypass grafting.

tension, low cardiac index), and (3) site, the magnitude and significance of these odds ratios for IHCT did not change.

Discussion

Patients and adverse events. Our results demonstrate that IHCT level after CABG is significantly related to adverse outcome. In multivariate analysis that examined a wide variety of possible predictors, IHCT was the most significant independent predictor of Q-wave MI. This finding suggests that anemia is well tolerated with respect to MI.

Confounding variables. The finding that low IHCT was associated with fewer ischemic events was unexpected. Therefore it was of paramount importance that confounding variables be examined. Transfusion and fluid administration were not greatly different between groups, and no independent relationship was detected between transfusion or fluid administration and MI. Although crystalloid fluid administration did statistically differ between low and high IHCT groups, the difference in volume (430 ml) was not clinically important. Although lower IHCT did appear to affect the use of hemostatic components and to be associated with increased bleeding, no relationship was identified

Fig. 2. Frequency of Q-wave MI, severe left ventricular dysfunction (intraaortic balloon pump use), all-cause mortality, and combined (all three) adverse ischemic outcome by the IHCT group. Low, HCT ≤24%; Medium, HCT 25% to 33%; High, HCT ≥34%.

between the use of these blood components and MI rates. Decreasing the value of the cut point for low HCT below or above 24% did not alter our findings.

If more severely ill patients (preoperatively or intraoperatively) were preferentially maintained at a higher IHCT (e.g., through transfusion, hemoconcentration, fluid restriction), then the association between high IHCT and adverse outcome could be easily explained. Therefore we examined whether patients with clinical signs of postbypass morbidity (low cardiac index, hypotension, hypertension, tachycardia, ischemia, or requirement for inotropic medications or intravenous nitroglycerin) were more likely to have higher IHCT levels. These seriously ill patients were equally distributed among the three IHCT groups. Thus perioperative morbidity was not a confounder.

Limitations. Limitations of our study include the definition of outcome. New Q waves were chosen as a very strict and exclusive definition of MI. If other, perhaps more liberal definitions of MI (e.g., creatine kinase MB, troponin, myoglobin, or echocardiographic findings) had been used, the frequency of these events by IHCT group may well have been different. No association was found between IHCT and other ischemic adverse outcomes such as stroke and renal failure. In addition, our study did not examine fibrinolytic state, platelet number, or function, and HCT was examined at only five time points. More HCT values with extensive hematologic correlates could potentially provide more information concerning cause and effect for the relationship found.

Prior work and potential causes. Prior research in animal models of anemia with both acute and

chronic coronary obstruction has been performed.²⁰⁻²² Ischemia occurs across a wide range of HCT values from 17% to 42.5%.²⁰⁻²² Previous case reports and single-center studies support our findings that anemia alone does not increase the risk of MI after CABG.¹ In two studies of eight and 224 patients, HCT levels did not affect myocardial lactate flux, a measure of ischemia.^{23,24} In a small study of 14 patients, the oxygen content of the coronary sinus did not change with either hemodilution (to 23%) or subsequent transfusion to 34%.²⁵ A case report of a patient with an HCT level of 5% described diffuse myocardial dysfunction, relieved with transfusion, but no postoperative MI.² In our study, even in patients with IHCT levels between 13% and 18% ($n = 13$), no Q-wave MI or ventricular dysfunction occurred, nor were there any deaths.

Perioperative MI and dysfunction are likely the result of multiple causes.⁹ An increased IHCT level may precipitate ischemic injury via several mechanisms: (1) Increased blood viscosity may require additional work by the myocardium, as well as decreasing tissue oxygen delivery.¹⁶ (2) Shear forces between the vessel walls and the blood increase as the concentration of red blood cells increases. In addition, platelets exposed to these greater shear forces are more likely to be activated, and increased lateral platelet migration exists.²⁶ Therefore the number of interactions per unit time between platelets and the endothelial walls increases.²⁷ These interactions between altered endothelium and activated platelets may be important.²⁸ (3) With increased IHCT, the availability of nitric oxide, an inhibitor of platelet and neutrophil binding to endothelial cells,²⁹ may be decreased. (4) Liberated hemoglobin taken up by endothelial cells increases free radical production,³⁰ perhaps worsening endothelial dysfunction.

In conclusion, on the basis of this study of 2202 patients, low IHCT (<24%) at the conclusion of CABG operations appears to protect against Q-wave MI. Therefore our data do not support arbitrary transfusion of RBC products to increase oxygen-carrying capacity after CABG. Furthermore, allowing a low IHCT to occur after CABG might decrease the morbidity and cost associated with transfusion and also preserve a scarce resource (allogeneic blood). Future randomized prospective trials will be required to discover the mechanisms involved, as well as to examine associations between IHCT and creatine kinase MB or ischemia by ST-T wave analysis.

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Appendix 1

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Appendix 2

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