Invited Commentary

Optimal Transfusion Trigger in Surgical Patients With Coronary Artery Disease

Steven M. Frank, MD; Aslam Ejaz, MD, MPH; Timothy M. Pawlik, MD, MPH, PhD

Among patients with known coronary artery disease (CAD), the ideal transfusion trigger based on nadir hemoglobin is still unclear. Three of the largest randomized clinical trials on transfusion triggers and perioperative outcomes were performed among cardiac patients undergoing cardiac surgery,[1-3] a clinical scenario that is very different from cardiac patients undergoing noncardiac surgery. In fact, other than 2 very small pilot studies in patients with myocardial infarction (MI) who were randomized to higher or lower transfusion triggers—one supporting a liberal[4] and the other a restrictive[5] transfusion strategy—the ideal hemoglobin trigger in the setting of MI (perioperative or nonperioperative) is unknown. The best evidence to date for the ideal transfusion trigger in noncardiac surgery is from the FOCUS Trial, which showed no benefit for any of the measured outcomes when a transfusion trigger of 10 g/dL (to convert to grams per liter, multiply by 10) was compared with a trigger of 8 g/dL among a cohort of elderly patients with a high incidence of CAD undergoing orthopedic procedures.[6] Furthermore, a large retrospective study reported that postoperative transfusions after noncardiac surgery were associated with increased adverse postoperative outcomes, with the exception of postoperative MI.[7]

Related article

Hollis and colleagues[8] reported that, among patients who experienced a postoperative MI (3.7%), those with a nadir hematocrit (Hct) of between 20% and 24% had a lower mortality rate when they received a red blood cell transfusion. For patients with a nadir Hct of more than 24%, there was no benefit of blood transfusion. Furthermore, for patients who did not experience an MI (96.3%), red blood cell transfusion did not confer benefit or harm when the nadir Hct was of 20% to 27%; however, mortality was increased with transfusion when nadir Hct was of 27% to 30%.

These findings hint at the need for a slightly higher transfusion threshold among patients with known CAD. As with all retrospective studies, confounding by indication is a potential weakness as patients receiving transfusion are often invariably sicker and undergo bigger operations compared with nontransfused patients. The use of propensity score matching did help to mitigate potential selection bias for transfusion. Given the scant evidence supporting an ideal transfusion trigger in patients with MI, among surgical patients, the authors' findings are novel and important. Future prospective studies should assess the impact of both transfusion triggers and targets, particularly among at-risk patients with known CAD.

The central tenet of any patient blood management program is: give the right product at the right dose to the right patient for the right reason and at the right time. Transfusion is good when you need it, and bad when you do not. The ultimate challenge in perioperative medicine is differentiating between these 2 scenarios. While future prospective studies are necessary, the study by Hollis and colleagues[8] helps begin to shed light on this important clinical challenge.

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Original Investigation | ASSOCIATION OF VA SURGEONS

Blood Transfusion and 30-Day Mortality in Patients With Coronary Artery Disease and Anemia Following Noncardiac Surgery

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IMPORTANCE Although liberal blood transfusion thresholds have not been beneficial following noncardiac surgery, it is unclear whether higher thresholds are appropriate for patients who develop postoperative myocardial infarction (MI).

OBJECTIVE To evaluate the association between postoperative blood transfusion and mortality in patients with coronary artery disease and postoperative MI following noncardiac surgery.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study involving Veterans Affairs facilities from January 1, 2000, to December 31, 2012. A total of 7361 patients with coronary artery disease who underwent inpatient noncardiac surgery and had a nadir postoperative hematocrit between 20% and 30%. Patients with significant bleeding, including any preoperative blood transfusion or transfusion of greater than 4 units during the intraoperative or postoperative setting, were excluded. Mortality rates were compared using both logistic regression and propensity score matching. Patients were stratified by postoperative nadir hematocrit and the presence of postoperative MI.

EXPOSURE Initial postoperative blood transfusion.

MAIN OUTCOMES AND MEASURES The 30-day postoperative mortality rate.

RESULTS Of the 7361 patients, 2027 patients (27.5%) received at least 1 postoperative blood transfusion. Postoperative mortality occurred in 267 (3.6%), and MI occurred in 271 (3.7%). Among the 5334 patients without postoperative blood transfusion, lower nadir hematocrit was associated with an increased risk for mortality (hematocrit of 20% to <24%: 7.3%; 24% to <27%: 3.7%; and 27% to 30%: 1.6%; $P < .01$). In patients with postoperative MI, blood transfusion was associated with lower mortality, for those with hematocrit of 20% to 24% (odds ratio, 0.28; 95% CI, 0.13-0.64). In patients without postoperative MI, transfusion was associated with significantly higher mortality for those with hematocrit of 27% to 30% (odds ratio, 3.21; 95% CI, 1.85-5.60).

CONCLUSIONS AND RELEVANCE These findings support a restrictive postoperative transfusion strategy in patients with stable coronary artery disease following noncardiac surgery. However, interventional studies are needed to evaluate the use of a more liberal transfusion strategy in patients who develop postoperative MI.

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Invited Commentary

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Perioperative anemia is associated with an increased risk for mortality among patients undergoing noncardiac surgery.[1-4] In patients with a history of cardiovascular disease, the risk for mortality with perioperative anemia is amplified.[5] Blood transfusion offers the most immediate therapy for anemia. However, liberal transfusion strategies that use a hemoglobin transfusion threshold of 9 to 10 g/dL (to convert to grams per liter, multiply by 10.0) have not been associated with improved mortality compared with restrictive transfusion strategies that use a hemoglobin transfusion threshold of 7 to 8 g/dL in various hospitalized patient populations.[6-10]

Prior studies of patients with cardiovascular disease undergoing surgery have shown similar outcomes with liberal and restrictive transfusion strategies. In patients undergoing hip surgery with risk factors or a history of cardiovascular disease, there was no significant difference in mortality or functional outcomes using a hemoglobin transfusion trigger of 8 vs 10 g/dL.[11] In a trial of patients undergoing cardiac surgery, there was no significant difference in a composite outcome of infection or ischemic events using a hemoglobin transfusion trigger of 7.5 vs 9 g/dL; however, analysis of secondary end points suggested higher rates of 90-day mortality with the lower hemoglobin trigger.[12] Importantly, these studies did not address differences with transfusions in patients who developed myocardial infarction (MI) in the postoperative period. Multiple studies have evaluated the role of blood transfusion in patients presenting with acute coronary syndrome and, to our knowledge, no clear consensus has been made regarding the appropriate hematocrit transfusion trigger.[13-15] Variation in hospital transfusion thresholds highlights the uncertainty of appropriate transfusion practices in patients with unstable coronary artery disease (CAD).[16,17] Whether restrictive or lower transfusion thresholds are generalizable for postoperative patients who develop postoperative MI is not clear.

To better determine the role of postoperative blood transfusions in patients with CAD and postoperative MI following noncardiac surgery, we examined the rates of mortality in patients based on receipt of blood transfusion and stratified by whether they developed postoperative MI. We hypothesized that postoperative blood transfusion would be associated with improved mortality rates at higher hematocrit values in patients with postoperative MI.

Methods

Study Population

We performed a retrospective cohort study of a sample of patients with a history of CAD who subsequently underwent noncardiac surgery from January 1, 2000, to December 31, 2012, at Veterans Affairs (VA) medical centers. The full details of the formation of this cohort have been described previously.[18] Briefly, all patients who underwent noncardiac surgery within 2 years after coronary stent placement at VA medical centers were identified and this population was then matched by surgical and cardiovascular disease risk factors to patients without coronary stents but with a history of CAD identified using *International Classification of Diseases, Ninth Revision* codes (410.xx, 411.xx, 412.xx, 414.xx, 429.2x, v4581, or 492.2x). Data for this study came from the VA Clinical Assessment Reporting and Tracking Program, VA Medical SAS data sets, and VA Surgical Quality and Improvement Program. The study was approved and granted waiver of consent by the local institutional review boards of the Birmingham VA Hospital, the VA Boston Healthcare System, and the VA Eastern Colorado Health System.

To identify patients with a potential exposure to blood transfusion, we limited the cohort to inpatient surgical procedures with signs of postoperative anemia defined as a nadir postoperative hematocrit of 30% or less (to convert to proportion of 1.0, multiply by 0.01). Because guidelines support consideration of blood transfusion in patients with preexisting cardiovascular disease with hematocrit of less than 20%, these patients were excluded from the study.[14] Given the possibility of major hemorrhage resulting in postoperative MI, we also excluded patients with signs of significant bleeding including any preoperative blood transfusion, intraoperative blood transfusion greater than 4 units, or blood transfusion greater than 4 units in the 72 hours following surgery.[19]

Study Variables

Our independent variable of interest was the initial postoperative blood transfusion identified using *International Classification of Diseases, Ninth Revision* procedure code 99.04 and the Healthcare Common Procedure Coding System codes P9016, P9021, P9022, P9038, P9039, and P9040. Our primary outcome was 30-day mortality rate identified in VA Vital Status file. Patients were considered to have postoperative MI if they had a diagnosis of MI identified by *International Classification of Diseases, Ninth Revision* code 410.xx in the VA Medical SAS data set or by VA Surgical Quality and Improvement Program nurse-abstracted MI during the 30 days after the index surgery. Patients were stratified by nadir postoperative hematocrit defined as the lowest-occurring hematocrit in the postoperative period or the lowest hematocrit preceding the initial blood transfusion. Hematocrit values were obtained through the Corporate Data Warehouse and supplemented with nurse-abstracted VA Surgical Quality and Improvement Program hematocrit values. The method for calculating revised cardiac risk index (CRI) has been previously defined.[20] High-risk surgery was excluded as a component of CRI to prevent procedure bias of CRI stratification. Intraoperative blood loss was calculated based on preoperative hematocrit, postoperative hematocrit, and number of intraoperative transfusions, as described elsewhere.[21] Race/ethnicity was unavailable for 200 patients (2.7%) and was coded as missing in these cases.

Statistical Analysis

Bivariate frequency comparisons were made using χ^2 tests. Change in average pretransfusion nadir hematocrit over time and the risk for mortality by nadir hematocrit were analyzed using linear regression. Logistic regression was used to adjust for confounding in patients receiving and not receiving postoperative blood transfusion. We initially included clinically rel-

evant covariates including age, race/ethnicity, history of smoking, recent MI, history of coronary stent, CRI, procedure type, relative value unit, high-risk surgery, calculated intraoperative blood loss, units of intraoperative blood transfused, emergent surgery status, operative time, preoperative hematocrit, and fiscal year of surgery. Because we were interested in whether the association between transfusion and mortality varied by the nadir hematocrit category and by the occurrence of postoperative MI, we included interactions between transfusion and nadir hematocrit category, as well as between transfusion and postoperative MI. Model selection was performed with backward-stepwise selection using $P \leq .10$ for inclusion. Because pretransfusion nadir hematocrit significantly varied by fiscal year, fiscal year was forced into the model. Model selection excluded relative value unit, high-risk surgery, and operative time as covariates. Estimates from the parsimonious model are reported. We further tested the full nonparsimonious model in our analysis and found similar results.

As an additional analysis, we performed propensity score matching for the likelihood of receiving a postoperative blood transfusion. The propensity score model included 23 variables (eTable 1 in the Supplement). Patients were matched 1:1 on propensity score using nearest-neighbor methods with caliper of 0.2 SDs. Because we were interested in the association of transfusions with outcomes across specific strata, the overall matching algorithm included exact matching by nadir hematocrit categories and for CRI. Nadir hematocrit categories included 20% to less than 24%, 24% to less than 27%, and 27% to 30%. To examine differences between patients who had postoperative MI, we produced new propensity score models for each stratum and included exact matching by nadir hematocrit category. Covariates were considered balanced if standardized mean differences were less than 0.2. Odds ratios in propensity score–matched groups were calculated using generalized estimating equations to adjust for clustering in matched pairs.[22] Fifteen patients had missing preoperative hematocrit values and were excluded in the regression and propensity score analysis.

All tests were 2-tailed with $\alpha = .05$. Statistical analysis was completed using SAS software (SAS Institute Inc). R package ggplot2 was used to produce smooth plots with LOESS.[23] Propensity score matching was performed using R package Matchit.[24]

Results

Of 28 173 patients with preexisting CAD undergoing noncardiac surgery during the study, 7361 (26.1%) met inclusion criteria (eFigure 1 in the Supplement). At least 1 postoperative blood transfusion was given in 2027 patients (27.5%). Thirty-day mortality occurred in 267 (3.6%), and 30-day MI occurred in 271 (3.7%). The characteristics of patients with and without postoperative blood transfusion are shown in **Table 1**. Coronary stents were present in 35.7% of patients, and stented patients had similar rates of postoperative blood transfusion compared with patients without coronary stents (28.8% vs 26.8%; $P = .06$).

Table 1. Characteristics of Patients With and Without Postoperative Blood Transfusion

Characteristic	No. (%)		*P* Value
	No Transfusion (n = 5334)	Transfusion (n = 2027)	
Demographics			
Age, y			
<60	1106 (74.4)	360 (24.6)	<.01
≥60	4228 (71.7)	1667 (28.3)	
Race/ethnicity			
White	4408 (72.4)	1681 (27.6)	.79
Black	731 (72.7)	274 (27.3)	
Other	49 (69.0)	22 (31.0)	
Sex			
Male	5202 (72.5)	1971 (27.5)	.48
Female	132 (70.2)	56 (29.8)	
Smoke			
Yes	1818 (72.6)	685 (27.4)	.81
No	3516 (72.4)	1342 (27.6)	
Anemia			
Preoperative hematocrit, %			
<24	22 (44.9)	27 (55.1)	<.01
24-<30	574 (65.3)	305 (34.7)	
30-36	1778 (72.4)	676 (27.5)	
>36	2949 (74.4)	1016 (25.6)	
Nadir postoperative hematocrit, %			
20-<24	712 (50.9)	686 (49.1)	<.01
24-<27	1795 (67.1)	881 (32.9)	
27-30	2827 (86.0)	460 (14.0)	
Comorbidities			
Cardiac stent			
None	3466 (73.2)	1270 (26.8)	.31
BMS	1055 (71.1)	429 (28.9)	
DES	793 (71.2)	321 (28.8)	
Both	20 (74.1)	7 (25.9)	
Cardiac risk index			
1	2960 (73.5)	1067 (26.5)	.06
2	1691 (71.6)	670 (28.4)	
≥3	683 (70.2)	290 (29.8)	
MI within 6 mo			
Yes	688 (72.0)	268 (28.0)	.71
No	4646 (72.5)	1759 (27.5)	
CVA within 1 y			
Yes	238 (73.5)	86 (26.5)	.68
No	5096 (72.4)	1941 (27.6)	
CHF within 2 y			
Yes	1404 (69.6)	1414 (30.4)	<.01
No	3930 (73.5)	1414 (26.5)	
Diabetes mellitus with insulin			
Yes	1102 (72.8)	412 (27.2)	.75
No	4232 (72.4)	1615 (27.6)	
Creatinine >2 mg/dL			
Yes	473 (69.0)	212 (31.0)	.04
No	4861 (72.8)	1815 (27.2)	
Liver disease			
Yes	333 (70.8)	137 (29.1)	.42
No	5001 (72.6)	1890 (27.4)	

(continued)

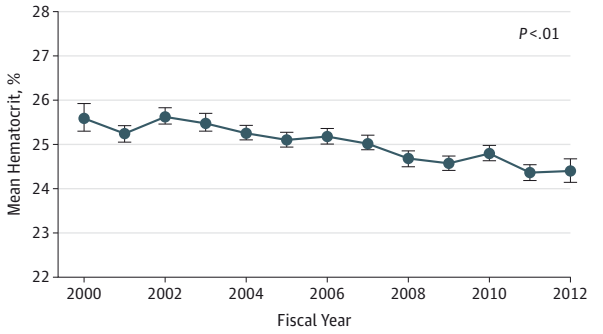
Table 1. Characteristics of Patients With and Without Postoperative Blood Transfusion (continued)

Characteristic	No. (%) No Transfusion (n = 5334)	No. (%) Transfusion (n = 2027)	*P* Value
Cancer related			
Yes	954 (73.8)	338 (26.2)	.22
No	4380 (72.2)	1689 (27.8)	
Operative Characteristics			
Operative time, h			
<2	1856 (73.3)	676 (26.7)	<.01
2-4	2362 (73.9)	835 (26.1)	
>4	1116 (68.4)	516 (31.6)	
Work RVU			
<10	442 (73.5)	159 (26.5)	<.01
10-20	1921 (75.6)	619 (24.4)	
>20	2971 (70.4)	1249 (29.6)	
Operation type			
Skin/eye/ear	76 (80.8)	18 (19.1)	<.01
Nervous	130 (82.8)	27 (17.2)	
Genital/urinary	401 (71.5)	160 (28.5)	
Musculoskeletal	1371 (67.1)	672 (32.9)	
Digestive	1077 (74.9)	360 (25.0)	
Vascular	1938 (73.9)	684 (26.1)	
Respiratory	282 (77.0)	84 (22.9)	
Other	59 (72.8)	22 (27.2)	
Classification			
Emergent	458 (68.4)	212 (31.6)	.01
Nonemergent	4876 (72.9)	1815 (27.1)	
High risk			
Yes	1668 (72.2)	643 (27.8)	.70
No	3666 (72.6)	1384 (27.4)	
Blood loss, mL			
<250	2491 (77.1)	742 (22.9)	<.01
250-<500	2120 (73.3)	772 (26.7)	
500-750	457 (64.0)	257 (36.0)	
>750	266 (51.0)	256 (49.0)	
Intraoperative transfusion, units			
≥2	429 (55.4)	345 (44.6)	<.01
<2	4905 (74.5)	1682 (25.5)	

Abbreviations: BMS, bare metal stent; CHF, congestive heart failure; CVA, cerebral vascular accident; DES, drug-eluting stent; MI, myocardial infarction; RVU, relative value unit.

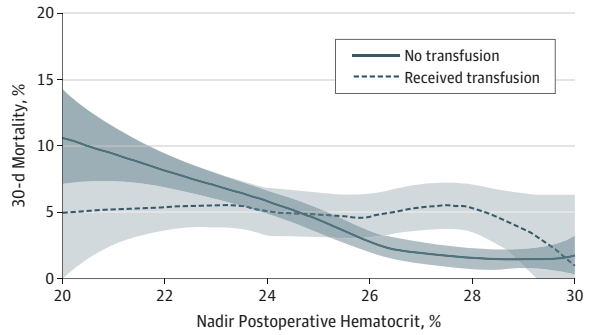
SI conversion factor: To convert creatinine to micromoles per liter, multiply by 88.4.

Figure 1. Mean Hematocrit Preceding Transfusion Over Time



Mean nadir hematocrit preceding blood transfusion across time. The error bars represent standard errors.

Figure 2. 30-Day Mortality Rate by Nadir Postoperative Hematocrit in Patients With and Without Postoperative Blood Transfusion



The solid and dashed lines represent estimated rates and the shaded areas represent 95% CIs.

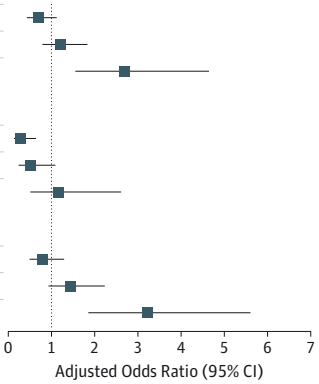
We examined the secular trend of nadir hematocrit values preceding transfusion over our study period. Mean nadir hematocrit prior to transfusion significantly decreased from 25.6% in 2000 to 24.4% in 2012 ($P < .01$) (**Figure 1**). A plot of unadjusted 30-day mortality by receipt of transfusion is displayed in **Figure 2**. Patients who did not receive a transfusion showed a linear increase in mortality with decreasing postoperative hematocrit ($P < .01$). Receiving a blood transfusion at higher hematocrit values was associated with increased mortality.

After adjustment for patient and procedure factors, different trends in mortality were observed in patients with and without transfusion across nadir hematocrit categories (**Figure 3**). The final model obtained a *c* statistic of 0.831. In general, transfusion with nadir hematocrit of 20% to 24% was associated with lower mortality compared with no transfusion, and as nadir hematocrit increased, transfusion was associated with increased rates of mortality. Among patients with a postoperative MI, transfusion was associated with significantly lower mortality, with nadir hematocrit of 20% to 24% (odds ratio [OR], 0.28; 95% CI, 0.13-0.64), but not with hematocrit of 24% to 27% (OR, 0.52; 95% CI, 0.24-1.09) or hematocrit of 27% to 30% (OR, 1.15; 95% CI, 0.51-2.61). In patients who did not have a postoperative MI, transfusion was not associated with mortality at a nadir hematocrit of 20% to 24% (OR, 0.80; 95% CI, 0.49-1.29) or 24% to 27% (OR, 1.44; 95% CI, 0.94-2.23) but significantly increased mortality with hematocrit of 27% to 30% (OR, 3.21; 95% CI, 1.85-5.60). Cardiac risk index and the presence of a coronary stent did not have a significant effect on the relationship between blood transfusion and mortality (data not shown).

As a sensitivity analysis, propensity score matching for likelihood of postoperative blood transfusion was performed for the overall cohort and separately for patients with and without postoperative MI. Patients who received a postoperative transfusion were successfully matched to a patient without

Figure 3. Multivariate Analysis of 30-Day Mortality Rates in Patients With and Without Transfusion

Value, %	30-d Mortality, No./Total No. (%) Transfusion	No Transfusion	Adjusted Odds Ratio (95% CI)
Overall			
Hct 20-<24	35/686 (5.1)	52/712 (7.3)	0.70 (0.43-1.12)
Hct 24-<27	43/881 (4.9)	67/1795 (3.7)	1.21 (0.79-1.83)
Hct 27-30	25/460 (5.4)	45/2827 (1.6)	2.68 (1.55-4.64)
MI			
Hct 20-<24	6/39 (15.4)	9/21 (42.9)	0.28 (0.13-0.64)
Hct 24-<27	9/57 (15.8)	16/62 (25.8)	0.52 (0.24-1.09)
Hct 27-30	5/29 (17.2)	5/63 (7.9)	1.15 (0.51-2.61)
No MI			
Hct 20-<24	29/647 (4.5)	43/691 (6.2)	0.80 (0.49-1.29)
Hct 24-<27	34/824 (4.1)	51/1733 (2.9)	1.44 (0.93-2.23)
Hct 27-30	20/431 (4.6)	40/2764 (1.5)	3.21 (1.85-5.60)



Results are presented from the overall cohort and stratified by occurrence of myocardial infarction (MI) in the postoperative period. HCT indicates hematocrit.

transfusion in 97.7% from the overall cohort, 70.4% from those with MI, and 98.7% from those without MI. Propensity score matching achieved improved balance of covariates (eTable 1, eTable 2, and eTable 3; eFigure 2, eFigure 3, and eFigure 4 in the Supplement). Mortality outcomes for each propensity score–matched group were similar to the findings from multivariate analysis: the mortality rate was significantly lower in patients with MI who received transfusion with nadir hematocrit of 20% to 24% (OR, 0.13; 95% CI, 0.02-0.72) but not with transfusions with nadir hematocrit of 24% to 27% (**Table 2**).

Table 2. 30-Day Mortality Rate in Propensity Matched Pairs From the Overall Cohort, Patients With Postoperative MI, and Patients Without Postoperative MI

Hematocrit, %	Mortality Rates, No./Total No. (%) Transfusion	No Transfusion	Odds Ratio (95% CI)[a]
Overall			
20-<24	32/660 (4.8)	46/660 (7.0)	0.68 (0.43-1.08)
24-<27	43/862 (5.0)	38/862 (4.4)	1.14 (0.73-1.78)
27-30	25/454 (5.5)	5/454 (1.1)	5.23 (1.97-13.9)
MI			
20-<24	2/19 (10.5)	9/19 (47.4)	0.13 (0.02-0.72)
24-<27	7/47 (14.9)	12/47 (25.5)	0.51 (0.20-1.32)
27-30	5/22 (22.7)	3/22 (13.6)	1.86 (0.42-8.30)
No MI			
20-<24	29/633 (4.6)	39/633 (6.2)	0.73 (0.44-1.21)
24-<27	34/815 (4.2)	26/815 (3.2)	1.32 (0.78-2.24)
27-30	20/427 (4.7)	11/427 (2.6)	1.86 (0.89-3.88)

Abbreviation: MI, myocardial infarction.

[a] Odds ratio of mortality with transfusion compared with no transfusion.

Discussion

In this study, we evaluated the association between postoperative blood transfusion and 30-day mortality in patients with CAD and MI following noncardiac surgery. One-quarter of patients with CAD had a postoperative hematocrit between 20% and 30%. In patients with no postoperative blood transfusion, lower nadir hematocrit values were associated with higher mortality. Overall, transfusions with nadir hematocrit of 27% to 30% were associated with higher mortality. Among postoperative patients with MI, transfusion was associated with lower mortality, with nadir hematocrit of 20% to 24%. These findings support a restrictive transfusion strategy in patients with stable CAD following noncardiac surgery; however, they suggest a potential role for higher hematocrit transfusion thresholds in patients with postoperative MI.

Several retrospective studies have supported the association of perioperative anemia and increased mortality.[1-5] However, the results from surgical trials have generally shown no overall differences with liberal vs restrictive transfusion strategies. Among 2016 patients undergoing hip surgery with a history of or risk factors for cardiovascular disease, similar outcomes for 30-day and 3-year mortality rates were observed using a hemoglobin transfusion trigger of 8 or 10g/dL.[11,25] In 2003 patients undergoing cardiac surgery who were randomized to a hemoglobin transfusion trigger of 7.5 vs 9 g/dL, no differences in ischemic events or serious infection were seen.[12] Analysis of secondary end points from this study suggested higher rates of 90-day mortality with the restrictive strategy; however, this could be attributed to spurious findings.[26] A smaller trial of 200 patients undergoing intraabdominal surgical oncology procedures did show higher rates of a composite 30-day mortality or severe complication when a lower transfusion trigger of 7 vs 9 g/dL was used.[27] Our findings support no benefit of postoperative blood transfusion in patients with stable CAD with nadir hematocrit of 27% to 30%.

To our knowledge, these results are the first to compare outcomes of blood transfusion in patients following surgery stratified by whether they had a postoperative MI. Retrospective studies have shown mixed evidence regarding the role of blood transfusion in patients with a diagnosis of acute coronary syndrome, and current guidelines are uncertain regard-

ing appropriate transfusion strategies for these patients.[13-15,28] Initial findings from a cohort of elderly patients with MI showed benefits with transfusion when the presenting hematocrit was less than 30%.[29] Follow-up studies have shown conflicting findings when analyzing the overall effect of blood transfusion in patients with acute coronary syndrome[16,17,30,31] or selective benefits when the hemoglobin level was less than 8 g/dL.[32] Two small pilot randomized trials of restrictive vs liberal transfusion strategies in patients with MI have shown opposite effects on composite adverse outcomes.[33,34] Our findings suggest that patients with MI in the postoperative setting may benefit from slightly higher transfusion thresholds.

Physician decision to administer blood transfusion is based on a multitude of clinical factors, and retrospective comparison of outcomes in patients with and without transfusion is subjected to unmeasured confounding.[28] However, when studies have created more appropriate comparison groups through stratifying patients by nadir hematocrit, an association between blood transfusion at low hematocrit levels and improved outcome has been shown.[17,21] The increased risk for blood transfusion at higher hematocrit levels may result as a risk-benefit trade-off.[35] Several mechanisms to explain the adverse effects of blood transfusions have been proposed including storage-related red blood cell changes, immunologic alterations, and potential prothrombotic effects.[36] These results have important implications for policies that seek to standardize blood transfusion practices and stress the importance of stratification by clinical scenario.

This study had several limitations. The generalizability of this study may be limited because it consisted of a VA population of mostly male patients. The cohort was a sample of patients with CAD undergoing surgery and may be weighted for having higher coronary disease burden. In addition, the sample size of patients with postoperative MI was limited. We could not account for the indication of the blood transfusion including whether the patient was symptomatic, and hematocrit transfusion thresholds may not readily translate to hemoglobin thresholds. We were limited in our ability to determine the temporal relationship between blood transfusion and MI. Previous studies have shown that most MI cases occur within 48 hours of surgery.[37] Because we did not limit to blood transfusions prior to the occurrence of MI, we were unable to determine whether postoperative blood transfusion is a risk factor for the development of MI. However, data from surgical trials have not suggested significant differences in MI rates based on transfusion strategy.[11,12,27] While we excluded patients with evidence of significant bleeding events, we could not account for the exact number of blood units administered in the postoperative period. The rate of MI may be underestimated by the occurrence of undocumented sudden fatal MI as a cause of death. Further, it is possible that patients with low hematocrit levels died before having a chance to receive a transfusion.

Conclusions

In patients with MI following noncardiac surgery, postoperative blood transfusion was associated with lower mortality when the hematocrit was 20% to 24%. In contrast, for patients with stable CAD, blood transfusion was associated with higher mortality, with nadir hematocrit of 27% to 30%. These findings support the benefits with restrictive transfusion strategies in patients with known CAD. In addition, intervention studies are needed to determine whether a higher hematocrit threshold in patients with postoperative MI is beneficial.

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Study concept and design: Hollis, McMurtrie, Holcomb, Hawn.
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