Impact of postoperative nadir hemoglobin and blood transfusion on outcomes after operations for atherosclerotic vascular disease

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Objective: Controversy surrounds the topic of transfusion policy after noncardiac operations. This study assessed the combined impact of postoperative nadir hemoglobin (nHb) levels and blood transfusion on adverse events after open surgical intervention in patients who undergo operative intervention for atherosclerotic vascular disease.

Methods: Consecutive patients who underwent peripheral arterial disease (PAD)-related operations were balanced on baseline characteristics by inverse weighting on propensity score calculated as their probability to have nHb greater than 10 gm/dL on the basis of operation type, demographics, and comorbidities, including the revised cardiac risk index. A multivariate generalized estimating equation analysis was performed to investigate associations between nHb, transfusion, and a composite outcome of perioperative death and myocardial infarction. Logistic and Cox proportional hazards regressions were used to assess the impact of nHb and transfusion on respiratory and wound complications; and a composite end point (CE) of death, myocardial infarction during a 2-year follow-up. Level of statistical significance was set at alpha of 0.0125 to adjust for the increased probability of type I error attributable to multiple comparisons.

Results: The analysis cohort included 880 patients (1074 operations). After adjusting for nHb level, the number of units transfused was not associated with the perioperative occurrence of the CE (odds ratio [OR], 1.13; $P = .025$). Adjusted for the number of units transfused, nHb had no impact on the perioperative CE (OR, 0.62; $P = .22$). An interaction term between transfusion and nHb level remained nonsignificant ($P = .312$), indicating that the impact of blood transfusion was the same regardless of the nHb level. Perioperative respiratory complications were more likely in patients receiving transfusions (OR, 1.22; $P = .009$), and perioperative wound infections were less common in patients with nHb >10 gm/dL (OR, 0.65; $P = .01$). During an average follow-up of 24 months, transfused patients were more likely to develop the CE (hazard ratio [HR], 1.15, $P = .009$), whereas nHb level did not impact the long-term adverse event rate (HR, 0.78; $P = .373$). The above associations persisted even after adjusting the Cox regression model for the occurrence of perioperative cardiac events.

Conclusions: Although nHb less than 10 gm/dL is not associated with death or ACS after PAD-related operations, maintaining nHb greater than 10 gm/dL appears to decrease the risk of wound infection. Blood transfusion is associated with increased risk of perioperative respiratory complications. Until a randomized trial settles this issue definitively, a restrictive transfusion strategy is justified in patients undergoing operations for atherosclerotic vascular disease. (J Vasc Surg 2013;57:1331-7.)

High demand for blood products has resulted in a fast increase in transfusion-related costs.[1-6] At the same time, blood transfusion-related morbidity accounts for approximately 17 billion in medical expenses annually.[7] Historically, the accepted clinical standard has been to transfuse patients when the hemoglobin (Hb) level drops below 10.0 gm/dL or the hematocrit falls below 30%. This "10/30 rule" was first proposed by Adams and Lundy in

1942 and served as red blood cell (RBC) transfusion guide for decades[6,8] under the premise that a minimal RBC mass is critical to avoid adverse cardiac events and death. Interestingly, this theoretical assumption has not been proven correct in practice, and blood transfusion has even been shown to be harmful. Large observational studies on this subject have been published analyzing findings in patients after myocardial infarction[9-13] and after a variety of noncardiac operative interventions,[14] but their results have been conflicting. Furthermore, randomized controlled trials[15-18] after coronary artery bypass, hip replacement, or in the context of acute myocardial infarction have indicated that a conservative strategy with a transfusion trigger at serum Hb of 8 gm/dL can be as safe as the liberal one that implies that a transfusion should be given when the serum Hb drops below 10 gm/dL.

Anemia has been shown to be present in up to 15% of patients presenting with acute coronary syndrome (ACS)[19] and is an important predictor of mortality in patients with heart failure and ischemic heart disease.[20] Ischemic heart disease is the leading cause of mortality in patients with atherosclerotic vascular disease (ASVD), accounting for

40% to 60% of deaths, and ACS is the most common complication after a ASVD-related vascular intervention.[21] Thus, patients with ASVD constitute an ideal initial cohort to assess the impact of transfusion strategies on cardiac events and mortality. However, relevant data are scarce. None of the large randomized controlled trials performed to date involved patients with peripheral arterial disease (PAD), and the only relevant study was too small to produce meaningful findings.[17] In this context, we designed this study to investigate associations between nadir postoperative Hb (nHb), blood transfusion, and outcomes after operations for ASVD.

METHODS

Patient population and data extraction. Using a retrospective cohort design, charts of consecutive patients who underwent elective operations for atherosclerotic vascular occlusive disease in a single institution were reviewed. We included patients who underwent carotid endarterectomy, open surgical reconstruction for aorto-iliac occlusive disease and infrainguinal occlusive disease, aneurysm repair (either open or endovascular) when this was associated with aorto-iliac occlusive disease, and amputations. Patients undergoing endovascular interventions only were excluded as these procedures are related with substantially less operative stress and blood loss than their open counterparts. Similarly, dialysis access and venous interventions were not included. Variables of interest were collected via review of charts located in the electronic medical record system. These included demographics, comorbidities, operative information, baseline and postoperative laboratory values, and outcomes. Baseline laboratory values were defined as the most recent value prior to the day of the operation. Perioperative period was defined as the time period starting from the day of the operation and ending on the 30th postoperative day.

Exposures of interest. The objective of the study was to assess the association between a postoperative nHb less than 10 gm/dL and postoperative outcomes. The choice of cutoff point was based on traditional clinical guidelines and was influenced by the fact that recent major randomized controlled trials on this subject have selected a similar cutoff as transfusion trigger for randomization purposes.[15,16,22] Blood transfusion was documented in units of packed red blood cells (PRBCs) transfused, intraoperatively and postoperatively, and was analyzed as a continuous variable. Since both nHb and units of blood transfused may change at any time during the perioperative period, we used in our analysis the value of these predictors prior to the occurrence of the event of interest. Consider for instance the hypothetical patient who has received 2 units PRBCs, develops ACS, and then receives 2 more units PRBCs at a later time. In modeling the contribution of blood transfusion as a predictor for ACS, we only take into consideration the 2 units transfused prior to ACS occurring. This approach was taken to capture the temporal effect between predictors and outcomes of interest and avoid bias introduced by practitioners who might have felt compelled

to more aggressively transfuse patients, particularly after a cardiac event.

Endpoints. The primary outcome was a composite "any vs none" end point (CE) of perioperative death and ACS. ACS was defined as (1) the presence of a new Q wave on electrocardiogram in diabetic patients, (2) the combination of elevated creatine kinase-MB or troponin I (at least twice of the upper normal limit) and chest pain, or (3) the combination of enzyme elevation and T wave inversion, left bundle branch block, ST segment depression of at least 1 mm, or new Q waves >40 ms in two contiguous leads as per recommendations of the American Heart Association.[23,24] The decision to use the specific CE was based on the clinical severity of the individual components, and the fact that sometime it is difficult to even distinguish between the two (for instance, the case in which a patient dies suddenly and it is uncertain whether ACS was the underlying cause).

Secondary outcomes included respiratory complications, wound complications, and a CE of midterm death and ACS. Respiratory complications included pneumonia (defined clinically with the development of fever and/or cough, and confirmed radiographically); unplanned reintubation; and prolonged ventilatory support (more than 48 hours after completion of the operation). Wound complications included wound infection (suspected clinically and confirmed with the presence of purulent discharge on exploration of positive wound culture) and wound dehiscence (defined as the presence of wound separation severe enough to justify either local wound care or wound exploration and formal closure). The time-to-event analysis for the midterm CE included information collected during a 2-year follow-up.

Statistical analysis. A propensity score was calculated as the probability of each patient to have postoperative nHb greater than 10 gm/dL. To calculate the propensity score, we fit a logistic regression model with nHb as a binary dependent variable (cutoff at 10 gm/dL). Predictors of this model included patient and operative characteristics that were thought to impact transfusion decisions and are listed in Table I. Propensity score was then included in the analysis models using the inverse-probability-weighting approach to adjust for baseline differences.

Primary end point. To analyze the binary composite outcome, we used a multivariate generalized estimating equation approach and calculated a distinct exposure effect for each of the components of the CE.[25] The average component-specific effect was then calculated and tested for the null hypothesis that the estimated log-odds equals zero.[25,26] Assessing the impact of each exposure (either nHb or transfusion) on the individual components of the end point using this approach minimized bias that could potentially occur because of different incidence rates of the individual components. Heterogeneity of treatment effects was evaluated performing an exposure-by-component interaction statistical significance test with the composite outcome being the dependent variable as previously described.[25] The model was adjusted for within patient

Table I. Distribution of variables used to calculate the propensity score between the groups and associated *P* value before and after propensity score matching

A, Categorical variables

	Group A (%)	Group B (%)	P value before PS	P value after PS
Aspirin	81	81	.896	.919
Statin	76	77	.768	.905
Plavix	23	12	.000	.936
Insulin	22	10	.000	.976
Beta blocker	69	62	.015	.963
ACE inhibitor	63	54	.004	.944
RCRI: II	33	37	.078	.927
RCRI: III	24	16	.000	.957
RCRI: IV	15	5	.000	.937
HTN	94	89	.006	.939
Hyperlipidemia	81	81	.886	.930
CAD	52	42	.002	.954
Renal history	25	12	.000	.835
DM	51	35	.000	.953
CHF	19	9	.000	.968
COPD	26	28	.371	.989
CVA	18	16	.333	.996
Smoking	86	86	.835	.957
ASA score 2	0	1	Ref	Ref
ASA score 3	57	70	.981	.980
ASA score 4	43	30	.980	.980
GETA	77	84	.003	.963
EVAR	17	26	Ref	Ref
AI occlusive open	6	6	.091	.982
Amputations	26	9	.000	.966
CEA	9	30	.000	.627
Infrainguinal open	41	27	.000	.988
Open AAA	1	2	.398	.930

B, Continuous variables

	Group A: mean (SD)	Group B: mean (SD)	P value before PS	P value after PS
Age	66.2 (8.5)	65.6 (8.3)	.294	.891
GFR	71.4 (31.6)	79.7 (25.8)	.000	.883
Albumin	3.3 (0.7)	3.6 (0.5)	.000	.814
BMI	26.2 (5.3)	26.9 (5.1)	.043	.851
Baseline Hb	-	-	-	-
Operative time	207.3 (139.5)	173.6 (96.4)	.000	.986
Operative blood loss	324.3 (368.9)	235.3 (265.2)	.000	.958
Crystalloids	1786.7 (1191.9)	1782.6 (1023.2)	-	-

AAA, Abdominal aortic aneurysm; *ACE,* angiotensin converting enzyme; *AI,* aortoiliac; *ASA,* American Society of Anesthesia; *BMI,* body mass index; *CAD,* coronary artery disease; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *CVA,* cerebrovascular accident; *DM,* diabetes mellitus; *EVAR,* endovascular aneurysm repair; *GETA,* general endotracheal anesthesia; *GFR,* glomerular filtration rate; *HTN,* hypertension; *PS,* propensity score matching; *RCRI,* revised cardiac risk index, *SD,* standard deviation.

outcome correlation to reflect the fact that some patients had more than one operation. For the given sample size of 1074 operations, this study had 90% power to detect a 50% reduction in the rate of the CE (from 15% to 7.5%); 85%

power to detect a 50% reduction in the rate of ACS (from 10% to 5%); and 32% power to detect 50% reduction in mortality (from 5% to 2.5%).

Secondary end points. The binary outcomes of respiratory complications and wound infection were compared using a random effects logistic regression model to account for within patient correlation of outcomes. Time-to-event analysis was performed with Cox proportional hazards regression, also adjusted for multiplicity of operations on the same patient using a shared frailty model. Level of statistical significance was set at alpha 0.0125 to account for the four comparisons performed when assessing the primary end point (two exposures tested against two individual outcomes). All analyses were performed using Stata IC v. 12.1 (StataCorp, College Station, Tex).

RESULTS

Descriptive statistics. Information was available on consecutive patients who underwent 1182 operations for atherosclerotic vascular disease. The analysis cohort that was used in the final analysis included 1074 operations (880 patients), separated into those with postoperative nHb ≥10 gm/dL (group A, n = 451 operations) and those with postoperative nHb <10 gm/dL (group B, n = 623 operations). Predictors included in the calculation of the propensity score and their relative presence in the two patient groups are listed in Table I, which indicates uniform distribution of covariates between the two groups of interest. The mean postoperative Hb for group A was 11.4 gm/dL (standard deviation, 1.2) vs 8.9 gm/dL (standard deviation, 0.8) for group B (*P* < .001). Transfusion of PRBCs was more frequent in group B (median, 2 units; interquartile range, 0-3) than group A (median, 0 units; interquartile range, 0-1) (*P* < .001), likely reflecting our tendency to transfuse these patients to a serum Hb around 10 gm/dL.

Primary end point. Univariate analysis demonstrated no association between nHb ≥10 gm/dL and the CE (odds ratio [OR], 0.68; 95% confidence interval [CI], 0.54-1.19; *P* = .12), whereas the number of units PRBCs transfused (OR, 1.13; 95% CI, 1.05-1.21; *P* < .001) was associated with the CE of death and ACS. On the multivariable model in which each one of these covariates was adjusted for the presence of the other, nHb ≥10 gm/dL was not associated with the CE (OR, 0.62; 95% CI, 0.33-1.14; *P* = .22). Number of PRBCs transfused remained associated with the CE even after adjusting for nHb (OR, 1.11; 95% CI, 1.01-1.22; *P* = .025). However, given the adjustment of the significance criterion to account for the effect of multiple comparisons, it is likely that even this association is due to chance. Analyzing the nHb as continuous variable in the multivariable model gave similar results. The test for heterogeneity of treatment effects was not statistically significant (*P* = .218), indicating no substantial difference in the effects of the individual exposures across the components of the CE. An interaction term between nHb and transfusion was introduced to the model but was found to be non-significant statistically (*P* = .312), indicating that the impact of transfusion on

outcomes was the same regardless of the level of post-operative nHb. Fig 1 demonstrates the predicted probability of the CE occurring at a range of units of blood transfused and for each level of the postoperative nHb. The multivariable analysis of associations between nHb, units of PRBCs, and each of the individual outcomes that comprised the CE is given in Table II.

Respiratory complications. In univariate analysis nHb ≥10 gm/dL (OR, 0.21; 95% CI, 0.09-0.85; $P = .007$) and number of PRBCs units transfused (OR, 1.29; 95% CI, 1.10-1.53; $P = .006$) were both associated with adverse respiratory events. In the multivariable adjusted model, however, nHb was no longer a statistically significant predictor (OR, 0.31; 95% CI, 0.09-1.21; $P = .13$); whereas the association between units transfused and adverse respiratory events persisted (OR, 1.22; 95% CI, 1.04-1.45; $P = .009$).

Wound complications. Transfusion had no impact on would complications in either univariate (OR, 1.07; 95% CI, 0.97-1.19; $P = .28$) or multivariable analysis (OR, 0.99; 95% CI, 0.90-1.09; $P = .93$). Maintaining nHb ≥10 gm/dL was associated with lower rate of perioperative wound complications in both univariate (OR, 0.48; 95% CI, 0.34-0.69; $P < .001$) and multivariable analysis (OR, 0.65; 95% CI, 0.4-0.93; $P = .01$).

Impact on midterm CE of death and ACS. We examined associations between nHb, blood transfusion and a composite of mortality and ACS during a 2-year follow-up. There was no association between nHb and the CE of death and ACS in either univariate (hazard ratio [HR], 0.71; 95% CI, 0.42-1.21; $P = .21$) or multivariable adjusted analysis (HR, 0.78; 95% CI, 0.45-1.35; $P = .373$). Blood transfusion was associated with the CE in both univariate (HR, 1.20; 95% CI, 1.09-1.34; $P < .001$) and bivariate adjusted analysis (HR, 1.15; 95% CI, 1.03-1.29; $P = .009$). Given the well-known impact of perioperative cardiac events on mid- and long-term mortality, we adjusted our Cox regression model even further by introducing a binary indicator variable for the presence of perioperative ACS or cardiac arrest. As anticipated, perioperative cardiac events were strongly associated with the CE (HR, 2.47; 95% CI, 1.32-5.41; $P = .008$). After adjusting for the presence of perioperative cardiac events, the association between transfusion and midterm outcome persisted (HR, 1.18; 95% CI, 1.04-1.30; $P = .007$). Fig 2 presents the Kaplan-Meier estimates of composite event at different levels of blood transfusion.

We also analyzed the impact of nHb, units of blood transfusion and perioperative cardiac events on the individual end points that comprised the composite outcome. In the multivariable model that included nHb, number of units PRBCs transfused and perioperative cardiac events as predictors, nHb had no impact on either midterm mortality (HR, 0.66; 95% CI, 0.33-1.32; $P = .247$) or ACS (HR, 0.89; 95% CI, 0.57-1.30; $P = .31$). There was a trend for association between blood transfusion and mortality (HR, 1.12; 95% CI, 1.02-1.34; $P = .02$), as well as between transfusion and ACS (HR, 1.45; 95%
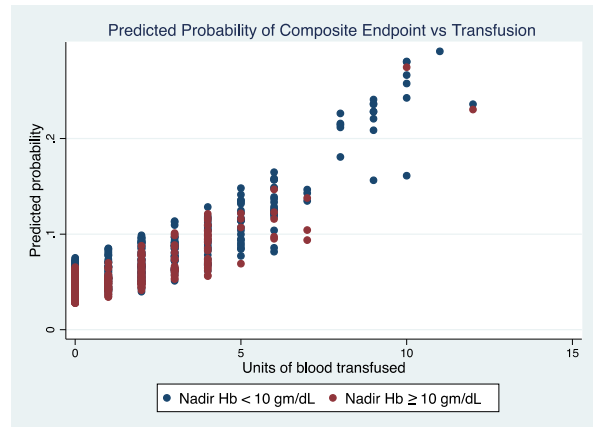
Fig 1. Predicted probability for the composite outcome of perioperative death, cardiac events, and stroke, as a function of number of packed red blood cells (PRBCs) transfused. The *blue dots* indicate patients with nHb <10 gm/dL, whereas the *red dotted line* those with nadir hemoglobin (*nHb*) ≥10 gm/dL.

Table II. Results of the adjusted bivariate analysis for the individual outcomes that comprised the primary CE

| Predictor	OR	95% CI	P value
Outcome: perioperative ACS			
nHb	0.61	0.33-1.12	.124
Units PRBCs	1.13	1.01-1.27	.031
Outcome: perioperative death			
nHb	0.81	0.31-2.62	.549
Units PRBCs	1.12	0.91-1.41	.262

ACS, Acute coronary syndrome; *CE*, composite end point; *CI*, confidence interval; *nHb*, nadir hemoglobin; *OR*, odds ratio; *PRBCs*, packed red blood cells.

CI, 1.2-4.21; $P = .025$). Perioperative cardiac events were associated with midterm mortality (HR, 2.69; 95% CI, 1.12-6.39; $P = .009$) but not midterm ACS. Figs 3 and 4 demonstrate Kaplan-Meier estimates of the individual end points of death and ACS at different levels of blood transfusion.
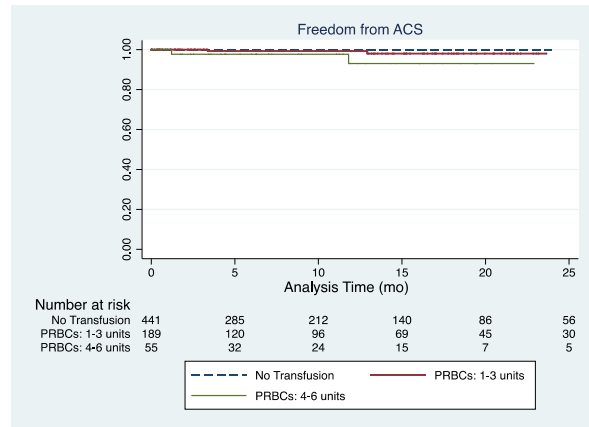
DISCUSSION

In this retrospective observational study, we used propensity score adjustment to analyze the impact of nadir postoperative Hb and blood transfusion on outcomes after open operations for ASVD. We showed that nHb levels below 10 gm/dL can be well tolerated and that there is a weak association between transfusion and a CE of perioperative death and cardiac events. We also showed that there is an association between perioperative blood transfusion and a composite of death and ACS during a 2-year follow-up. Those findings are of importance in health care practitioners treating patients with ASVD.
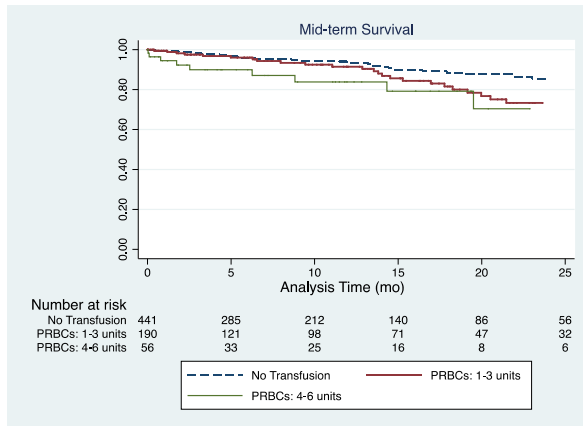
The topic of transfusion threshold has been of relatively strong interest in a variety of settings; however, observational studies on this subject have produced conflicting
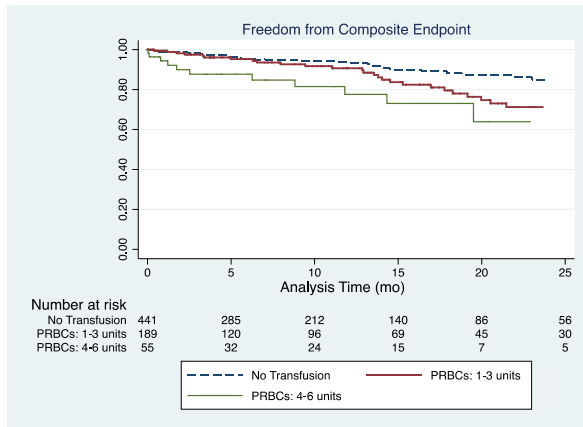
Fig 2. Kaplan-Meier estimates for freedom from the midterm composite end point (CE) of death and acute coronary syndrome (ACS) during the 2-year follow-up. *PRBCs*, Packed red blood cells.

Fig 3. Kaplan-Meier estimates for survival during the 2-year follow-up. *ACS*, Acute coronary syndrome; *PRBCs*, packed red blood cells.

Fig 4. Kaplan-Meier estimates for freedom from acute coronary syndrome (*ACS*) during the 2-year follow-up. *PRBCs*, Packed red blood cells.

results. Findings that indicate a protective role for transfusions include those by Sabatine[11] who performed a post-hoc analysis of patients enrolled in clinical trials for acute coronary syndrome, and indicated that baseline anemia increases the risk for cardiovascular mortality and ischemic cardiac events. Similarly, Aronson[9] demonstrated a protective effect of transfusion in patients admitted with ACS who had nadir Hb levels less than 8 gm/dL during their hospital stay. Wu[14] studied perioperative mortality in veterans who underwent a variety of surgical procedures, and also suggested a progressive increase of mortality and cardiac morbidity with declining preoperative Hb mass, a finding confirmed later by Musallam in non-veteran patient population.[27] And Foss showed that in patients undergoing elective hip replacement procedures, a restrictive policy with transfusion trigger at serum Hb of 8 gm/dL is associated with increased mortality and cardiac

events.[28] Other published studies, however, disagree with the above findings. In a post-hoc analysis of a trial[29] that studied the impact of transfusion policy in the intensive care unit setting, transfusion policy did not impact survival or incidence of cardiac events in a subset of patients with known cardiac disease.[30] Rao[10] showed that transfusion was associated with increasing mortality rates in patients who became anemic after they received thrombolytic treatment for acute coronary syndrome, results that persisted even after correction for the level of nadir Hb level observed in the patients.

Our study fills a gap in the literature of transfusion triggers that pertains to the management strategy of patients with ASVD who are typically treated as being of high cardiac risk even in the absence of known coronary artery disease. This is particularly true when multiple atherosclerotic risk factors are present. Randomized controlled trials on the topic of transfusion strategy fall short on assessing patients at high cardiac risk, but indicate that a conservative transfusion policy is reasonable in critical care setting,[2] after coronary artery bypass,[16] after acute myocardial infarction,[18] and after hip replacement surgery.[15] The latter recruited patients with multiple cardiovascular risk factors but without formal cardiac risk assessment. In the only available relevant trial on vascular patients, Bush et al[17] found no difference in the overall complication and mortality rates between conservative and liberal transfusion groups using a cutoff Hb 9 gm/dL. Patients who dropped their postoperative Hb below that level, however, tended to have more cardiac complications (14% vs 23%), and the fact that this difference did not reach statistical significance in that study is likely due to sample-size limitations. Given the paucity of data for high cardiac risk patients, the recent recommendations[31] from the American Association of Blood Banks support the notion of a conservative transfusion approach in patients with pre-existing cardiac disease under a weak recommendation based on moderate quality evidence.

Since the decisions on blood transfusions are guided by the physiologic need to provide a critical mass of oxygen

carriers to assure that metabolic processes proceed uninterrupted, a physiologic test would be ideal to assist with clinical decision-making. Unfortunately, such a test has not been found yet. In fact, several candidate tests or set of tests have been tried but dismissed as either over-sensitive, or easily confounded by operation or resuscitation-related physiologic changes.[6] Similarly, clinical indicators of hemodynamic status are often misleading. The lack of sophisticated physiologically driven algorithms led to the development of the "transfusion trigger" concept, which dictates that a specific level of serum Hb can be used to guide transfusion decisions. This task is deceptively simple, as it appears that although anemia increases the risk for perioperative cardiovascular events and mortality, transfusion (currently the main treatment that can rapidly correct the effects of anemia) often fails to provide any benefit and has been noted to even increase the risk of perioperative adverse events. This complex interplay was the reason why we simultaneously analyzed both anemia and transfusion in a bivariate model to precisely define their relative contribution to the outcomes of interest. Clearly, a "single number strategy" oversimplifies the physiologic complexities that underlie blood transfusion and unique circumstances, such as prolonged tachycardia, recent cardiac events, and overall volume status should be taken into consideration prior to making transfusion decisions.

Our adjusted analysis demonstrated that nHb less than 10 gm/dL can be well tolerated after operations for ASVD. The association between blood transfusion and outcomes was more difficult to define. There was a trend for increased incidence of the primary end point with increasing blood transfusions; given the adjustment to correct for multiple comparisons, however, this did not reach statistical significance. Another complicating factor in this analysis was the fact that nHb and units of blood transfusion are correlated variables, and the dynamics of their relationship were difficult to capture in a retrospective study. It is possible that increasing transfusion needs were related to lower nHb or a greater physiologic stress of the operation, but these confounders were not captured objectively because of the timing of blood sample collection. Therefore, interpretation of transfusions as having a harmful effect in the perioperative period should be made with caution.

The association between blood transfusion and the composite of mortality and ACS during the follow-up was more clearly defined. Other authors[32] have also indicated an unexpected harmful effect for blood transfusion that is fairly linear, similar to our analysis. This has been a rather counterintuitive finding, but it is consistent with studies that have failed to demonstrate an increase in tissue oxygenation associated with blood transfusion.[33] The reason for this phenomenon is poorly understood and may be related to alteration in nitric oxide biology, decreased 2,3-diphosphoglyceric acid levels, and release of inflammatory mediators.[10] Regardless of the underlying pathophysiologic mechanism and cognizant of the fact that observational studies like ours are not meant to address questions of causality, we believe that our findings when taken in conjunction with results from major randomized trials indicate that a conservative transfusion policy is reasonable in the population we studied.

Limitations of this study are inherent to its retrospective design. Although propensity score analysis can adjust for known confounders, unknown covariates that have a confounding effect may still bias the results. Some important variables, such as the presence of intraoperative or postoperative hypotension or tachycardia, were not available for analysis. Also, this was a study that included almost exclusively male patients; as such, our results cannot be extended to women undergoing the operations under consideration.

In conclusion, we have shown that nadir postoperative Hb less than 10 gm/dL is well tolerated after operations for ASVD and does not increase the risk of a CE of death and cardiac events. Perioperative transfusion is associated with a higher rate of a perioperative respiratory complications and an increased risk of death and ACS during a 2-year follow-up. Until a randomized controlled trial settles this issue definitively, a conservative transfusion approach is reasonable in male patients undergoing elective operative intervention for ASVD.

AUTHOR CONTRIBUTIONS

Conception and design: PK, NB
Analysis and interpretation: PK, NB, GP, BC
Data collection: PK, NB, GP, BC, TP, PL, SO
Writing the article: PK, NB, GP, BC, TP, PL, SO
Critical revision of the article: PK, NB, GP, BC, TP, PL, SO
Final approval of the article: PK, NB, GP, BC, TP, PL, SO
Statistical analysis: PK, NB
Obtained funding: PK
Overall responsibility: PK

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DISCUSSION

Dr Ronald Fairman (*Philadelphia, Pa*). My first question is, did you look at the timing of transfusion and did that have an impact on your results, whether the transfusions were administered only during the surgery as opposed to the early postoperative or late postoperative periods?

Dr Panos Kougias. We sure did look at that and it had a minor impact. The intraoperative transfusion actually had less of an impact than the postop. But overall, data were collected up to the point of the event. We tried to avoid the temporal bias that some observational centers have by collecting data that included transfusions even after the event of interest had occurred. So I would say that the postoperative, actually, transfusions were a more significant predictor than the intraoperative.

Dr Rabih Chaer (*Pittsburgh, Pa*). My question really pertains to the high cardiac risk patient. Your propensity score is as good as what goes into your model. I briefly looked at the list of the elements that you included in your analysis, but perhaps the highest effect of anemia is dependent on how much it increases myocardial demand. Did you look at whether those patients were beta blocked or not, because this might impact on the coronary outcomes of anemia.

Dr Kougias. Absolutely. Beta blockade, use of statin and, more interestingly, use of aspirin or Plavix were introduced in the model. We also included, when we did the propensity score calculation, the patient's risk status in terms of revised cardiac risk index. So the propensity score we had was all adjusted for all those covariates.