Should asymptomatic patients discharged with lower hemoglobin expect worse outcomes after valve surgery?

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ABSTRACT

Objective: Blood transfusion in cardiac surgery patients is associated with increased morbidity and cost. The decision to transfuse patients after surgery varies but is often based on low hemoglobin (Hgb) levels, regardless of symptom status. This study examined whether asymptomatic patients discharged with lower Hgb levels had increased risk for perioperative complications and 1-year mortality.

Methods: Between 2008 and mid-2014, a total of 1107 valve-only procedures were performed. Patients discharged alive with complete data (N = 1044) were divided into 2 groups with discharge Hgb levels of ≤ 8 g/dL (n = 153) or > 8 g/dL (n = 891). Propensity score matching was conducted between Hgb groups, resulting in 152 patient pairs.

Results: In multivariate analyses, discharge Hgb level did not predict 30-day mortality (odds ratio [OR] = 1.01, $P = .991$), 1-year survival (hazard ratio [HR] = 0.87, $P = .34$), or readmission < 30 days (OR = 0.92, $P = .31$). Furthermore, after propensity score matching, no differences were found between groups with Hgb levels ≤ 8 versus > 8 g/dL in 30-day mortality (0% vs 0.7%, $P > .99$) or readmissions (14% vs 16%, $P = .52$). Cumulative 1-year survival was similar between matched groups with discharge Hgb level of ≤ 8 versus > 8 g/dL (89.3% vs 91.4%, $P = .67$). Matched groups with Hgb level ≤ 8 versus > 8 g/dL had similar physical (28% vs 18% increase; $P = .27$) and mental (7% vs 6% increase; $P = .94$) health-related quality of life (HRQL) improvements at 6 months.

Conclusions: Asymptomatic patients discharged with lower Hgb levels did not manifest inferior outcomes, including perioperative morbidity/mortality, readmission < 30 days, HRQL, and 1-year survival. The practice of blood transfusion to correct lower Hgb levels in asymptomatic patients should be eliminated, as it may be associated with increased morbidity without apparent clinical benefits after valve surgery. (J Thorac Cardiovasc Surg 2015;150:1322-9)

Cumulative survival for propensity score-matched groups, by discharge Hgb level.

Central Message

In asymptomatic valve surgery patients, hemoglobin level at discharge was not predictive of early outcomes or 1-year survival.

Perspective

This study found no association between adverse outcomes and a lower Hgb level at discharge in asymptomatic patients after valve surgery. The practice of blood transfusion after valve surgery to correct lower Hgb levels in asymptomatic patients before discharge should be eliminated, as it may be associated with increased morbidity without apparent clinical benefits.

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The great majority of transfusions of blood and blood products in the United States are given to cardiac surgery patients.¹ For many decades, common practice has been to transfuse surgery patients when hemoglobin (Hgb) levels fall to < 10 g/dL, regardless of whether the patient is

symptomatic.² This practice is based on evidence that shows an association between anemia and increased morbidity and mortality.^{3,4} Yet with some exceptions,⁵ the preponderance of literature shows transfusion itself to be associated with an increased risk of morbidity and mortality, a longer length of stay, and increased costs.⁶⁻⁹

Several associations and organizations have set forth guidelines for perioperative blood transfusion.^{1,10-12} Despite these guidelines, however, actual transfusion practices vary widely both within and among institutions.¹³⁻¹⁶ Moreover, although the most recent blood conservation guidelines from the Society of Thoracic Surgeons (STS) and the Society of Cardiovascular Anesthesiologists are based on an extensive survey of the published literature, those

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Abbreviations and Acronyms

Hgb	= hemoglobin
HR	= hazard ratio
HRQL	= health-related quality of life
OR	= odds ratio
SF-12	= Medical Outcomes Study Short-Form 12
STS	= Society of Thoracic Surgeons

organizations found almost no evidence to stratify blood conservation interventions.¹

To date, there is no established, widely recognized no Hgb threshold below which blood transfusion can be consistently recommended for patients undergoing cardiac surgery.² This threshold is especially important for patients who have lower Hgb levels well after the intensive phase of their postoperative care, when they are asymptomatic, ambulating very well, and awaiting discharge from the hospital. The purpose of this study was to determine whether lower Hgb levels at discharge in asymptomatic patients who have undergone valve surgery are associated with an increased risk of perioperative complications and 1-year mortality.

METHODS

All study procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. This prospective study was conducted at a single center with a cohort of consecutive patients who underwent valve-only cardiac surgical procedures between April 2008 and June 2014 and were discharged alive from the hospital. During that period, 2551 patients underwent valve surgery, and 1107 valve-only procedures were performed (Figure 1).

All patients included in these analyses (N = 1044) had complete data available on presurgery and discharge Hgb and on blood transfusion. Blood transfusion was managed in accordance with our rigorous institutional protocol and the STS guidelines.^{1,17} Patients were divided into 2 groups based on discharge Hgb levels: ≤ 8 g/dL (n = 153) and > 8 g/dL (n = 891). Within the former group, 24 (16%) patients had a discharge Hgb level of ≤ 7 g/dL.

The value of 8 g/dL was selected for the Hgb cut-point to represent patients with significant anemia, because it additionally represents a strong relationship with blood product transfusion, even in asymptomatic patients.¹⁸ Asymptomatic patients were defined as clinically stable, ambulating well on the floor, and maintaining normal blood pressure with no orthostatic hypotension, dizziness, tachycardia, tachypnea, or shortness of breath. These factors were evaluated daily as part of our institutional clinical protocol.

Data were collected prospectively using our local STS database and institutional cardiac surgery database. Outcome measures included STS-defined morbidity, readmissions within 30 days, postdischarge mortality within 30 days of surgery, mortality during the first year of follow-up, and health-related quality of life (HRQL) using the Medical Outcomes Study Short Form-12 (SF-12) before surgery and at the 6-month follow-up after surgery. This study was approved by our local institutional review board (IRB nos. 06.022 and 12.055). Patient consent was waived for our registry.

Statistical Analysis

All analyses were performed with SPSS Version 17.0 (SPSS Inc, Chicago, Ill) or R 2.10.1 (R Foundation for Statistical Computing, Vienna,

Austria), and a 2-sided P value $< .05$ was used to determine significance. Continuous data are presented as mean $\pm$ SD, or median (interquartile range); categorical data are presented as frequency (percentage), unless otherwise noted. Comparisons of the discharge Hgb groups were conducted using independent-samples t tests or the Mann-Whitney U test for continuous variables, and χ^2 analysis or the Fisher exact test for categorical variables.

Outcome analyses were first conducted in the unmatched full sample to evaluate the relationship of discharge Hgb level as a continuous variable to the primary outcomes, including 30-day postdischarge mortality and 1-year survival, as well as discharge location and readmission within 30 days after discharge. These analyses were conducted using multivariate logistic and Cox regressions with the following covariates: age, gender, body mass index, chronic pulmonary disease, diabetes, ejection fraction, cerebrovascular disease, preoperative Hgb level, year of surgery, cardiopulmonary bypass time, and receipt of blood products during surgical hospitalization. Box-Tidwell testing revealed that the interaction term of discharge Hgb with the natural log of discharge Hgb level was not significant in any of the logistic regression analyses.

As a second step, propensity score matching was conducted to improve clinical covariate balance between the discharge Hgb groups, using the MatchIt package within R.¹⁹⁻²¹ Propensity scores were estimated via a logistic model that examined discharge Hgb group as the dependent variable and the following independent variables selected a priori: age, gender, chronic pulmonary disease, diabetes, ejection fraction, cerebrovascular disease, preoperative Hgb level, year of surgery, cardiopulmonary bypass time (minutes), and blood product transfusion during the surgical hospitalization.

Patients with a discharge Hgb level of ≤ 8 g/dL were matched to patients with a discharge Hgb level of > 8 g/dL, using propensity scores and a caliper of 0.25 propensity score SD.¹⁹ After matching, balance was improved for all covariates in the logistic model (Table 1), and almost all patients with a discharge Hgb level of ≤ 8 g/dL were able to be matched (Figure 2). A total of 152 pairs of patients remained after propensity score matching (N = 304), and this sample was used in analyses where noted.

Outcome analyses on the propensity score-matched sample (N = 304) utilized independent-samples t tests or Mann-Whitney U tests for continuous variables, and χ^2 analysis or the Fisher exact test for categorical variables. Kaplan-Meier survival analysis was used to compare the discharge Hgb groups on 1-year survival. Changes in HRQL between Hgb groups were examined using repeated measures ANOVA.

RESULTS

Patients

The mean age of patients in this sample (N = 1044) was 62.1 ± 14.0 years, and 37% were women. The sample collectively underwent 918 single-valve, 114 double-valve, and 12 triple-valve surgeries. The breakdown of which valve types were involved in these operations is: 514 mitral, 593 aortic, 72 tricuspid, and 3 pulmonary. Given that some patients had surgeries on multiple valves simultaneously, these numbers are not mutually exclusive. The mean Hgb level at discharge was 9.9 ± 1.7 g/dL; the distribution of discharge Hgb level is shown in Figure 3. Before matching, patients with a discharge Hgb level of ≤ 8 g/dL differed from patients with a discharge Hgb level of > 8 g/dL in preoperative and intraoperative characteristics (Table 2).

In particular, patients with discharge Hgb level of ≤ 8 g/dL were more likely to be women (44% vs 36%, $P = .041$) and to have cerebrovascular disease (23% vs 11%,

FIGURE 1. Flowchart illustrating inclusion criteria for the study sample.

$P < .001$). Patients with a discharge Hgb level of ≤ 8 g/dL were, additionally, less likely to have had an elective valve surgery (78% vs 89%, $P < .001$) and a single-valve procedure (76% vs 90%, $P < .001$). Patients with a discharge Hgb level of ≤ 8 g/dL had lower mean preoperative Hgb levels (11.3 vs 13.1 g/dL, $P < .001$) and longer mean cardiopulmonary bypass time (135 vs 123 minutes, $P = .010$). After matching, the 2 groups were balanced on all preoperative and intraoperative characteristics, particularly those included in the propensity score model (Table 3).

Multivariate Analyses With Discharge Hemoglobin

Discharge Hgb as a continuous variable was not predictive of incidence of postdischarge mortality within 30 days (odds ratio [OR] = 1.01, 95% confidence interval [CI] = 0.45-2.25, $P = .991$), discharge to home (OR = 1.06, 95% CI = 0.89-1.25, $P = .542$), or readmission within 30 days (OR = 0.92, 95% CI = 0.78-1.08, $P = .313$) in the entire sample, after adjustment for clinical covariates, as described earlier. Similarly, discharge Hgb as a continuous variable was not related to 1-year survival

TABLE 1. Covariate balance achieved from propensity score-matching technique

Characteristic	Std diff Before PSM	Std diff After PSM	Percentage Improvement
Age (y)	0.008	−0.001	89
Female	0.173	−0.026	85
Chronic pulmonary disease	0.246	0.029	88
Diabetes mellitus	0.295	0.044	85
Ejection fraction (%)	0.062	0.001	99
Cerebrovascular disease	0.274	0.062	77
Preoperative Hgb (g/dL)	−1.007	−0.054	95
Cardiopulmonary bypass time (min)	0.224	0.047	79
Blood product transfusion	0.562	0.000	100
Year of surgery	0.041	−0.032	22

Std diff, Standard difference; PSM, propensity score matching; Hgb, hemoglobin.

Distribution of Propensity Scores

FIGURE 2. Distribution of propensity scores for control (discharge Hgb level >8 g/dL) and treatment (discharge Hgb level ≤ 8 g/dL) units.

(hazard ratio [HR] = 0.87, 95% CI = 0.65-1.16, $P = .344$) after multivariate adjustment.

Propensity Score-Matched Outcome Analyses

During the postoperative course, patients who were discharged with an Hgb level of ≤ 8 or >8 g/dL did not differ in the incidence of reoperations for bleeding (3% vs 5%, $P = .357$), prolonged ventilation >24 hours (15% vs 16%, $P = .874$), pneumonia (4% vs 5%, $P = .584$), stroke/transient ischemic attack (1% vs 1%, $P > .999$), or

FIGURE 3. Histogram illustrating the distribution of Hgb levels at discharge within the entire sample.

TABLE 2. Patient characteristics before propensity score matching

Characteristic	Hgb >8 g/dL (n = 891)	Hgb ≤8 g/dL (n = 153)	P value
Age	62.0 ± 13.8	62.2 ± 15.1	.924
Female	319 (36)	68 (44)	.041
Diabetes mellitus	132 (15)	43 (28)	<.001
Body mass index (kg/m ²)	28.0 ± 6.2	28.2 ± 5.8	.728
Hypertension	527 (59)	104 (68)	.039
Congestive heart failure	260 (29)	68 (44)	<.001
Ejection fraction (%)	57.7 ± 10.4	58.3 ± 9.6	.507
Previous cerebrovascular accident	63 (7)	20 (13)	.011
Cerebrovascular disease	101 (11)	35 (23)	<.001
Chronic pulmonary disease	162 (18)	45 (29)	.001
Creatinine >2 mg/dL	34 (4)	15 (10)	.001
Peripheral vascular disease	51 (6)	13 (9)	.187
Preoperative Hgb (g/dL)	13.1 ± 1.9	11.3 ± 1.8	<.001
STS mortality risk (%)	1.9 ± 2.6	3.8 ± 6.1	.001
EuroSCORE II (%)	2.8 ± 4.9	6.0 ± 9.3	<.001
Elective status	793 (89)	119 (78)	<.001
Single valve procedure	802 (90)	116 (76)	<.001
Type of surgery			
Aortic valve	495 (56)	98 (64)	.050
Mitral valve	444 (50)	70 (46)	.351
Tricuspid valve	48 (5)	24 (16)	<.001
Pulmonary valve	2 (0.2)	1 (0.7)	.379
Cardiopulmonary bypass time (min)	123 ± 44	135 ± 53	.010
Length of stay (d)	4 (3-6)	6 (4-11)	.002

Data are presented as frequency (%), median (interquartile range), or mean ± SD. For the “type of surgery” category, values are not mutually exclusive because some patients had surgery on >1 valve. *Hgb*, Hemoglobin; *STS*, Society of Thoracic Surgeons; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation.

renal failure (3% vs 1%, $P = .448$). The mean discharge Hgb level was 7.5 ± 0.5 g/dL in the group with an Hgb level of ≤ 8 g/dL, and 9.6 ± 1.2 in the group with an Hgb level of >8 g/dL ($P < .001$). The matched groups of Hgb level ≤ 8 and >8 g/dL were not different on the primary outcomes of postdischarge 30-day mortality (0% vs 0.7%, $P > .999$), incidence of readmission (14% vs 16%, $P = .522$), or mortality within 1 year (9% vs 7%, $P = .515$). The primary indications for readmissions in patients with an Hgb level of ≤ 8 g/dL were any effusions (7 of 21), tachyarrhythmias, or bradyarrhythmias (6 of 21), and fluid overload (3 of 21).

In patients with an Hgb level of >8 g/dL, the primary indications for readmissions were any effusions (6 of 25), and tachyarrhythmias or bradyarrhythmias (5 of 25). The mode of discharge disposition to home did not differ between matched patients discharged with an Hgb level of ≤ 8 or >8 g/dL (81% vs 80%, $P = .667$). Kaplan-Meier analysis found that cumulative 1-year survival was similar between matched patients discharged with an Hgb level of ≤ 8 g/dL or >8 g/dL (89.3% vs 91.4%, log rank = 0.19, $P = .67$; Figure 4).

TABLE 3. Patient characteristics after propensity score matching

Characteristic	Hgb >8 g/dL (n = 152)	Hgb ≤8 g/dL (n = 152)	P value
Age (y)	62.1 ± 14.2	62.1 ± 15.1	.994
Female	70 (46)	68 (45)	.818
Diabetes mellitus	40 (26)	43 (28)	.699
Body mass index (kg/m ²)	28.4 ± 7.1	28.3 ± 5.8	.808
Hypertension	102 (67)	103 (68)	.903
Congestive heart failure	65 (43)	68 (45)	.729
Ejection fraction (%)	58.2 ± 9.6	58.2 ± 9.7	.994
Previous cerebrovascular accident	17 (11)	19 (13)	.723
Cerebrovascular disease	30 (20)	34 (22)	.574
Chronic pulmonary disease	42 (28)	44 (29)	.799
Creatinine >2 mg/dL	17 (11)	15 (10)	.709
Peripheral vascular disease	15 (10)	13 (9)	.692
Preoperative Hgb (g/dL)	11.4 ± 2.0	11.3 ± 1.8	.651
STS mortality risk (%)	2.9 ± 3.4	3.8 ± 6.1	.140
EuroSCORE II (%)	4.3 ± 6.0	6.0 ± 9.3	.063
Elective status	118 (78)	118 (78)	>.999
Single valve procedure	120 (79)	116 (76)	.582
Type of surgery			
Aortic valve	86 (57)	98 (65)	.159
Mitral valve	84 (55)	69 (45)	.085
Tricuspid valve	17 (11)	23 (15)	.309
Pulmonary valve	0	1 (0.7)	>.999
Cardiopulmonary bypass time (min)	131 ± 53	134 ± 52	.680
Length of stay (d)	6 (4-10.75)	6 (4-11)	.115

Data are presented as frequency (%), median (interquartile range), or mean ± SD. For the “type of surgery” category, values are not mutually exclusive because some patients had surgery on >1 valve. *Hgb*, Hemoglobin; *STS*, Society of Thoracic Surgeons; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation.

Health-Related Quality-of-Life Analyses

In the subset of matched patients who completed HRQL measures before surgery and at 6 months after surgery

FIGURE 4. Cumulative survival for groups matched on their discharge Hgb levels. *Hgb*, Hemoglobin; *CI*, confidence interval.

FIGURE 5. Box plots illustrating HRQL improvement in the physical composite scale from the SF-12 from before surgery to 6 months after surgery by groups matched on their discharge Hgb levels. *HRQL*, Health-related quality of life; *Hgb*, hemoglobin.

($n = 78$), a significant improvement was found in the physical composite score ($F = 31.1$, $P < .001$), mental composite score ($F = 5.4$, $P = .023$), and the general health subscale from the SF-12 ($F = 28.8$, $P < .001$). The matched Hgb ≤ 8 and > 8 g/dL groups had similar improvements in physical composite score (a 28% vs 18% increase; $F = 1.25$, $P = .268$; Figure 5) and mental composite score (a 7% vs 6% increase; $F = 0.01$, $P = .943$) from before to 6 months after surgery. Although lower general health scores were reported before surgery in the group with Hgb level ≤ 8 g/dL, those patients reported similar general health scores at the 6-month time point after surgery (48.9 vs 47.7, $t = -0.6$, $P = .569$).

Effect of Blood Product Transfusion

The transfusion rate for the entire sample ($N = 1044$) was 22%. Patients with a discharge Hgb level of ≤ 8 g/dL had a higher incidence of transfusion during their hospital course (46%) than the entire sample. As a result of the propensity score matching process, which included transfusion as a covariate, matched patients with a discharge Hgb level of > 8 g/dL were identical to patients with a discharge Hgb level of ≤ 8 g/dL in the incidence of any blood product transfusion during the hospital course (46% vs 46%, $P > .999$).

In general, patients with a discharge Hgb level of ≤ 8 g/dL were sicker (Table 2), and the propensity score matching technique resulted in a group of comparable patients (including in transfusion rate) who had a discharge Hgb level of > 8 g/dL. When the analyses were separated by time at which blood products were given, no differences remained between matched patients with a discharge Hgb level of ≤ 8 and > 8 g/dL in intraoperative blood product

transfusion (28% vs 34%, $P = .215$) and postoperative blood product transfusion (29% vs 34%, $P = .324$).

Secondary analyses examined the independent effect of blood product transfusion on outcomes, first in multivariate analyses with the entire sample, then in the propensity score-matched sample. In contrast to the discharge Hgb results, multivariate Cox regression analysis found that blood product transfusion was in fact a significant predictor of poorer 1-year survival ($HR = 2.27$, 95% CI = 1.06-4.88, $P = .036$), but it was not related to readmissions within 30 days ($OR = 1.51$, 95% CI = 0.75-3.04, $P = .244$).

In the sample that was propensity score matched on discharge Hgb level ($N = 304$), patients with transfusions did not differ from patients without transfusions in 30-day mortality (0.7% vs 0%, respectively, $P = .461$) or readmissions (17% vs 13%, respectively, $P = .366$). Discharge to home was less likely for patients with transfusion than for patients without transfusions (69% vs 89%, respectively, $P < .001$). Last, 1-year cumulative survival was significantly worse for patients with transfusions than for patients without transfusions (85.7% vs 94.8%, respectively; log rank = 6.27, $P = .012$). The negative effect of blood transfusion on 1-year survival remained significant after adjustment for discharge Hgb level as a continuous variable ($HR = 3.00$, 95% CI = 1.18-7.60, $P = .021$).

DISCUSSION

In this study of patients who underwent valve surgery at our institution, asymptomatic patients discharged with a low Hgb level (≤ 8 g/dL) had outcomes that were comparable to those of patients discharged with an Hgb level > 8 g/dL; these outcomes include similar survival at 30 days and 1 year, similar readmission rate, and similar improvements in HRQL. On the other hand, blood and blood product transfusion during hospital course was associated with poorer 1-year cumulative survival.

Blood transfusion is most often given to cardiac surgery patients to address anemia.² Preoperative anemia is well known to confer increased risks after cardiac surgery.^{22,23} The association of transfusion itself with postoperative adverse outcomes has been widely reported.²⁴⁻²⁷ Conversely, blood conservation protocols were shown to be associated with improved surgical outcomes across a region²⁸ in a study based on our institutional blood transfusion protocol, which has been in place since 2007; its success has led to regional implementation. Under our transfusion management protocol, $< 20\%$ of our valve patients receive intraoperative or postoperative blood transfusion, and asymptomatic patients with Hgb levels of < 8 g/dL are discharged with appropriate iron and/or other supplements.

Several reports support the use of a more restrictive strategy for transfusion (ie, at lower Hgb levels).^{6,17,29,30} The transfusion requirements in the septic shock trial³¹ found

no significant differences in 90-day mortality, severe adverse reactions, use of life support, or survival after discharge between 2 groups of patients who received blood transfusion at Hgb thresholds of ≤ 7 and ≤ 9 g/dL. In another study²⁹ evaluating transfusion thresholds, no differences were found in morbidity, mortality, or self-assessed fatigue or anemia with the use of Hgb thresholds of < 8 and < 9 g/dL. In the Transfusion Requirements in Critical Care study, maintenance of Hgb at 7 to 9 g/dL, and a transfusion threshold of as low as 7 g/dL, was not inferior to a more liberal transfusion threshold of 10 g/dL and a maintenance range of 10 to 12 g/dL.³²

Despite what has been shown in these studies,^{6,17,29,30,32} the variation in transfusion incidence across US health care facilities reflects the evidence gap in the literature with regard to best practices for blood transfusion.^{2,18} The discrepancy between guideline recommendations and actual practice is exacerbated in part by studies such as the recent report by Murphy and colleagues,⁵ which found that a restrictive transfusion threshold after cardiac surgery was not superior to a liberal threshold with respect to morbidity or health care costs. That single prospective randomized study, however, stands in contrast to an abundance of studies^{6,8,9,24-27,33,34} conducted during the past decade—including one by Murphy and colleagues themselves⁷—showing an association between transfusion and an increased risk of complications, adverse outcomes, and cost as well as those^{2,28,29,31,35} demonstrating the benefits of blood conservation strategies.

In this study, 153 (15%) patients were discharged with an Hgb level of ≤ 8 g/dL. Although the vast majority of patients in our center are discharged with Hgb levels of > 8 g/dL (Figure 3), our results were achieved in a significant subgroup of asymptomatic patients who were discharged with lower Hgb levels and had comparable early outcomes and 1-year survival rates. The results of our study add to the body of evidence showing that, in considering perioperative transfusion strategies to correct anemia in asymptomatic patients, a restrictive Hgb threshold is not associated with compromised outcomes and may have a positive impact on 30-day results and 1-year survival for patients after valve surgery.

Limitations

Our study has several limitations that should be taken into account. The results are in agreement with the bulk of the literature in this area. However, they do require validation in a larger patient sample because our results were obtained in a single center with a rigorous multidisciplinary transfusion protocol and thus may not be generalizable to other centers. In addition, the transfusion rate in our propensity score-matched sample was higher than our usual institutional rate, owing to the fact that the analysis was performed on subgroups. However, the transfusion

rate in the full sample of this study ($N = 1044$) was 22%, which is in line with the rate found for our entire population of valve patients.

In addition, although > 1000 patients were included in the entire study sample, patients discharged with Hgb levels of ≤ 8 g/dL represented only 15% of the sample. The propensity score-matched analyses may therefore have been affected by this relatively small sample size, which further highlights the need for validation of these findings in a larger sample. Finally, because patients were not prospectively randomized to discharge Hgb groups, unmeasured factors may have confounded our results. However, the propensity score-matching methodology was included as a means to replicate the random occurrence of confounders that would be present in randomized studies. Although the results of the propensity score-matched analyses were in agreement with the unmatched analyses of the entire cohort, future studies utilizing a randomized controlled design are warranted to evaluate the association between discharge Hgb levels and outcomes in asymptomatic patients.

CONCLUSIONS

The ongoing challenge in treating anemic patients after cardiac surgery is multifactorial and can present difficulties in making treatment decisions for individual patients. Based on our experience with thousands of patients, however, we believe that an important element in meeting this challenge is to change the culture around transfusion. Implementation of blood conservation protocols has been clearly associated with improved outcomes and cost savings.^{28,35,36} The important message of our study lies in the demonstration that adverse outcomes are not associated with lower Hgb level at discharge in asymptomatic patients, for all age groups.

A more conservative approach to transfusion is often challenged by physicians accustomed to transfusion, owing to old habits and a belief that any risks associated with transfusion are outweighed by the greater risk of postoperative anemia and the inferior outcomes with which it is associated. The results of this study demonstrate that asymptomatic patients with a lower Hgb level can be safely discharged from the hospital after valve surgery, and that blood transfusion, rather than lower Hgb level at discharge, represents the greater risk of inferior outcomes. The hope is that this study will serve as a model for a prospective randomized study in a larger group of patients to clarify and answer additional clinical questions.

Conflict of Interest Statement

Niv Ad, MD, is a consultant and a member of the speaker's bureau for Medtronic, Inc, and AtriCure. Alan M. Speir, MD, is on the Medtronic, Inc, advisory board. All other

authors have nothing to disclose regarding commercial support.

You can watch a Webcast of this AATS meeting presentation by going to: http://webcast.aats.org/2015/Video/Tuesday/04-28-15_4E_0945_Ad.mp4

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Key Words: valve surgery, hemoglobin, anemia, outcomes

Discussion

Dr Glenn Whitman (Baltimore, Md). I want to thank the American Association for Thoracic Surgery (AATS) for allowing me this opportunity. I also want to thank Dr Ad for sending me his paper several months ago.

When the review committee for the AATS saw this abstract, every one of us was enthusiastic. This paper takes aim at all of us cardiovascular surgeons because we represent the primary group of transfusers in the world, yet we exhibit no standardized behavior.

As much as I want to agree with the authors' conclusion that whether the discharge level of hemoglobin (Hgb) is <8 g/dL or >8 g/dL does not matter in valvular heart disease patients, I think we have to approach the conclusion with skepticism. Just recently, Dr Colleen Koch from the Cleveland Clinic published a paper on 153,000 discharged patients, without regard to diagnoses; utilizing the University Health-System Consortium, Inc, (UHC) database, she showed that in the group that had an Hgb level of <9 g/dL, there was an almost 4-fold increase in readmissions at 30 days, compared with those female patients who had an Hgb level >12 g/dL and with male patients with an Hgb level >13 g/dL. These findings were adjusted for confounding factors.

Furthermore, just last month, the Transfusion Indication Threshold Reduction study came out in the *New England Journal of Medicine* (Murphy GJ, Pike K, Rogers CA, Wordsworth S, Stokes EA, Angelini GD, et al. Liberal or restrictive transfusion after cardiac surgery. *N Engl J Med*. 2015;372:997-1008). Seventeen institutions in England looked at all cardiac surgery patients, randomized them, 1000 in each group, to a triggered threshold of 9 g/dL versus 7.5 g/dL in the immediate postoperative period. When they looked at those discharged patients—in the transfusion trigger group of 9 g/dL, the Hgb level at discharge averaged 10 g/dL; in the trigger group of 7.5 g/dL, the Hgb level averaged 9 g/dL.

The investigators found no difference in their primary endpoint, which was ischemic or infection-related events at 90 days, including myocardial infarction, stroke, acute kidney injury, and gut infarctions. However, a secondary endpoint was 90-day mortality, which was lower in the group that was liberally transfused. In all fairness, though, comparing that study to this one is not entirely appropriate, as two thirds of that study population had coronary artery disease, whereas in the study presented today, none had coronary disease, because they were all isolated valve patients.

I have 2 questions that I want to raise with Dr Ad. One, what were, in fact, the Hgb concentrations in your 2 different populations? If there was very little difference in the Hgb concentrations, that might explain why the 2 groups behaved similarly.

The second question gets at the value of propensity matching. In all of the studies that are retrospective, non-randomized, and utilize propensity matching, the quality of the study depends upon how well matched the 2 populations were. As an example, the fact that frailty, which we all understand is difficult to measure, is not included in these 2 populations might be viewed as a major drawback of the propensity matching. I think that not one of us, as disciplined as we might be, would sit at the foot of an extremely frail patient and withhold a transfusion if that patient were anemic.

The subjective assessment of frailty may have played a large role in who was permitted to be discharged with an

Hgb level <8 g/dL. It must be acknowledged that, to the degree that frailty was not measured, and more-anemic patients were less frail, the conclusion that there is no difference in patients discharged with an Hgb level <8 g/dL versus >8 g/dL may be incorrect.

Thank you.

Dr Niv Ad. Well, it was a long discussion, but I think you made some valid points. However, here is the point I am trying to make, and for those who work with me, this approach is very familiar. I want to raise a philosophical question, which is: Should we transfuse patients just because they are anemic, with no physiologic merit? I believe that the answer is no; and not all patients are the same.

Now, as far as our statistical method, I believe that it is important for you to understand what we did here. We did not base this study on a propensity-matched analysis only. We based this study on 2 very robust analyses: One is discharge Hgb level as a continuous variable; the other is a propensity match to supplement that, and it seems like you missed that.

No study is perfect, and it is very hard to randomize patients in multicenter studies in cardiac surgery in general, because the quality of the surgery is also important, and we do not talk about that. So, our study basically shows, with legitimate prospectively collected data, not a chart review, because we have a registered database, and data are being collected as we move on, that showed that, based on those 2 analyses, it is safe to discharge patients with low Hgb levels if they are asymptomatic.

Now, when we consider specific individual patients, then it is a question of individuality and variability, and this question probably should be answered with a more robust analysis of a subgroup of patients with lower Hgb level, different ages, frailty, renal failure, and so on. That was not the aim of our study. Our study was designed to answer one question, which is a philosophical question: Should we transfuse patients that are anemic just because they are anemic, even if their Hgb level is <8 g/dL, and the answer is no.

Dr Whitman. Dr Ad—just for everybody's knowledge—what were the Hgb concentrations in these 2 groups?

Dr Ad. The average one?

Dr Whitman. Exactly.

Dr Ad. We clearly showed the average with a nice, simple figure; you probably missed it, because the distribution of Hgb level at discharge was demonstrated; 153 patients with an Hgb level <8 g/dL, and about 70 patients with an Hgb level <7 g/dL. The average for the entire group was 9.9 g/dL.

But I do not understand your point. The study points to the fact that, based on our 2 valid analyses, done by a superb statistician, Hgb level at discharge was not associated with a negative outcome.

Dr Whitman. Dr Ad, thank you. I was simply asking what the Hgb concentrations were in the 2 groups.