Predictors and Outcomes of Postoperative Hemoglobin of <8 g/dL in Total Joint Arthroplasty

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Background: Restrictive transfusion practices have decreased transfusions in total joint arthroplasty (TJA). A hemoglobin threshold of <8 g/dL is commonly used. Predictors of this degree of postoperative anemia in TJA and its association with postoperative outcomes, independent of transfusions, remain unclear. We identified predictors of postoperative hemoglobin of <8 g/dL and outcomes with and without transfusion in TJA.

Methods: Primary elective TJA cases performed with a multimodal blood management protocol from 2017 to 2018 were reviewed, identifying 1,583 cases. Preoperative and postoperative variables were compared between patients with postoperative hemoglobin of <8 and ≥8 g/dL. Logistic regression and receiver operating characteristic curves were used to assess predictors of postoperative hemoglobin of <8 g/dL.

Results: Positive predictors of postoperative hemoglobin of <8 g/dL were preoperative hemoglobin level (odds ratio [OR] per 1.0-g/dL decrease, 3.0 [95% confidence interval (CI), 2.4 to 3.7]), total hip arthroplasty (OR compared with total knee arthroplasty, 2.1 [95% CI, 1.3 to 3.4]), and operative time (OR per 30-minute increase, 2.0 [95% CI, 1.6 to 2.6]). Negative predictors of postoperative hemoglobin of <8 g/dL were tranexamic acid use (OR, 0.42 [95% CI, 0.20 to 0.85]) and body mass index (OR per 1 kg/m^2 above normal, 0.90 [95% CI, 0.86 to 0.94]). Preoperative hemoglobin levels of <12.4 g/dL in women and <13.4 g/dL in men best predicted postoperative hemoglobin of <8 g/dL. Overall, 5.2% of patients with postoperative hemoglobin of 7 to 8 g/dL and 95% of patients with postoperative hemoglobin of <7 g/dL received transfusions. Patients with postoperative hemoglobin of <8 g/dL had longer hospital stays ($p < 0.001$) and greater rates of emergency department visits or readmissions ($p = 0.001$) and acute kidney injury ($p < 0.001$). Among patients with postoperative hemoglobin of <8 g/dL, patients who received transfusions had a lower postoperative hemoglobin nadir ($p < 0.001$) and a longer hospital stay ($p = 0.035$) than patients who did not receive transfusions.

Conclusions: Postoperative hemoglobin of <8 g/dL after TJA was associated with worse outcomes, even for patients who do not receive transfusions. Optimizing preoperative hemoglobin levels may mitigate postoperative anemia and adverse outcomes.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Blood management strategies to minimize blood loss and the need for transfusions are integral to total joint arthroplasty (TJA). Blood transfusions in TJA have been associated with poor outcomes, including increased infection rate and length of stay[1-4]. Multimodal strategies including anesthetic and surgical techniques, as well as tranexamic acid (TXA) use and restrictive transfusion thresholds, have been implemented to reduce the need for transfusions in TJA[5-9].

Evidence shows that avoiding transfusions until patients are symptomatic, have a hemoglobin concentration of <7 or <8 g/dL, or have a hemoglobin concentration of <8 g/dL with cardiac disease leads to shorter hospital stays, lower infection rates, and fewer in-hospital deaths compared with more liberal transfusion thresholds[10-12]. These restrictive thresholds have likely led to a greater prevalence and severity of postoperative anemia[13]. Postoperative anemia alone has been associated with adverse outcomes in TJA, including myocardial infarction[14] and acute kidney injury[15], as well as worse functional recovery[16] and quality of life[17]. Many studies have sought to determine predictors of and adverse outcomes associated with postoperative

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Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJS/G735).

transfusions after TJA[1,18-21]. However, few studies have assessed modern blood management protocols in TJA and the effects of severe postoperative anemia that does not require transfusions. Most blood conservation efforts in orthopaedic surgery focus on perioperative modalities and intraoperative techniques to limit blood loss and subsequent anemia[13,22]. A better understanding of preoperative risk factors will enable enhanced patient optimization to limit the extent of postoperative anemia.

The primary aim of this study was to identify preoperative and intraoperative variables that are predictive of anemia (hemoglobin of <8 g/dL) after primary elective TJA performed using a multimodal blood management program. A threshold of 8 g/dL was chosen because transfusions triggers are commonly set below this value. Thus, it both serves as a surrogate for avoiding transfusions and enables the evaluation of patients with severe anemia who do not require transfusions. Our secondary aims were to determine preoperative hemoglobin cutoff values that best predict postoperative hemoglobin of <8 g/dL and to investigate the associations between this degree of anemia and acute kidney injury, length of stay, and emergency department (ED) visits or hospital readmissions in patients who underwent elective TJA and who did not require transfusions.

Materials and Methods

After approval by our institutional review board, a retrospective review was conducted of all primary elective TJA cases performed at our academic tertiary care center from January 1, 2017, to December 31, 2018. We excluded cases performed for patients who were <18 years of age, cases that were nonelective, cases involving a concomitant procedure (for example, removal of instrumentation or core decompression), and cases lacking postoperative complete blood cell count results.

Blood Management Protocol

All patients in this study were treated in the context of our standardized blood management protocol. Anticoagulants were withheld preoperatively in accordance with the evidence-based guidelines established by the American Society of Regional Anesthesia and Pain Medicine[23]. At the time of incision, 1 g of intravenous TXA was administered unless the patient had a history of a vascular stent. A restrictive transfusion protocol was used, with transfusion thresholds of hemoglobin of <7 g/dL in asymptomatic patients and <8 g/dL in symptomatic patients not responding to fluid resuscitation or patients with preexisting cardiac disease. Transfusions were given on the basis of a single-unit-per-occurrence policy. Decisions to administer transfusions were made by the orthopaedic surgery team according to these guidelines. Intraoperatively, the anesthesia team made transfusion decisions with the surgical team's input according to patients' intraoperative hemodynamic status and hemoglobin value. No patients received surgical drains. For postoperative venous thromboembolism prophylaxis, low-risk patients received 325 mg of aspirin twice daily for 1 month and sequential compressive devices while in the hospital. Patients with a history of venous thromboembolism or other comorbidities receiving anticoagulation preoperatively were given prophylactic doses of their preoperative anticoagulant for 1 month after the surgical procedure and then they returned to their normal dose. Rivaroxaban at 10 mg daily was given for 1 month postoperatively to patients with a history of venous thromboembolism who did not take anticoagulants preoperatively, unless their insurance did not approve, in which case enoxaparin was given for 1 month at a dosage of 30 mg twice daily for patients undergoing total knee arthroplasty (TKA) and 40 mg daily for patients undergoing total hip arthroplasty (THA). No preoperative hemoglobin threshold was required prior to the surgical procedure during the study period.

Data Collection

Data on preoperative, intraoperative, and postoperative variables were extracted from the institutional electronic medical records. Preoperative variables were patient age, sex, race or ethnicity, body mass index (BMI), comorbidities (diabetes, chronic kidney disease, congestive heart failure, and coronary artery disease), and preoperative hemoglobin level. Intraoperative variables were procedure (TKA or THA), type of anesthesia (general or spinal), TXA use, and operative time. Postoperative variables were hemoglobin level, postoperative anticoagulant regimen, transfusion occurrence, duration of hospital stay, and ED visit or readmission within 90 days after discharge. Postoperative acute kidney injury was calculated on the basis of the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines for Acute Kidney Injury (AKI)[24]. The postoperative hemoglobin nadir was also assessed, defined as the lowest hemoglobin level measured postoperatively during admission.

Statistical Analysis

Cases were grouped according to whether the postoperative hemoglobin nadir was <8 g/dL or ≥8 g/dL. Descriptive statistics for categorical variables are reported as the frequency and percentage, and those for continuous variables are reported as the mean and the standard deviation. Charlson Comorbidity Index values were calculated for all patients[25]. Categorical variables were compared between the 2 cohorts using the Pearson chi-square and Fisher exact tests, as appropriate. When significant, post hoc pairwise comparisons were performed with the Bonferroni correction for multiple testing. Continuous variables were assessed for differences between the 2 cohorts using Student t tests with unequal variances. Differences in length of stay, acute kidney injury, and ED visits or readmissions between the 2 cohorts were analyzed both with and without the inclusion of patients who received transfusions. We also performed subanalyses comparing length of stay, acute kidney injury, postoperative hemoglobin nadir, and ED visits or hospital readmissions between patients who received transfusions and those who did not receive transfusions who had a postoperative hemoglobin nadir of <8 g/dL. An additional subanalysis was

conducted to assess differences in length of stay and rates of postoperative hemoglobin of <8 g/dL, acute kidney injury, and ED visits or readmissions across the various postoperative anticoagulation regimens.

A multivariable logistic regression model was constructed to identify variables independently associated with the development of postoperative hemoglobin of <8 g/dL. The following variables were chosen for inclusion in the regression model prior to analysis: preoperative hemoglobin level, procedure type, operative time, sex, anesthesia type, Charlson Comorbidity Index, age, BMI, and use of TXA. The results of this regression model are reported as odds ratios (ORs) with 95% confidence intervals (CIs). An additional linear regression model was constructed to assess the relationship between postoperative hemoglobin of <8 g/dL in patients who did not receive transfusion and the length of stay after adjusting for age, sex, procedure type, and Charlson Comorbidity Index. The results of this model are reported as regression coefficients with 95% CIs. Significance was set at $p < 0.05$ for all analyses.

The preoperative hemoglobin value that was most strongly associated with the development of postoperative hemoglobin of <8 g/dL was calculated separately for men and women. A receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was calculated. The optimal cutoff value was determined by the highest value of Youden index, which is calculated to maximize sensitivity and specificity (sensitivity + specificity – 1 = Youden index)[26]. Statistical analyses were conducted using Stata, version 15 (StataCorp) and SPSS, version 26.0 (IBM).

Source of Funding
There was no funding received for this study.

Results

Patient Population

There were 1,635 primary TJA cases in which the surgical procedure was performed during the study period. Cases were excluded due to lack of complete blood cell count data (n = 33), nonelective cases (n = 10), concomitant procedure(s) (n = 8), and patient age of <18 years (n = 1). This resulted in 1,583 eligible cases performed in 1,448 patients. Among these cases, 887 (56%) were TKA and 696 (44%) were THA. There were 98 cases (6.2%) with a postoperative hemoglobin of <8 g/dL; of these 98 cases, 45 (46%) underwent TKA and 53 (54%) underwent THA. There were 21 cases (1.3%) with a postoperative hemoglobin nadir of <7 g/dL. Complete preoperative and intraoperative variables among cohorts are shown in Appendix 1. Among all 1,583 cases, 27 (1.7%) received transfusions. Transfusions were received in 5.2% of patients (4 of 77) with postoperative hemoglobin from 7 to 8 g/dL and 95% of patients (20 of 21) with postoperative hemoglobin of <7 g/dL. The mean postoperative hemoglobin nadir (and standard deviation) was 10 ± 1.5 g/dL. Among cases with hemoglobin of <8 g/dL, the mean postoperative hemoglobin nadir was 7.3 ± 0.6 g/dL. With regard to postoperative anticoagulation regimens, aspirin was used in 1,337 cases (84%), novel oral anticoagulants (rivaroxaban, apixaban, or dabigatran) were used in 174 cases (11%), coumadin was used in 59 cases (3.7%), and enoxaparin was used in 13 cases (0.82%).

Postoperative Outcomes

The differences in postoperative outcomes are shown in Table I. Patients with postoperative hemoglobin of <8 g/dL had a greater length of stay ($p < 0.001$) and higher rates of transfusion ($p < 0.001$), acute kidney injury ($p < 0.001$), and ED visits or readmissions within 90 days after discharge (p =

TABLE I Postoperative Outcomes of 1,583 Primary TJA Cases from 2017 to 2018, by Development of Postoperative Anemia with Hemoglobin of <8 g/dL

Outcome	All Cases	Cases with Postoperative Hemoglobin <8 g/dL	Cases with Postoperative Hemoglobin ≥8 g/dL	P Value
All cases				
No. of cases	1,583	98	1,485	
Lowest postoperative hemoglobin level* *(g/dL)*	10 ± 1.5	7.3 ± 0.6	11 ± 1.3	<0.001
Any transfusion administered†	27 (2%)	24 (24.5%)	3 (0.2%)	<0.001
Duration of hospital stay* *(hr)*	41 ± 27	82 ± 69	38 ± 18	<0.001
Acute kidney injury†	33 (2%)	8 (8.2%)	25 (1.7%)	<0.001
ED visit or readmission within 90 days†	79 (5%)	12 (12.2%)	67 (4.5%)	0.001
Excluding 27 cases with transfusions				
No. of cases after exclusion	1,556	74	1,482	
Duration of hospital stay* *(hr)*	40 ± 20	70 ± 39	38 ± 18	<0.001
Acute kidney injury†	30 (2%)	5 (6.8%)	25 (1.7%)	0.002
ED visit or readmission within 90 days†	76 (5%)	9 (12.2%)	67 (4.5%)	0.003

*The values are given as the mean and the standard deviation. †The values are given as the number of cases, with the percentage in parentheses.

TABLE II Multivariable Regression Analysis of Postoperative Hemoglobin of <8 g/dL After Primary TJA in 1,583 Cases from 2017 to 2018

Variable	OR*	P Value
Preoperative hemoglobin level, per 1-g/dL increase	3.0 (2.4 to 3.7)	<0.001
THA compared with TKA	2.1 (1.3 to 3.4)	0.004
Surgical duration, per 30-minute increase	2.0 (1.6 to 2.6)	<0.001
Female sex	1.4 (0.77 to 2.5)	0.274
General anesthesia compared with neuraxial anesthesia	1.1 (0.55 to 2.4)	0.717
Charlson Comorbidity Index, per 1-point increase	1.1 (0.99 to 1.3)	0.072
Age, per 5-year increase	1.1 (0.92 to 1.2)	0.443
BMI, per 1-kg/m^2 increase	0.90 (0.86 to 0.94)	<0.001
TXA use	0.42 (0.20 to 0.85)	0.016

*The values are given as the OR, with the 95% CI in parentheses.

0.001) than those with postoperative hemoglobin of ≥8 g/dL. After excluding patients who received transfusions, patients with postoperative hemoglobin of <8 g/dL still had a greater length of stay ($p < 0.001$) and higher rates of acute kidney injury ($p = 0.002$) and ED visits or readmissions ($p = 0.003$) than those with postoperative hemoglobin of ≥8 g/dL. Postoperative anticoagulant use was not associated with rates of acute kidney injury ($p = 0.40$) or development of postoperative hemoglobin of <8 g/dL ($p = 0.06$). Patients taking novel oral anticoagulants for postoperative anticoagulation had a greater length of stay ($p = 0.028$) and a higher rate of ED visits or readmissions ($p = 0.048$) (see Appendix 2). After adjusting for age, sex, procedure type, and Charlson Comorbidity Index, postoperative hemoglobin of <8 g/dL was independently associated with a greater length of stay by 28 hours (95% CI, 24 to 33 hours), even after excluding patients who received transfusions. When comparing patients with a postoperative hemoglobin nadir of <8 g/dL who received transfusions and those who did not, those who received transfusions had a greater mean length of stay (4.8 ± 4.9 compared with 2.6 ± 1.6 days; $p = 0.035$) and lower mean postoperative hemoglobin nadir (6.5 ± 0.7 compared with 7.5 ± 0.3 g/dL; $p < 0.001$) but no differences in rates of acute kidney injury (12.5% compared with 6.8%; $p = 0.40$) or ED visits or hospital readmissions (12.5% compared with 12.2%; $p = 0.99$).

Predictors of Postoperative Hemoglobin Level of <8 g/dL

Results of multivariate regression to assess predictors of a postoperative hemoglobin level of <8 g/dL are shown in Table II. The following factors were independently associated with greater odds of postoperative hemoglobin of <8 g/dL: lower preoperative hemoglobin level (OR per 1-g/dL decrease, 3.0 [95% CI, 2.4 to 3.7]), THA (OR compared with TKA, 2.1 [95% CI, 1.3 to 3.4]), and longer operative time (OR per 30-minute increase, 2.0 [95% CI, 1.6 to 2.6]). The following factors were independently associated with lower odds of postoperative hemoglobin of <8 g/dL: higher BMI (OR per 1-kg/m^2 increase, 0.90 [95% CI, 0.86 to 0.94]) and TXA use (OR, 0.42 [95% CI, 0.20 to 0.85]). Age, sex, Charlson Comorbidity Index, and anesthesia type were not independently associated with postoperative hemoglobin of <8 g/dL.

Preoperative Hemoglobin Thresholds to Predict Postoperative Hemoglobin of <8 g/dL

In women, a preoperative hemoglobin level of 12.4 g/dL maximized the sensitivity (75%) and specificity (73%) for predicting postoperative anemia with hemoglobin of <8 g/dL, with a positive predictive value of 20% and a negative predictive value of 99.7% (AUC = 0.79) (Fig. 1). In men, the optimal preoperative hemoglobin cutoff value for predicting postoperative anemia with hemoglobin of <8 g/dL was 13.4 g/dL, with a sensitivity of 78% and specificity of 88%, a positive predictive value of 11%, and a negative predictive value of 88% (AUC = 0.87) (Fig. 2). These cutoff values correctly classified development of postoperative anemia with hemoglobin of <8 g/dL in 75% of cases involving women and 78% of cases involving men.

Discussion

Lower preoperative hemoglobin level, THA (compared with TKA), and longer operative time independently increased the odds of postoperative hemoglobin of <8 g/dL in patients who underwent elective TJA, whereas higher BMI and TXA use independently decreased the odds. Sex and Charlson Comorbidity Index were not associated with postoperative hemoglobin of <8 g/dL. Preoperative hemoglobin cutoffs of 12.4 g/dL in

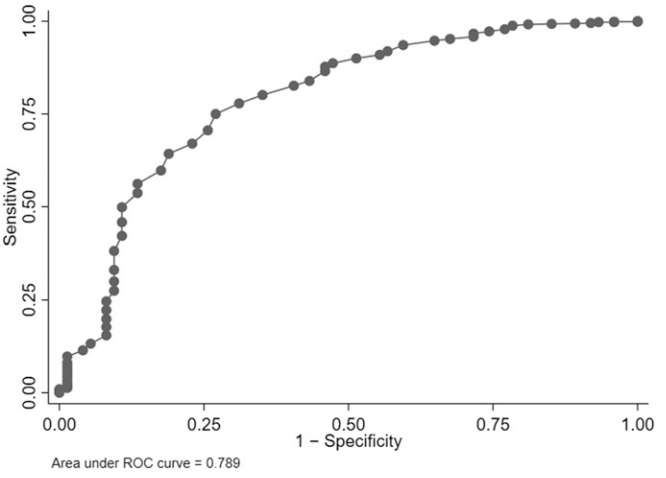

Fig. 1

The ROC curve for prediction of the development of postoperative hemoglobin of <8 g/dL using preoperative hemoglobin levels in women who underwent TJA. A preoperative hemoglobin level of 12.4 g/dL was the cutoff value that maximized sensitivity (75%) and specificity (73%).

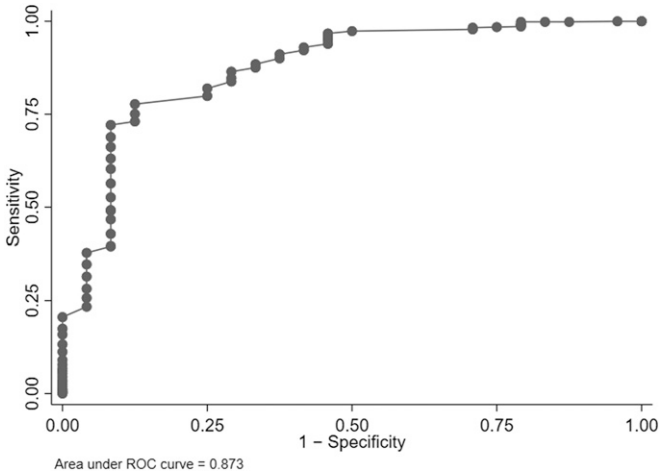

Fig. 2

The ROC curve for prediction of the development of postoperative hemoglobin of <8 g/dL using preoperative hemoglobin levels in men who underwent TJA. A preoperative hemoglobin level of 13.4 g/dL was the cutoff value that maximized sensitivity (78%) and specificity (88%).

women and 13.4 g/dL in men most accurately predicted a postoperative hemoglobin level of <8 g/dL after TJA. Patients with postoperative hemoglobin levels of <8 g/dL had greater length of stay and higher rates of acute kidney injury and ED visits or readmissions compared with those whose postoperative hemoglobin levels were ≥8 g/dL, independent of transfusions.

Lower preoperative hemoglobin, longer operative time, and THA have been associated with greater risk of postoperative transfusions in TJA in previous studies[1,19,20]. Our findings are consistent with those studies and further demonstrate the association with worse outcomes in patients with severe anemia who do not require transfusions. Previous studies showed an increased risk of acute kidney injury in orthopaedic patients with postoperative anemia; however, all of these studies included patients who received transfusions[15,27]. Choi et al.[15] found that patients who underwent THA and had postoperative hemoglobin of <10 g/dL had twice the odds of acute kidney injury after adjusting for transfusion, and Walsh et al.[27] found that a decrease in hemoglobin of >2.0 g/dL below preoperative values in orthopaedic patients was associated with increased odds of acute kidney injury after adjusting for transfusion. In our study, patients with a postoperative hemoglobin level of <8 g/dL who did not receive transfusions had 4 times the rate of acute kidney injury and nearly 3 times as many ED visits or hospital readmissions compared with patients with postoperative hemoglobin of ≥8 g/dL. These findings underscore the importance of minimizing the extent of postoperative anemia, which in itself is a risk factor for worse outcomes after TJA. An additional finding from our study was that postoperative anticoagulant choice was not associated with acute kidney injury rates. Although this analysis was limited because of small numbers of patients taking certain anticoagulants, it provides additional evidence that aspirin is a safe and effective postoperative anticoagulant despite concerns about its potential nephrotoxic effects[28]. This finding is particularly important in light of the widespread adoption of aspirin as the anticoagulant of choice in recent years[29,30].

In this study, only 1.7% of all patients received a transfusion, but 5.7% of those with a hemoglobin level from 7 to 8 g/dL received a transfusion. After we excluded patients who received transfusions, those with a postoperative hemoglobin nadir of <8 g/dL had a mean length of stay that was nearly twice that of patients with a postoperative hemoglobin nadir of ≥8 g/dL. Patients with this degree of postoperative anemia may be at greater risk for hypotension, fatigue, and delayed physical therapy, which could explain their longer hospitalizations. Despite not requiring transfusion, this degree of anemia affects short-term recovery and outcomes. This effect is particularly important to recognize in the setting of outpatient joint arthroplasty.

We found that the optimal preoperative values predictive of a postoperative hemoglobin level of <8 g/dL were <12.4 g/dL in women and <13.4 g/dL in men. These levels are higher than the World Health Organization's definitions for anemia (12 g/dL for women and 13 g/dL for men)[13] and similar to or higher than those described for predicting transfusions after TKA, reported as 12.5 g/dL for men and 12.4 g/dL for women in 1 study[19], 13.75 g/dL for men and 12.75 g/dL for women in another study[31], and 12.4 g/dL for patients who were ≥70 years of age and 12.1 g/dL for patients who were <70 years of age in a third study[21]. Our findings highlight that patients who, by definition, do not have anemia, are still at risk for developing a postoperative hemoglobin level of <8 g/dL and of having worse outcomes, irrespective of transfusion requirements. Preoperative evaluation and optimization of hemoglobin to the highest possible level will likely benefit patients.

This study had several limitations. First, it was a retrospective study. Second, our sample size prevented multivariable regression analyses of THA and TKA separately. Third, we did not assess the preoperative use of anticoagulants; however, all patients taking anticoagulants preoperatively stopped taking them before the surgical procedure in accordance with evidence-based guidelines[23], so this is unlikely to have influenced rates of postoperative anemia. Fourth, our analysis to determine preoperative hemoglobin values that best predicted postoperative anemia of <8 g/dL did not account for other variables besides sex.

In conclusion, although transfusions have decreased and can often be avoided in THA and TKA, postoperative anemia continues to affect outcomes. Only 25% of patients in our study with postoperative hemoglobin of <8 g/dL and 5.2% of those with postoperative hemoglobin between 7 and 8 g/dL received a transfusion; however, postoperative anemia with hemoglobin of <8 g/dL was independently associated with a longer hospital stay and higher rates of ED visits or hospital readmission and acute kidney injury after elective TJA, regardless of transfusion status. Preoperative hemoglobin levels of <12.4 g/dL in women and <13.4 g/dL in men best predicted postoperative hemoglobin of <8 g/dL. These findings suggest that before elective TJA, it is important to optimize hemoglobin levels and evaluate and treat anemia to the extent possible. The work-up and treatment often entail a delay of the surgical procedure, further work-up, and specialty consultation. Future

studies should investigate the efficacy of preoperative optimization of hemoglobin levels in reducing the extent of postoperative anemia.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/G736). ■

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