Original research

Transfusion Avoidance in Severely Anemic Total Hip and Total Knee Arthroplasty Patients: An Analysis of Risk

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A B S T R A C T

Background: Allogenic blood transfusions increase the risk of multiple complications. We evaluated the influence of restricting transfusions in adults with osteoarthritis that underwent total hip or knee arthroplasty (THA/TKA) with severe postoperative anemia.
Material and methods: Patients that underwent THA/TKA for osteoarthritis with postoperative hemoglobin (Hb) $\leq$ 8 g/dl were retrospectively identified. We evaluated characteristics and adverse postoperative outcomes of patients not transfused and compared them to those of patients who received postoperative transfusion. Adverse outcomes were 90-day readmission, reoperation, infection, and falls, as well as inpatient cardiovascular events and deaths.
Results: One thousand eighty-seven patients meeting inclusion criteria underwent THA and TKA. The 399 patients (36.7%) who did not undergo transfuion were younger (67.4 vs 69.5 years, $P = .008$), healthier (American Society of Anesthesiologist $\leq$ 2: 64.2% vs 56%, $P = .006$), comprised a lower proportion of cardiovascular disease patients (13.8% vs 24.7%, $P < .001$), a lower proportion of patients with Medicare/Medicare Managed Care (57.2% vs 65.5%, $P = .05$), received tranexamic acid more frequently (66.4% vs 52.9%, $P < .01$), had a shorter procedure time (92.7 vs 103.1, $P < .01$), a lower postoperative drop in Hb (4.0 vs 4.2 g/dl, $P = .022$), a later drop in Hb (2.6 vs 2.2 days, $P = .003$), and a shorter length of stay (3.5 vs 4.8, $P < .01$). TKA patients underwent transfusion more frequently than THA patients (67.5% vs 59%, $P = .004$). There were no postoperative deaths. Adverse events were similar between the 2 groups.
Conclusion: Findings suggest that younger and healthier patients that have lower Hb later during their hospital stay need not undergo transfusion solely based on Hb levels. Routine transfusion triggers can be avoided even in more anemic patients.

Introduction

Major joint replacement entails an expected blood loss with a postoperative drop in hemoglobin (Hb) of approximately 2-3 g/dL, depending on tranexamic acid (TXA) use [1]. Historic allogeneic blood transfusion rates have been as high as 46%-90% [2-4], while after modern hip and knee replacement, rates are below 1% [5]. Although transfusion has become less common following hip and knee arthroplasty, risks of adverse events still exist.

Patients that receive allogenic blood transfusions are at risk of complications that range from mild to severe. Human error is one of the leading causes of complications related to transfusions; most translate into minor reactions, but massive hemolytic transfusion reaction and even death can occur. The most serious risks are transfusion-associated circulatory overload and transfusion-related acute lung injury—the latter is associated with increased mortality [6].

In addition to the known risk of transmissible disease, blood transfusion after joint replacement increases the chance of major periprosthetic joint infections (PJIs) [7]. PJI after hip and knee replacement is a devastating complication, as treatment is a financial and psychological burden and can lead to subpar patient outcomes [8]. Transfusion after arthroplasty also increases length of stay [9] and costs by 10% to 20% [10].

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The traditional approach has been to transfuse those patients with a Hb $\leq$ 10 g/dl after surgery, with a lower threshold to transfuse those with a history of cardiovascular disease [10]. However, there is evidence that morbidity and mortality after surgery are only significantly increased when Hb level drops below 6 g/dl [11]. The introduction of restrictive transfusion thresholds has significantly decreased the rate of transfusions and associated risk, without affecting clinical outcomes [10,12]. This evidence is compelling toward lowering the transfusion threshold in patients who undergo total joint arthroplasty (TJA).

Therefore, we studied the influence of restrictive transfusions on patients with postoperative Hb equal to or less than 8 g/dl following total hip arthroplasty (THA) and total knee arthroplasty (TKA). We evaluated patient and perioperative characteristics as well as adverse postoperative outcomes of those not transfused and compared them to those who received postoperative allogenic blood transfusion. The adverse outcomes of interest were 90-day readmission, reoperation, infection, and falls; inpatient adverse cardiovascular events; and death.

Material and methods

After obtaining institutional review board approval, we retrospectively identified all patients with a postoperative Hb of 8 g/dl or less that underwent primary THA and TKA for osteoarthritis at a single academic hospital between February 1, 2016, and July 30, 2019. Patients younger than 18 years and those undergoing bilateral TJA or that had subsequent unrelated surgery within 90 days of the index procedure were excluded. If a patient was symptomatically anemic with a Hb of 8 g/dl or less, transfusion was considered by the inpatient medical team, with ultimate approval required by the treating surgeon.

Demographic and perioperative data obtained from the electronic medical record (EMR) included age, sex, race, body mass index, American Society of Anesthesiologist classification, insurance type, number of allogenic packed red blood cells transfused, preoperative and postoperative Hb, hip or knee joint, laterality, procedure duration, type of anesthesia, length of stay, and use of TXA.

Comorbidities that are considered significant drivers for readmissions and reoperations were identified with International Classification of Disease, Tenth Revision codes: history of cardiovascular or chronic pulmonary disease, diabetes, renal failure, neoplasia, coagulopathies, dementia, mood disorders, and history of substance abuse [13,14].

Data on adverse outcomes were collected from the EMR, and once identified, a chart review was performed to subclassify 90-day readmissions, reoperations, and infections. Our hospital keeps track of inpatient and outpatient patient falls, which allowed us to identify patients that fell within 90 days of the index surgery either in the hospital or after being discharged. Inpatient cardiovascular adverse events were identified using International Classification of Disease, Tenth Revision codes and included angina, myocardial infarction, acute ischemic heart disease, pulmonary embolism,

Table 1
Patient demographic characteristics, TJA patient with postop Hb $\leq$ 8 g/dl.

Characteristics	Total	Not transfused	Transfused	*P* value
	N = 1087	N = 399	N = 688	
Age (y)	68.7 (12.7)	67.4 (12.1)	69.5 (13.0)	.008[a]
Sex				.059
Male	218 (20.1%)	68 (17.0%)	150 (21.8%)	
Female	869 (79.9%)	331 (83.0%)	538 (78.2%)	
Race				.66
Native American	1 (0.1%)	1 (0.3%)	0 (0.0%)	
Asian	28 (2.6%)	8 (2.0%)	20 (2.9%)	
Black	117 (10.8%)	41 (10.3%)	76 (11.0%)	
Other	67 (6.2%)	23 (5.8%)	44 (6.4%)	
Patient Declined	15 (1.4%)	4 (1.0%)	11 (1.6%)	
Unavailable	6 (0.6%)	3 (0.8%)	3 (0.4%)	
White	853 (78.5%)	319 (79.9%)	534 (77.6%)	
BMI (kg/m^2)	29.0 (7.1)	29.2 (7.1)	28.8 (7.1)	.39
ASA status				.006[a]
1 (Normal)	17 (1.6%)	3 (0.8%)	14 (2.0%)	
2 (Mild systemic)	618 (56.9%)	253 (63.4%)	365 (53.1%)	
3 (Severe systemic)	431 (39.7%)	137 (34.3%)	294 (42.7%)	
4 (Life-threatening)	12 (1.1%)	3 (0.8%)	9 (1.3%)	
Hx of CVD	225 (20.7%)	55 (13.8%)	170 (24.7%)	<.001[a]
Hx of COPD	19 (1.7%)	6 (1.5%)	13 (1.9%)	.64
Hx of diabetes	64 (5.9%)	19 (4.8%)	45 (6.5%)	.23
Hx of renal failure	46 (4.2%)	14 (3.5%)	32 (4.7%)	.37
Neoplasm/metastasis	122 (11.2%)	46 (11.5%)	76 (11.0%)	.81
Hx of coagulopathies	33 (3.0%)	12 (3.0%)	21 (3.1%)	.97
Hx of dementia	5 (0.5%)	2 (0.5%)	3 (0.4%)	.88
Hx of mood disorders	92 (8.5%)	38 (9.5%)	54 (7.8%)	.34
Hx of drug abuse	3 (0.3%)	1 (0.3%)	2 (0.3%)	.90
Insurance type				.05[a]
Medicare	637 (58.6%)	213 (53.4%)	424 (61.6%)	
Medicare Managed Care	42 (3.9%)	15 (3.8%)	27 (3.9%)	
Commercial	365 (33.6%)	156 (39.1%)	209 (30.4%)	
Work Comp	1 (0.1%)	0 (0.0%)	1 (0.1%)	
Medicaid	7 (0.6%)	2 (0.5%)	5 (0.7%)	
Medicaid Managed Care	15 (1.4%)	7 (1.8%)	8 (1.2%)	
Other	13 (1.2%)	2 (0.5%)	11 (1.6%)	
Unspecified	7 (0.6%)	4 (1.0%)	3 (0.4%)	

ASA, American Society of Anesthesiologists classification; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; Hx, history.
[a] Statistically significant difference. Continuous variables are reported as means and standard deviations, and discrete variables are reported as frequencies and percentages.

acute heart failure, chronic heart failure exacerbation, cardiac or respiratory arrest, and cerebrovascular disease. Inpatient deaths were first screened via EMR and then verified with the social security death index.

Continuous variables are reported as means and standard deviations, while discrete variables are reported as frequencies and percentages in the descriptive analysis. Group demographic and perioperative characteristics were initially compared utilizing t-test and chi-square test. Multivariable logistic regression was planned to adjust for baseline comorbidities. Statistical significance was defined as $P \leq .05$. Post-hoc power analysis was performed to calculate the power achieved to detect a difference in total adverse event rate between the 2 groups. All analyses were performed with Stata, version 14.2 (StataCorp., College Station, TX).

Results

Patient demographic and perioperative characteristics

Of 30,723 TJAs, a total of 1087 patients met inclusion criteria. Incidence of anemia, and inclusion in the study, decreased by year with the introduction of TXA (4.5% in 2016, 4.1% in 2017, 2.8% in 2018, 2.3% in 2019). Detailed patient demographic characteristics are listed in Table 1. In the overall group, the mean age was 68.7 years (±12.7 years), 79.9% were female, and 78.5% were white. Mean body mass index was 29 kg/m^2 (±7.1 kg/m^2). Most patients had Medicare/Medicare Managed Care insurance (62.5%), followed by commercial insurance (33.6%).

Three hundred and ninety-nine patients (36.7%) did not undergo transfusion. Patients that did not receive transfusion were slightly younger (67.4 ± 12.1 vs 69.5 ± 13 years, $P = .008$), healthier, had American Society of Anesthesiologist ≤ 2 (64.2% vs 56%, $P = .006$), comprised less number of patients with a history of cardiovascular disease (13.8% vs 24.7%, $P < .001$), and a lower proportion of coverage with Medicare/Medicare Managed Care (57.2% vs 65.5%, $P = .05$).

Overall perioperative characteristics were similar for both groups and are found in Table 2. The mean preoperative Hb was 11.8 (±1.4) g/dl and was collected on average 13.7 (±6.8) days prior to surgery. Evaluating patients for preoperative anemia was left to the discretion of the perioperative medical team. Anesthesia type was similar: 91.7% of patients received regional anesthesia, and 6.8% received general anesthesia.

Patients that did not receive transfusion had a higher mean postoperative Hb (7.7 vs 7.5 g/dl, $P < .001$), with a lower drop in Hb (4 vs 4.2 g/dl, $P = .022$) that was seen at a later time (2.6 vs 2.2 days, $P = .003$). The nontransfused group received TXA more frequently (66.4% vs 52.9%, $P < .01$), had a shorter procedure duration (92.7 vs 103.1 minutes, $P < .01$), and a shorter length of stay (3.5 vs 4.8 days, $P < .01$). Transfused patients received an average of 2.1 units of packed red blood cells. TKA patients underwent transfusion more frequently (67.5%) than THA patients (59%, $P = .004$).

Adverse outcomes

Adverse outcomes for both groups are listed in Table 3. There were no statistically significant differences in adverse events between the nontransfused and transfused groups prior to adjusting for demographic and perioperative group differences.

Overall readmission and reoperation rates were 5.8% and 4%, respectively. The most common reason for readmission was reoperation (3.9%). In both groups, the most common cause of reoperation was local infection (1.3% PJI and 0.8% superficial surgical site superficial infection), followed by periprosthetic fracture (0.6%), hematoma incision and drainage (0.6%), extensor mechanism disruption in TKA (0.5%), and hip instability in THA (0.3%). Systemic infection rate was 0.8%, including respiratory infection (0.7%) and sepsis (0.1%). One patient had a postoperative course complicated by sepsis due to endocarditis and epidural abscess and would ultimately undergo reoperation. The overall inpatient fall rate was 0.6%—5 patients who did not receive transfusion fell vs 2 that did receive transfusion. There were no outpatient falls recorded in our database. The overall rate of adverse inpatient cardiovascular events was 0.7%. Three patients in the nontransfused group developed new-onset A-fib (vs 7 in the transfused group), 1 patient in the nontransfused group had a nonfatal pulmonary embolism, and 1 patient in the transfused group experienced bradycardia. One patient, who received transfusion, had a readmission for adverse

Table 2
Patient perioperative characteristics after TJA with postop Hb ≤ 8 g/dl.

Perioperative data	Total	Not transfused	Transfused	P value
	N = 1087	N = 399	N = 688	
Number of transfusions			2.1 (2.1)	
Preop Hb (g/dl)	11.8 (1.4)	11.7 (1.2)	11.8 (1.4)	.87
Preop Hb (days before surgery)	13.7 (6.8)	14.0 (7.2)	13.6 (6.6)	.34
Lowest postop Hb (g/dl)	7.6 (0.4)	7.7 (0.4)	7.5 (0.4)	<.001[a]
Postop Hb (d)	2.4 (2.1)	2.6 (3.0)	2.2 (1.4)	.003[a]
Postop Hb drop (g/dl)	4.2 (1.4)	4.0 (1.3)	4.2 (1.5)	.022[a]
Joint				.004[a]
Knee	553	180 (32.5%)	373 (67.5%)	
Hip	534	219 (41%)	315 (59%)	
Procedure duration (min)	99.3 (42.7)	92.7 (32.7)	103.1 (47.2)	<.001[a]
Anesthesia				.33
Unspecified	14 (1.3%)	6 (1.5%)	8 (1.2%)	
General	74 (6.8%)	21 (5.3%)	53 (7.7%)	
Neuroaxial nerve block	43 (4.0%)	13 (3.3%)	30 (4.4%)	
Peripheral nerve block	3 (0.3%)	2 (0.5%)	1 (0.1%)	
Regional	953 (87.7%)	357 (89.5%)	596 (86.6%)	
Length of stay (d)	4.3 (3.1)	3.5 (1.6)	4.8 (3.6)	<.001[a]
Tranexamic acid				<.001[a]
None	458 (42.1%)	134 (33.6%)	324 (47.1%)	
IV	500 (46.0%)	223 (55.9%)	277 (40.3%)	
Topical	129 (11.9%)	42 (10.5%)	87 (12.6%)	

IV, intravenous.

[a] Statistically significant difference. Continuous variables are reported as means and standard deviations, and discrete variables are reported as frequencies and percentages.

Table 3
Patient adverse outcomes (not adjusted) after TJA with postop Hb $\leq$ 8 g/dl.

Postoperative adverse events	Total	Not transfused	Transfused	P value
	N = 1087	N = 399	N = 688	
Readmission (90 d)	63 (5.8%)	29 (7.3%)	34 (4.9%)	.11
Readmission reason				.63
MUA	16 (1.5%)	7 (1.8%)	9 (1.3%)	
CV adverse event	1 (0.1%)	0 (0.0%)	1 (0.1%)	
Reoperation	42 (3.9%)	19 (4.8%)	23 (3.3%)	
Hematoma nonop	3 (0.3%)	2 (0.5%)	1 (0.1%)	
Symptomatic anemia	1 (0.1%)	1 (0.3%)	0 (0.0%)	
Reoperation (90 d)	44 (4.0%)	19 (4.8%)	25 (3.6%)	.36
Reason for reoperation				.67
Periprosthetic fracture	6 (0.6%)	4 (1.0%)	2 (0.3%)	
Hip instability	3 (0.3%)	2 (0.5%)	1 (0.1%)	
Hematoma I&D	7 (0.6%)	3 (0.8%)	4 (0.6%)	
Infection	22 (2.0%)	8 (2.0%)	14 (2.0%)	
Extensor mechanism disruption	5 (0.5%)	2 (0.5%)	3 (0.4%)	
Epidural abscess I&D	1 (0.1%)	0 (0.0%)	1 (0.1%)	
Infection (90 d)	31 (2.9%)	10 (2.5%)	21 (3.1%)	.60
Infection type				.9
PJI	14 (1.3%)	5 (1.3%)	9 (1.3%)	
Superficial surgical site infection	9 (0.8%)	3 (0.8%)	6 (0.9%)	
Respiratory infection	8 (0.7%)	3 (0.8%)	5 (0.7%)	
Sepsis/endocarditis	1 (0.1%)	0 (0.0%)	1 (0.1%)	
Falls (inpatient)	7 (0.6%)	5 (1.3%)	2 (0.3%)	.056
Adverse CV event (inpatient)	8 (0.7%)	2 (0.5%)	6 (0.9%)	.49
Adverse CV event type				.17
Bradycardia	1 (0.1%)	0 (0%)	1 (0.1%)	
New-onset Afib	6 (0.6%)	1 (0.3%)	5 (0.7%)	
Pulmonary embolism	1 (0.1%)	1 (0.3%)	0 (0%)	
Deaths	0 (0%)	0 (0%)	0 (0%)	

Afib, atrial fibrillation; CV, cardiovascular; I&D, incision and drainage; MUA, manipulation under anesthesia.
Variables are reported as frequencies and percentages.

cardiovascular event. One patient in the nontransfused group was readmitted for symptomatic anemia. There were no postoperative deaths.

Because there was no association between transfusion and adverse events, a multivariable analysis controlling for demographic and preoperative variables was not performed. Statistical power achieved to detect a difference in total adverse event rate between the 2 groups was 0.33.

Discussion

We performed a retrospective review of adult patients undergoing consecutive unilateral THA or TKA for osteoarthritis who had a postoperative Hb equal to or less than 8 g/dl. We described patients' demographic and perioperative characteristics and sought to identify any differences in adverse postoperative outcomes between patients that received transfusions vs those who did not. Our primary findings were that patients who received transfusion tended to be older with more comorbidities but that there was no statistical difference in adverse events between the 2 groups.

In patients with postoperative Hb below 8 g/dl after TJA, the observed transfusion rate was 63.3%. Compared with historical transfusion rates, this does not seem higher than average, but some groups have recently reported transfusion rates in patients with Hb below 8 g/dl to start around 6.5% and to decrease to 1.3% after the implementation of a quality initiative program [15]. Low preoperative Hb is a risk factor for transfusion [2-4]. Both groups started with a similarly low preoperative Hb level (11.7 g/dl in the nontransfused group vs 11.8 g/dl in the transfused group, P = .87).

Blood management programs combine different interventions before, during, and after surgery. These programs focus on optimizing the preoperative Hb, decreasing blood loss, and ultimately decreasing the need for transfusion. Wong et al. noted a reduction

in allogenic transfusion rates after THA, from 26.1% at hospitals that provided usual care to 16.5% at hospitals that implemented a blood management program [2]. Bonfante also saw a reduction in transfusion rates from 31% to 17% after implementing a new transfusion order set and eliminating the practice of autologous blood donation [16]. Modern recommendations in the United States have called for reducing the transfusion threshold to Hb below 7 g/dl for most patients and below 8 g/dl for those with a history of major comorbidities [10]. The ultimate benefits of blood management programs included decreasing the risk of infection, length of stay, cardiovascular events, mortality, and costs.

Restricting transfusions did not increase the 90-day readmission rate (7.3% in nontransfused vs 4.9% for transfused, P = .11). This is in agreement with the systematic review performed by Mitchell et al., whereby restrictive transfusion protocols did not associate with a relative risk of readmission [12]. Markel et al. demonstrated that odds of readmission was increased in transfusion patients (odds ratio 1.79, 95% confidence interval: 1.06-3.01) and decreased after implementation of a quality-improvement transfusion protocol [17]. In addition to reduced length of stay, Kotze et al. also noticed a decrease in 90-day readmission rates from 13.5% to 8.2% (P = .02) after implementing a blood management protocol [18].

Reoperation rates were similar between the nontransfused (4.8%) and transfused groups (3.6%, P = .36). Rhee et al. found that blood transfusions did not increase odds of revision surgery after TKA or THA at 90 days and 1 year after surgery [15]. Infection was found to be similar between our groups (2.5% in the nontransfused vs 3.1% in the transfused group, P = .60). This contrasts with the reported increased risk of infection with allogenic blood transfusions [2,3,7,15], as well as the report of a decreased risk of infection with a restrictive transfusion strategy [12].

There was a low overall incidence of inpatient cardiovascular events (average 0.7%) that did not significantly differ between

groups. Restrictive strategies in additional studies did not demonstrate an increase in cardiovascular events [2,17]. No postoperative deaths occurred in either group, in agreement with a systematic review, in which restrictive transfusions in 9 randomized controlled trials did not associate with a change in the relative risk of mortality [12].

Our study had several limitations. First, it was retrospective in nature, was not designed to evaluate a restrictive transfusion protocol, and the ultimate decision for transfusion may have differed between providers. Second, we did not analyze hemodynamic status or fluid management, thus we cannot ascertain to what extent fluids could have been utilized prior to transfusion. Third, 78.5% of patients were white, potentially making the study less generalizable. Fourth, while TXA was administered to almost all patients in the final year of our study, adoption increased during the study period to reflect the national standard of care. This likely contributed to a decline in both blood loss and transfusions over the study period. Fifth, we conducted an observational study, which may have been susceptible to type II error. Further study with a larger number of patients, potentially multicenter or registry study, would allow for greater statistical power. Sixth, we did not compare our anemic patients to a control group of patients without anemia to determine the standard rates of complications we studied. Nevertheless, the results seem promising and encourage revisiting institutional policies to enhance our blood management program.

In conclusion, restricting transfusions in younger, healthier anemic patients did not associate with increased adverse outcomes in our cohort of 1087 TJA patients. Our findings suggest that younger and healthier patients that experience Hb below 8 g/dl later during their hospital stay may not need to undergo transfusion solely based on Hb levels. Further study with a larger number of patients may detect differences that were not found in our cohort.

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: D. S. Iacobelli is in the editorial or governing board of *Journal of Arthroplasty*. F. Cushner receives royalties from Smith & Nephew; is in the speakers' bureau of or gave paid presentations for KCI and Orthalign; is a paid consultant for Smith & Nephew, KCI, and Orthalign; is an unpaid consultant for and has stock or stock options in Canary Medical; and receives financial or material support from Elsevier and Thieme. F. Boettner receives royalties from Orthodevelopment Inc and Smith & Nephew; is in the speakers' bureau of or gave paid presentations for DePuy, a Johnson & Johnson company, and Medtronic; is a paid consultant for DePuy, a Johnson & Johnson company, Medtronic, and Smith & Nephew; receives research support as a principal investigator from Smith & Nephew and Hospital for Special Surgery; is in the editorial or governing board of OrthoForum GmbH. J. A. Rodriguez receives

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For full disclosure statements refer to https://doi.org/10.1016/j.artd.2022.01.033.

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