Patient Blood Management Program Improves Blood Use and Clinical Outcomes in Orthopedic Surgery

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ABSTRACT

Background: Although randomized trials show that patients do well when given less blood, there remains a persistent impression that orthopedic surgery patients require a higher hemoglobin transfusion threshold than other patient populations (8 g/dl *vs.* 7 g/dl). The authors tested the hypothesis in orthopedic patients that implementation of a patient blood management program encouraging a hemoglobin threshold less than 7 g/dl results in decreased blood use with no change in clinical outcomes.

Methods: After launching a multifaceted patient blood management program, the authors retrospectively evaluated all adult orthopedic patients, comparing transfusion practices and clinical outcomes in the pre- and post-blood management cohorts. Risk adjustment accounted for age, sex, surgical procedure, and case mix index.

Results: After patient blood management implementation, the mean hemoglobin threshold decreased from 7.8 ± 1.0 g/dl to 6.8 ± 1.0 g/dl ($P < 0.0001$). Erythrocyte use decreased by 32.5% (from 338 to 228 erythrocyte units per 1,000 patients; $P = 0.0007$). Clinical outcomes improved, with decreased morbidity (from 1.3% to 0.54%; $P = 0.01$), composite morbidity or mortality (from 1.5% to 0.75%; $P = 0.035$), and 30-day readmissions (from 9.0% to 5.8%; $P = 0.0002$). Improved outcomes were primarily recognized in patients 65 yr of age and older. After risk adjustment, patient blood management was independently associated with decreased composite morbidity or mortality (odds ratio, 0.44; 95% CI, 0.22 to 0.86; $P = 0.016$).

Conclusions: In a retrospective study, patient blood management was associated with reduced blood use with similar or improved clinical outcomes in orthopedic surgery. A hemoglobin threshold of 7 g/dl appears to be safe for many orthopedic patients. **(Anesthesiology 2018; 129:1082-91)**

BLOOD transfusions are the most frequently performed hospital procedure in the United States,[1] and according to the Joint Commission in 2012, they are also one of the top five overused procedures.[2] Because of the risks, costs, and adverse outcomes associated with blood transfusions,[3–8] recent studies have focused on investigating methods to reduce the number of unnecessary transfusions performed. According to the AABB (formerly the American Association of Blood Banks), erythrocyte transfusions in hospital settings nationwide have significantly decreased (by approximately 25%) during the past 5 yr.[9,10] In particular, patient blood management programs implementing techniques such as restrictive hemoglobin triggers, clinical decision support, educational efforts, and technologic advances in surgery and blood conservation across hospitals and health systems have been effective in decreasing blood use.[11–20]

A number of reports, including nine landmark randomized controlled trials,[21–29] have investigated clinical outcomes in patients after decreased blood transfusions. These studies demonstrate that giving less blood through restrictive hemoglobin triggers results in similar outcomes for most patients or improved outcomes for some subgroups of patients. Only one of these nine studies, however, the Functional Outcomes in Cardiovascular Patients Undergoing Surgical Repair of Hip Fracture (FOCUS) trial,[27] specifically enrolled

Editor's Perspective

What We Already Know about This Topic

- A transfusion threshold of 8 g/dl of hemoglobin is considered safe for asymptomatic orthopedic surgery patients, but lower thresholds have not been tested

What This Article Tells Us That Is New

- A blood management program using a hemoglobin transfusion threshold of 7 g/dl in asymptomatic orthopedic patients reduces blood use by 32.5% and results in similar or improved clinical outcomes
- Improved outcomes occurred primarily in patients 65 yr of age and older

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orthopedic surgery patients, and these patients were elderly with hip fracture and high-risk with a high prevalence (more than 60%) of cardiovascular disease. Based primarily on this study, and several others that also included elderly high-risk patients,[30–33] recent AABB-endorsed transfusion guidelines recommend a hemoglobin trigger of 8 g/dl for orthopedic surgery patients (strong recommendation, moderate quality evidence), but a hemoglobin trigger of 7 g/dl even for critically ill hospitalized patients (also strong recommendation, moderate quality evidence[34]). The guidelines recognize, however, that a hemoglobin trigger of 7 g/dl is likely comparable to 8 g/dl, but not enough evidence is available for orthopedic patients to make this determination.

In light of this suggestion that orthopedic patients may require more liberal transfusion than other patients, and thus may be vulnerable at lower hemoglobin levels, we were specifically interested in the effect of a patient blood management program on orthopedic surgery patients. During the past 5 yr, in alignment with recent trends in blood management, our health system instituted a comprehensive patient blood management program with an aim to decrease unnecessary blood transfusion across the health system. The various methods we endorse are evidence-based best practices that result in reduced overall transfusions, and in the interest of safety and quality, we want to ensure that we are not putting our orthopedic patients at risk by giving them less blood than is needed. Therefore, we did a retrospective analysis to test the hypothesis that after implementation of a patient blood management program, orthopedic patients would receive fewer allogeneic blood transfusions without an increase in adverse outcomes.

Materials and Methods

Institutional review board approval with a waiver for written informed consent was obtained to assess changes in blood use and clinical outcomes across The Johns Hopkins Health System. The patient blood management database with clinical outcomes covers the period from January 2013 to May 2017. At The Johns Hopkins Bayview Medical Center (Baltimore, Maryland), the primary orthopedic center at our institution, the patient blood management program was phased in over time; however, for the purposes of this study, patient blood management was considered to be initiated in January 2015, when the majority of patient blood management efforts were implemented. Further details on the timing of individual interventions are outlined in the section, "Phasing In of Patient Blood Management Interventions." These methods were implemented as part of larger health system-wide patient blood management program. All patients aged 18 and over admitted to the orthopedic surgery service during this period were included in the current study. Categories of surgical procedure included hip fracture repair, hip and knee arthroplasty (primary and revision), and "other" (all patients except those mentioned). Spine surgery was not included because orthopedic spine cases are done at another hospital in our health system.

Patient Blood Management Program

The patient blood management program employed several strategies outlined in table 1, which included (1) obtaining support from hospital leadership; (2) assembling multidisciplinary teams of stakeholders and holding monthly meetings; (3) providing education based on rigorous peer-reviewed studies; (4) implementing transfusion guidelines; (5) implementing clinical decision support with best-practice advisory alerts; (6) performing data acquisition and analytics[35]; (7) creating blood use electronic dashboards[35]; (8) providing transfusion guideline compliance audit reports with feedback[15]; and (9) enacting specific methods to decrease blood use, including a "Why Give 2 When 1 Will Do?" Choosing Wisely campaign,[16] use of intraoperative antifibrinolytics (primarily tranexamic acid), anesthetic management such as controlled hypotension and maintaining normothermia, surgical methods such as newer cautery techniques,[36] topical hemostatics, and reduction of phlebotomy blood loss by using smaller tubes and reducing unnecessary laboratory test ordering. Diagnosis and treatment of preoperative anemia was not emphasized, and there was no preoperative anemia clinic in the pre- or post-patient blood management time periods.

Phasing In of Patient Blood Management Interventions

For the purposes of describing the incremental onset of our patient blood management program, we have defined four stages over time, which are (1) pre-patient blood management, before any activities began; (2) early patient blood management, when education on evidence-based transfusion practice at The Johns Hopkins Hospital campus began, and tranexamic acid at The Johns Hopkins Bayview campus

Table 1. Methods for Implementing the Patient Blood Management Program

1. Obtain support from health system leadership
2. Assemble multidisciplinary team with monthly meetings
3. Education (with emphasis on the randomized control trials supporting restrictive transfusion)
4. Implement transfusion guidelines
5. Decision support with best-practice advisories
6. Data acquisition and analytics
7. Blood management data dashboards
8. Transfusion guideline compliance audits with feedback (reports) to providers
9. Methods to improve blood use
Evidence-based transfusion triggers
"Why Give 2 When 1 Will Do?" Choosing Wisely campaign for erythrocytes
Antifibrinolytics (tranexamic acid)
Anesthetic management (*e.g.,* controlled hypotension, normothermia)
Surgical methods (*e.g.,* newer cautery methods, topical hemostatics, and sealants)
Reduce phlebotomy blood loss (smaller tubes, eliminate unnecessary testing)

Table is modified from Frank SM, *et al.* Anesthesiology 2017; 127:754–64.[20]

was introduced; (3) post-patient blood management, when harmonized transfusion guidelines across the health system, a "Why Give 2 When 1 Will Do?" single-unit transfusion campaign, data dashboards, audits for transfusion guideline compliance with feedback, and an early version of clinician decision support for hemoglobin triggers were implemented; and (4) enhanced patient blood management, when the Epic (USA) electronic record was launched with improved decision support and best-practice advisories notifying clinicians about out-of-guideline orders, as well as enhanced guideline compliance audits with feedback sent to all departments and providers. These patient blood management intervention phases are illustrated in figure 1.

Data Collection and Clinical Outcomes

Transfusion and laboratory data were collected from two platforms of electronic medical records (Meditech [USA] before September 2015, and Epic thereafter). Quality

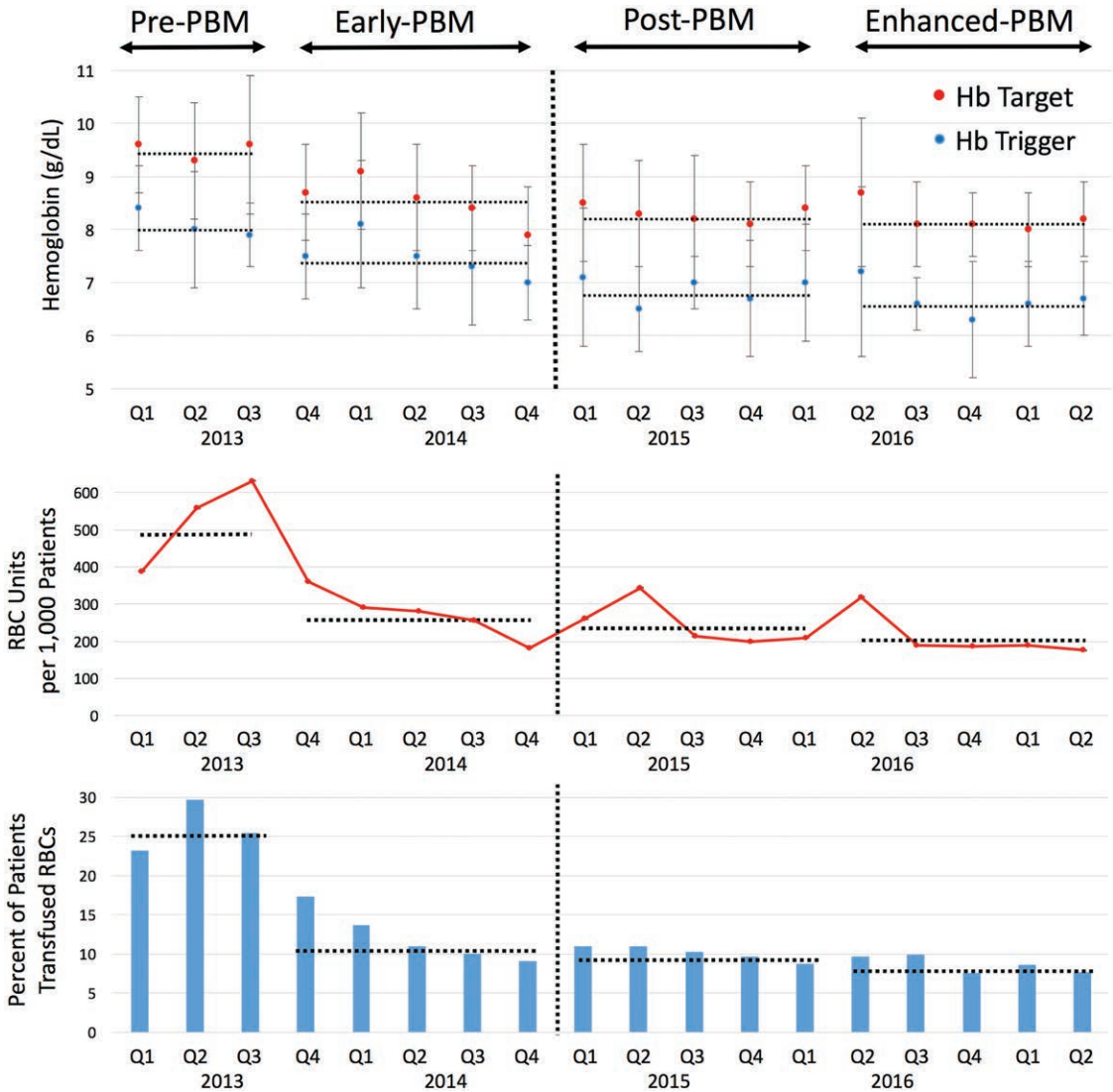

Fig. 1. Changes in hemoglobin trigger and target, number of units per 1,000 patients, and percentage of patients transfused erythrocytes are shown over time. The *vertical dotted line* divides the pre- and post-patient blood management (PBM) periods that were compared in the analysis. The *horizontal dotted lines* are averages over the four periods, which are (1) pre-PBM, before patient blood management began; (2) early PBM, when education on evidence-based transfusion practice at The Johns Hopkins Hospital campus began, and tranexamic acid at The Johns Hopkins Bayview campus was implemented; (3) post-PBM, when harmonized transfusion guidelines, a "Why Give 2 When 1 Will Do?" single-unit transfusion campaign,[16] data dashboards,[35] audits for transfusion guidelines compliance with feedback,[15] and an early version of clinician decision support for Hb triggers were implemented in the electronic record system; and (4) enhanced PBM, when the Epic (USA) electronic record was launched with improved decision support and best-practice advisories notifying clinicians about out-of-guideline orders, as well as enhanced guideline compliance audits with feedback sent to all departments and providers.[35] Of note is the decrease in mean Hb trigger from above 7 g/dl over the first two periods to less than 7 g/dl over the latter two periods. Hb, hemoglobin; RBC, erythrocyte; Q, calendar year quarter (3-month intervals). Hb concentration shown as mean ± SD.

control for these two sources was confirmed by our Clinical Analytics team and by an outside consultant, and the data were consolidated onto our blood management dashboard, as previously described.[35] Blood use data were verified by comparison with blood bank records. Clinical outcomes, as described below, were assessed with administrative data obtained from our health system's administrative database.

The primary clinical outcome assessed was composite morbidity or mortality. Secondary outcomes included (1) composite morbidity, (2) mortality (during the hospitalization), (3) length of stay, and (4) 30-day readmissions. Composite morbidity was defined as the occurrence of any of the following hospital-acquired morbid events, defined by International Classification of Diseases, Ninth Revision, or International Classification of Diseases, Tenth Revision, codes, as we have previously described.[37] Morbid events included (1) infection (*Clostridioides difficile,* sepsis, surgical site infection, or drug-resistant infection), (2) thrombotic event (deep venous thrombosis, pulmonary embolus, or disseminated intravascular coagulation), (3) kidney injury, (4) respiratory event, and (5) ischemic event (myocardial infarction, transient ischemic attack, or cerebrovascular injury). Conditions that were flagged as present on admission were not considered to be hospital-acquired morbid events.

Assessment of Blood Use

For erythrocyte-transfused patients, the lowest (nadir) hemoglobin concentration during the hospital stay was used to define the hemoglobin trigger, and the last measured hemoglobin concentration before discharge was used to define the hemoglobin target, as we have previously described.[38] Preoperative hemoglobin concentrations were unavailable in our database. Blood use was assessed two ways: (1) the percentage of patients receiving any erythrocyte units, and (2) the number of units transfused per 1,000 patients during their entire hospital stay.

Data and Statistical Analysis

The analysis was designed as a pre- and post-patient blood management comparison, comparing two periods: (1) January 2013 to December 2014, and (2) January 2015 to May 2017. The methods of analysis were planned before accessing the data, and the sample size needed was estimated on the basis of experience with morbid event rates from our previous outcome studies.[39–41] In an effort to reduce bias, analysis of blood use and clinical outcomes was first performed for the entire patient population and then by preplanned subgroup analyses with two age-defined subgroups (younger than 65 yr and 65 yr of age and older). The subgroup analysis was done to determine whether older orthopedic surgery patients showed differing results compared to younger patients, given that several previous orthopedic surgery studies made their conclusions based on elderly patients alone.

We performed a multivariable logistic regression to assess the risk-adjusted effect of the patient blood management program on adverse outcomes (any morbidity or mortality). The independent variables entered into the model for risk adjustment were age, case mix index (weighted All Patients Refined–Diagnosis-Related Groups), hip fracture, surgical procedure, and sex. We chose the weighted All Patients Refined–Diagnosis-Related Groups since this variable accounts for both complexity of procedure and severity of illness, and it correlates with both transfusion requirements[42] and clinical outcomes.[43] The logistic regression model included those independent variables that were (1) the design variable in the study (pre- and post-patient blood management), (2) variables that have been linked to outcomes in previous studies, or (3) variables with $P < 0.1$ on univariate analysis.

Continuous data are given as mean ± SD or median (interquartile range) if normally or not normally distributed, respectively. Ordinal and nominal values are given as percentages. Means were compared by unpaired Student's *t* tests, and medians by Mann–Whitney U tests, while percentages were compared by chi-square tests or the Fisher exact test when the numerator had five or fewer patients or events. Analyses were generated with JMP version 12.1.0 and SAS version 9.4.2 (SAS Institute, USA). For all analyses, $P < 0.05$ (two-tailed) was considered significant.

Sensitivity Analysis

To further control for confounding, we performed a sensitivity analysis using a propensity score, derived for each individual on the basis of the predictor variables from a multivariable logistic regression as the probability of being in the post-patient blood management group. These variables included age, sex, case mix index, hip fracture, and hip or knee arthroplasty. After adjustment, by forcing propensity score into the multivariable model, the association of patient blood management with composite morbidity or mortality was recalculated.

Results

There were 1,507 patients in the pre-patient blood management cohort and 2,402 patients in the post-patient blood management cohort. The clinical characteristics between the two groups are shown in table 2. Mean age was 1 yr older in the post-patient blood management cohort, and there was no change in male and female sex distribution. Case mix index assessed by median weighted All Patients Refined–Diagnosis-Related Groups was slightly but significantly decreased in the post-patient blood management cohort, indicating a small decrease in aggregate severity of illness and/or complexity of procedure. The percentage of patients requiring surgery for hip fracture was similar in the two periods. The percentage of patients undergoing total hip arthroplasty increased in the post-patient blood management period. The percentage of revision total joint

Table 2. Patient Characteristics before and after Patient Blood Management (All Patients)

Parameter	Pre-patient Blood Management (n = 1,507)	Post-patient Blood Management (n = 2,402)	*P* Value
Age, yr, mean ± SD	61 ± 16	62 ± 15	0.010
Age ≥ 65 yr, n (%)	620 (41.1)	1,042 (43.4)	0.17
Sex, n (% male)	685 (45.5)	1,114 (46.4)	0.57
CMI, median (IQR)	1.89 (1.65–1.98)	1.84 (1.53–1.98)	< 0.0001
Patient category, n (%)			
Hip fracture	124 (8.2)	194 (8.1)	0.87
Total hip	321 (21.3)	647 (26.9)	< 0.0001
Total knee	490 (32.5)	818 (34.1)	0.32
Total hip revision	49 (3.3)	81 (3.4)	0.84
Total knee revision	39 (2.6)	48 (2.0)	0.23
Other orthopedic	484 (32.1)	614 (25.6)	< 0.0001

CMI, case mix index (All Patient Refined–Diagnosis-Related Groups).

Table 3. Blood Use and Clinical Outcomes before and after Patient Blood Management (All Patients)

Parameter	Pre-patient Blood Management (n = 1,507)	Post-patient Blood Management (n = 2,402)	*P* Value
Trigger Hb, g/dl*, mean ± SD	7.8 ± 1.0	6.8 ± 1.0	< 0.0001
Target Hb, g/dl*, mean ± SD	9.0 ± 1.1	8.3 ± 1.0	< 0.0001
% Tx RBC, n (%)	242 (16.1)	226 (9.4)	< 0.0001
RBC units/1,000 patients	338	228	0.0007
LOS, days, median (IQR)	3 (1–4)	2 (1–3)	< 0.0001
Morbidity, n (%)	20 (1.3)	13 (0.54)	0.01
Mortality, n (%)	2 (0.13)	6 (0.25)	0.72
Morbidity or mortality, n (%)	22 (1.5)	18 (0.75)	0.035
30-day readmit†, n (%)	133 (9.0)	135 (5.8)	0.0002

*Trigger is defined as the nadir Hb during the hospital stay, and target as the last measured Hb before discharge. †Twenty-six patients in the pre-patient blood management period and 79 patients in the post-patient blood management period had missing data for this outcome.

Hb, hemoglobin; LOS, length of stay; RBC, erythrocyte; Tx, transfused.

arthroplasty patients was similar in the two cohorts. The number of patients having "other" procedures decreased in the post-patient blood management cohort.

The phasing in of different patient blood management program interventions over time along with changes in hemoglobin trigger and target, percentage of patients transfused, and mean number of units per patient are shown in figure 1. There was an incremental stepwise decrease in each parameter shown for each of the four periods. The changes shown in the early patient blood management phase are likely due to education at The Johns Hopkins Hospital campus, which carried over to the Bayview campus (as they share staff), and perioperative tranexamic acid use. Of significance is the average hemoglobin trigger, which was more than 7 g/dl during the first two periods and less than 7 g/dl during the second two periods.

Changes in blood use between the pre- and post-patient blood management time periods are shown in table 3. The mean hemoglobin transfusion trigger decreased by 1 g/dl, and the mean hemoglobin target decreased by 0.7 g/dl (both $P < 0.0001$). The percentage of patients transfused erythrocytes decreased from 16.1% to 9.4% ($P < 0.0001$), and there was a 32.5% decrease in the number of erythrocyte units per 1,000 patients ($P = 0.0007$). The percentages of patients transfused plasma (pre-patient blood management 1.6% *vs.* post-patient blood management 1.4%; $P = 0.66$) and platelets (pre-patient blood management 0.53% *vs.* post-patient blood management 0.37%; $P = 0.48$) were low and unchanged.

Clinical outcomes comparing the pre- and post-patient blood management periods are also shown in table 3. The composite outcome of any morbidity or mortality (primary outcome) decreased by half ($P = 0.035$). The median (interquartile range) length of stay decreased by 1 day ($P < 0.0001$). The morbid event rate decreased by more than half ($P = 0.01$), and mortality was unchanged ($P = 0.72$). The 30-day readmission rate significantly decreased from 9.0% to 5.8% ($P = 0.0002$). In the pre- and post-patient blood management periods, 26 patients and 79 patients had missing readmission data, respectively. In summary, when all adult orthopedic patients are included (both young and old cohorts), the implementation of patient blood management was associated with improvement in all measured outcomes, except for mortality, which remained unchanged.

Clinical characteristics for the younger and older subgroups are shown in table 4. Mean age was approximately 25 yr greater in the older (65 yr old and older) subgroup. Median case mix index was slightly but significantly decreased in the post-patient blood management period for both age subgroups. The percentage of patients requiring surgery for hip fracture was similar in the pre- and post-patient blood management periods for both subgroups. The percentage of patients undergoing total hip arthroplasty increased in the post-patient blood management period for both subgroups.

Changes in blood use and clinical outcomes are shown for the younger and older subgroups in table 5. The percentage of patients transfused decreased post-patient blood management in both subgroups; however, erythrocyte use (erythrocyte units per 1,000 patients) decreased significantly in the older subgroup only (by 43%; $P < 0.0001$). Median length of stay decreased by 1 day for both the younger and older subgroups in the post-patient blood management period (both $P < 0.0001$). Morbidity was unchanged in the younger subgroup but decreased in the older subgroup in the post-patient blood management period ($P = 0.039$). Mortality remained unchanged in both younger and older subgroups, as did the composite outcome (morbidity or mortality). The 30-day readmission rate was unchanged in the younger subgroup, but for the older subgroup, there was a decrease in readmission rate post-patient blood management ($P < 0.0001$). In summary, the improved outcomes with patient blood management were more apparent in the

Table 4. Patient Characteristics before and after Patient Blood Management (Younger and Older Subgroups)

	Younger Patients (<65 yr; n = 2,247)			Older Patients (≥65 yr; n = 1,662)		
Parameter	Pre-patient Blood Management (n = 887)	Post-patient Blood Management (n = 1,360)	*P* Value	Pre-patient Blood Management (n = 620)	Post-patient Blood Management (n = 1,042)	*P* Value
Age, yr, mean ± SD	51 ± 12	52 ± 11	0.009	75 ± 8	75 ± 8	0.93
Sex, n (% male)	488 (55.0)	701 (51.5)	0.11	197 (31.8)	412 (39.6)	0.001
CMI, median (IQR)	1.84 (1.65–1.98)	1.70 (1.51–1.98)	< 0.0001	1.89 (1.65–2.04)	1.84 (1.58–1.98)	< 0.0001
Patient category, n (%)						
Hip fracture	25 (2.8)	46 (3.4)	0.45	99 (16.0)	148 (14.2)	0.31
Total hip	207 (23.3)	396 (29.1)	0.002	114 (18.4)	251 (24.1)	0.006
Total knee	279 (31.5)	435 (32.0)	0.79	211 (34.0)	383 (36.8)	0.26
Total hip revision	30 (3.4)	41 (3.0)	0.63	19 (3.1)	40 (3.8)	0.40
Total knee revision	20 (2.3)	26 (1.9)	0.58	19 (3.1)	22 (2.1)	0.23
Other orthopedic	326 (36.8)	416 (30.6)	0.003	158 (25.5)	198 (19.0)	0.002

CMI, case mix index (All Patients Refined–Diagnosis-Related Groups).

Table 5. Blood Use and Clinical Outcomes before and after Patient Blood Management (Younger and Older Subgroups)

	Younger Patients (<65 yr; n = 2,247)			Older Patients (≥65 yr; n = 1,662)		
Parameter	Pre-patient Blood Management (n = 887)	Post-patient Blood Management (n = 1,360)	*P* Value	Pre-patient Blood Management (n = 620)	Post-patient Blood Management (n = 1,042)	*P* Value
Trigger Hb, g/dl*, mean ± SD	7.9 ± 1.0	6.7 ± 0.9	< 0.0001	7.8 ± 1.0	6.9 ± 1.1	< 0.0001
Target Hb, g/dl*, mean ± SD	9.0 ± 1.3	8.1 ± 0.9	< 0.0001	9.0 ± 1.1	8.3 ± 1.0	< 0.0001
% Tx RBC, n (%)	89 (10.0)	86 (6.3)	0.0015	153 (24.5)	139 (13.4)	<0.0001
RBC units/1,000 patients	192	163	0.39	547	313	0.0001
LOS, days, median (IQR)	2 (1–3)	1 (1–3)	< 0.0001	3 (2–4)	2 (1–4)	< 0.0001
Morbidity, n (%)	8 (0.9)	5 (0.4)	0.15	12 (1.9)	8 (0.8)	0.039
Mortality, n (%)	1 (0.1)	1 (0.1)	1.0	1 (0.2)	5 (0.5)	0.42
Morbidity or mortality, n (%)	9 (1.0)	6 (0.4)	0.11	13 (2.1)	12 (1.2)	0.13
30-day readmit†, n (%)	62 (7.1)	74 (5.6)	0.15	71 (12)	61 (6.1)	< 0.0001

In the older patient cohort, 17 patients in the pre-patient blood management period and 38 patients in the post-patient blood management period had missing data for this outcome.

*Trigger is defined as the nadir Hb during the hospital stay, and target as the last measured Hb before discharge. †In the younger patient cohort, 9 patients in the pre-patient blood management period and 41 patients in the post-patient blood management period had missing data for this outcome.

Hb, hemoglobin; LOS, length of stay; RBC, erythrocyte; Tx, transfused.

older patient subgroup (age 65 yr or older), whereas in the younger patients, the outcomes were unchanged.

In the multivariable model with risk adjustment for age, case mix index, sex, hip fracture, and type of surgery, there were reduced odds of an adverse outcome (composite morbidity or mortality; odds ratio, 0.44; 95% CI, 0.22 to 0.86; $P = 0.016$) in the post-patient blood management period than in the pre-patient blood management period (table 6). Case mix index, hip fracture, and total joint arthroplasty were also independent predictors of adverse outcomes, but age and sex were not. These findings indicate that patient blood management was associated with improvement in clinical outcomes even after adjustment for these potential confounders. On sensitivity analysis using risk adjustment with propensity scores in the logistic regression model, the results remained robust, and patient blood management remained associated

Table 6. Multivariable Logistic Regression—Predictors of Adverse Outcome (Morbidity or Mortality)

Parameter	Odds Ratio	95% CI	*P* Value
Age, <65 yr/≥65 yr	1.57	(0.74–3.38)	0.24
Sex, male/female	0.92	(0.45–1.90)	0.82
CMI, per unit change in regressor	3.66	(2.59–5.32)	< 0.0001
Hip fracture	3.28	(1.39–7.81)	0.0067
Total joint arthroplasty	0.31	(0.13–0.74)	0.008
Pre- / Post-patient blood management	0.44	(0.22–0.86)	0.016

On sensitivity analysis when adding propensity score into the above model, the results remained robust, and patient blood management was associated with a decrease in the composite adverse outcome (morbidity or mortality; odds ratio, 0.37; 95% CI, 0.18–0.74; $P = 0.005$).

CMI, case mix index (All Patients Refined–Diagnosis-Related Groups).

with a decrease in the composite outcome (morbidity or mortality; odds ratio, 0.37; 95% CI, 0.18 to 0.74; $P = 0.005$).

Discussion

The results of this study demonstrate that for orthopedic surgery patients, a comprehensive patient blood management program is a successful method for significantly reducing blood use, while maintaining or improving clinical outcomes. Even after age and risk adjustment in the post-patient blood management cohort, patients did just as well or better with a lower hemoglobin trigger and target, resulting in an overall decrease in the percentage of patients transfused and erythrocyte units transfused per patient. Importantly, morbidity, length of stay, and readmission rates all improved, while mortality was unchanged. It is likely that with the overall low incidence of mortality (about 2 per 1,000 patients), the sample size was too small and/or the patients too healthy to assess mortality. Regarding age, the older patients showed more benefit than younger patients with the changes in transfusion practice, perhaps because both morbidity and readmissions occurred with about half the frequency at baseline in the younger subgroup. The finding that older patients do as well or better with a restrictive transfusion strategy than with a liberal strategy is also supported by clinical trials in orthopedic[27] and cardiac surgery.[29]

The FOCUS trial,[27] published in 2011, enrolled more than 2,000 hip fracture patients, who were randomized to hemoglobin triggers of 8 or 10 g/dl, and the primary result was no difference in any of the major outcomes. Our study also included orthopedic patients, although the mean age of our patients was about 20 yr younger than the mean age in the FOCUS trial (61 yr *vs*. 83 yr). This age difference is likely because elderly patients are more prone to hip fractures, and the FOCUS inclusion criteria specified a history of risk factors for cardiovascular disease. Our study's results are in agreement with the results of the FOCUS trial,[27] in that a restrictive transfusion strategy is safe in orthopedic patients, with the caveat (from both studies) that symptomatic anemia and not just hemoglobin concentration be used as criteria for transfusion. However, our results differ from the FOCUS results because we describe a decrease to an even lower hemoglobin threshold for transfusion (less than 7 g/dl rather than less than 8 g/dl). Our results also differ in that we showed improvement in some clinical outcomes. Even the older subgroup in our analysis had the same or better outcomes with this lower hemoglobin threshold. Granted, even our older subgroup (mean age 75 yr) was still younger than the average FOCUS patient (83 yr), but our findings suggest that a blanket statement for orthopedic patients to be transfused at a hemoglobin trigger of 8 g/dl is overstated.

The findings in the current study have implications regarding the most recent AABB transfusion guidelines,[34] where 8 g/dl is suggested as the ideal trigger for orthopedic patients, with a statement recognizing that 7 g/dl *versus* 8 g/dl has not been compared. Of interest is the average hemoglobin trigger above 7 g/dl, decreasing to less than 7 g/dl, in what we defined as the pre- and post-patient blood management periods in our study (fig. 1). It should be recognized that before blood management, approximately one third of all erythrocyte transfusions at our institution were ordered with a preceding hemoglobin concentration between 7 and 8 g/dl.[15,35] Thus, when Choosing Wisely and AABB guidelines recommend a hemoglobin threshold between 7 and 8 g/dl,[34,44] this leaves a substantial number of transfusions that could potentially be avoided with preceding hemoglobin levels between 7 and 8 g/dl. Perhaps the best conclusion is that we treat the whole patient, and not just their laboratory values. In fact, the FOCUS trial allowed transfusion in the restrictive group even when the hemoglobin was more than 8 g/dl, if symptoms of anemia were present (cardiac chest pain, congestive heart failure, or tachycardia or hypotension unresponsive to fluid), and our hospital guidelines are similar. In fact, about 15% of patients assigned to the FOCUS trial restrictive group were transfused for such symptoms. The same criteria would be important to consider as indications for transfusion if a hemoglobin threshold of 7 g/dl was to be used for orthopedic patients.

Other studies that describe a before and after patient blood management analysis of outcomes include the study by Goodnough *et al.*,[45] who retrospectively investigated clinical outcomes across all patients hospital-wide after starting a blood management program. These investigators noted similar trends but slightly different results than ours, with an improvement in mortality rates and unchanged readmission rates, yet a similar reduction in mean erythrocyte units per patient (≈25 to 30%). Another recent study by Leahy *et al.*[19] retrospectively examined blood use and patient outcomes after a health system–wide patient blood management program. In this study, which also included all hospitalized patients, they noted a decrease in erythrocyte transfusions (≈40%), as well as a decrease in hemoglobin trigger and length of stay; however, they also noted a decrease in mortality. A patient blood management program specifically for hip and knee arthroplasty patients showed a 30 to 50% decrease in percentage of patients transfused, along with a decreased length of stay.[46] Interestingly, their patient blood management methods included postoperative blood salvage and postoperative intravenous iron, which were not included in our patient blood management program. Tranexamic acid was also used.

Other orthopedic studies on transfusion triggers have assessed ability to ambulate,[47] quality of life,[48] delirium,[32] cardiac ischemia,[49] and infections,[31] and these studies almost universally found no benefit to liberal transfusion; however, the hemoglobin transfusion triggers ranged from 8 to 11.3 g/dl. To our knowledge, ours is the first study in orthopedics to assess hemoglobin thresholds as low as 7 g/dl. Given the potential risk of anemia from undertransfusion in the era of patient blood management, our findings are reassuring in this regard. Certainly, monitoring for undertransfusion should be considered in a patient blood management program,

since severe anemia can result in impaired oxygen delivery with an increase in ischemic events and/or mortality.[50,51]

There are some limitations that should be recognized in our study. In a retrospective observational analysis, controlling for multiple confounding variables that change over time or issues such as missing data is challenging, and identifying a true causal effect of a patient blood management program on blood use and clinical outcomes is not possible. There may have also been unreported changes, such as quality improvement efforts in surgical practice, some of which are designed, for example, to decrease length of stay. Cohort characteristics were relatively similar before and after patient blood management, with the exceptions of an increase in the proportion of total hip replacements, a small increase in age, and a small decrease in case mix index. Furthermore, since all adult orthopedic inpatients were included, there were likely a considerable number of low-risk (primarily younger) patients in our study population. Interestingly, however, there appeared to be more improvement for clinical outcomes in the older subgroup of patients (65 yr and older). Thus, we can only say that in the setting of our current orthopedic care standards, patient blood management was associated with decreased blood use and similar or better outcomes, without a clear causal relationship to outcomes. In addition, after adding surgical procedure (total joint and hip fracture) to the multivariable model, the risk-adjusted odds ratio showing decreased adverse clinical outcome remained significant. The exact beginning of patient blood management is difficult to determine because there were 10 or more methods that were implemented in a gradual, stepwise fashion (fig. 1). For the purposes of the outcomes analysis, we chose to define the start as when pre-patient blood management activities were completed and the majority of the primary interventions had been initiated. Of note is the mean hemoglobin trigger, decreasing from above to less than 7 g/dl when our pre- and post-time periods are compared. Regarding the various different patient blood management methods, we cannot clearly determine the most impactful initiatives because many of them were implemented as a "bundle." Because preoperative anemia is associated with increased transfusion and adverse outcomes,[52] but was not specifically addressed in our study, we are unable to comment on the importance of anemia management. Tranexamic acid for total joints was phased in gradually at least 1 yr before these interventions. The single-center nature of this study is also a limitation, as results in other centers may differ from ours. Other centers may have sicker or older patients, such as those with hip fractures, which result in a higher-risk population, like that in the FOCUS trial. In fact, our overall adverse event rates were lower than those reported in other studies.

In conclusion, our results suggest that patient blood management is efficacious for orthopedic patients and that a hemoglobin trigger of 7 g/dl rather than 8 g/dl is well tolerated, even by elderly patients on an orthopedic service. Our study adds to the growing body of literature regarding the efficacy of patient blood management programs on reducing transfusion overuse while maintaining good outcomes. By reducing risks and costs while improving outcomes, we can promote high-value practice with effective patient blood management programs.

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Competing Interests

Dr. Frank has been on advisory boards for Haemonetics (Braintree, Massachusetts) and Medtronic (Minneapolis, Minnesota). The other authors declare no competing interests.

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