Predicting Perioperative Transfusion in Elective Hip and Knee Arthroplasty

A Validated Predictive Model

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ABSTRACT

Background: Preoperative anemia is a significant predictor of perioperative erythrocyte transfusion in elective arthroplasty patients. However, interactions with other patient and procedure characteristics predicting transfusion requirements have not been well studied.

Methods: Patients undergoing elective primary total hip arthroplasty or total knee arthroplasty at a tertiary hospital in Adelaide, South Australia, Australia, from January 2010 to June 2014 were used to identify preoperative predictors of perioperative transfusion. A logistic regression model was developed and externally validated with an independent data set from three other hospitals in Adelaide.

Results: Altogether, 737 adult patients in the derivation group and 653 patients in the validation group were included. Binary logistic regression modeling identified preoperative hemoglobin (odds ratio, 0.51; 95% CI, 0.43 to 0.59; $P < 0.001$ for each 1 g/dl increase), total hip arthroplasty (odds ratio, 3.56; 95% CI, 2.39 to 5.30; $P < 0.001$), and females 65 yr of age and older (odds ratio, 3.37; 95% CI, 1.88 to 6.04; $P = 0.01$) as predictors of transfusion in the derivation cohort.

Conclusions: Using a combination of patient-specific preoperative variables, this validated model can predict transfusion in patients undergoing elective hip and knee arthroplasty. The model may also help to identify patients whose need for transfusion may be decreased through preoperative hemoglobin optimization. **(Anesthesiology 2017; 127:317-25)**

PREOPERATIVE anemia is a significant predictor for requiring postoperative blood transfusion.[1–6] These transfusions increase costs *via* direct costs of blood and resources required to process and administer and *via* indirect costs through associated increased length of stay and infection. Additional risks associated with transfusion include transfusion-related acute lung injury, transfusion-associated circulatory overload, and transfusion-transmitted infections.[6–8]

As a result, patient blood management (PBM) programs have sought to identify and manage predisposing factors for postoperative blood transfusion. PBM programs have optimization of preoperative hemoglobin, minimizing blood loss through improved surgical techniques, including the use of tranexamic acid, and application of restrictive transfusion thresholds[9–13] as the three key strategies. Of these, preoperative hemoglobin concentration is the strongest predictor and remains the most readily modifiable patient risk factor leading to a major focus on optimizing hemoglobin concentrations before surgery.[14–17]

What We Already Know about This Topic

- Anemia is a predictor of transfusion, but other predictive factors are less well established
- A logistic model was developed in 737 patients having hip or knee replacements, and validated in 653 other patients

What This Article Tells Us That Is New

- Preoperative hemoglobin and hip (rather than knee) replacement predicts transfusion requirement
- There was an interaction between age and gender, with transfusions being more often given in women more than 65 yr old

While this strategy is largely accepted as best practice, there has been little understanding of what the optimum preoperative hemoglobin target is other than a normal hemoglobin. However, this does not take into account the observation that the need for transfusion is continuous and not bimodal, which a single threshold would imply; although the transfusion rate is lower in nonanemic patients, they are still transfused. This pattern suggests that there is an incremental,

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inverse relationship between preoperative hemoglobin and need for transfusion.[18–21] A range of hemoglobin thresholds has been suggested, but a model that suggests a more specific hemoglobin target based on comorbidities, age, gender, and procedure type may better capture the variable level of transfusion need. The aim of the study was to develop a model using preoperative factors to predict erythrocyte transfusion in patients undergoing primary hip and knee arthroplasty.

Materials and Methods

The study was approved by the Royal Adelaide Hospital Human Research Ethics Committee (Adelaide, South Australia, Australia; approval No. R20160227). All data were collected retrospectively, and analysis was completed using deidentified data.

Derivation Cohort

The Royal Adelaide Hospital is a tertiary referral hospital in South Australia with an orthopedic surgery service that performs both emergency and elective lower-limb arthroplasty surgery. The Orthopaedic Patient Management Outcomes Documentation Database (OPMOD) is a centralized database of procedures performed by the Department of Orthopaedic and Trauma Services at the Royal Adelaide Hospital. It collects patient demographic data including indications for surgery, postoperative complications, and date of discharge.

Patient demographic data were extracted from OPMOD for patients who underwent elective primary hip or knee joint arthroplasty between January 2010 and June 2013. Extracted data included date of birth, sex, date of operation, procedure performed (total hip arthroplasty or total knee arthroplasty), and indication for surgery. Patients were excluded if surgery was the result of trauma, revision of a previous arthroplasty, or required for acute fracture management or malignant bone disease. Hence only primary elective arthroplasty was selected to reduce sample heterogeneity.

Preoperative hemoglobin concentration levels were extracted from a centralized laboratory database for all patients. The Network for Advancement of Transfusion Alternatives guidelines[14] recommend preoperative hemoglobin concentration level screening as close to 28 days of operation date; however, preoperative assessments are usually conducted within 5 weeks at the Royal Adelaide Hospital. For this reason, patients who did not have a hemoglobin concentration level recorded in the 35 days before their surgery were excluded.

The American Society of Anesthesiologists (ASA) Physical Classification Status,[22] which assesses the physical status of the patient before surgery, was extracted from the operating room management information system used by the theaters. Previous studies[23–25] have identified ASA status as a predictor of transfusion, and patients who did not have this recorded were excluded. Erythrocyte transfusion use for the month before surgery to the end of the acute hospital admission was extracted from electronic transfusion medicine records. A hemoglobin of at least 13 g/dl in males and at least 12 g/dl in females was considered normal hemoglobin using the World Health Organization definition.

Validation Cohort

The validation cohort consisted of patients operated on at three other hospitals in Adelaide, South Australia, Australia (Repatriation General Hospital, Queen Elizabeth Hospital, and Lyell McEwin Hospital) between July 2013 and June 2014. A different time period was used based on data availability at the time. Patient demographic, procedure type using International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD AM-10), preoperative hemoglobin concentration, and transfusion data were obtained from the South Australia Blood Utilisation database. This links South Australian public hospital morbidity with pathology data sets of the statewide pathology service.

Statistical Analysis

Statistical calculations were performed using Stata 14.1 (Stata Corp, USA). The probability of erythrocyte transfusion was modeled using the binary logistic regression model using the derivation cohort from a single hospital. Age (as a flag whether patient was 65 yr and older or not), gender, preoperative hemoglobin, ASA score (as categorical variable), and procedure were examined to be included in the model as predictors. We also included interaction term between age and sex to improve the model fit; however, other interaction terms among variables included in the final model were not considered nor examined to be included in the final model. A backward selection method was employed, and a variable was not included in the final model if the variable does not have *P* values of less than 0.05 in adjusted model. The preoperative hemoglobin (g/dl) was tested for the linearity assumption before being included as a continuous variable in the logistic regression model; then to satisfy the linearity assumption, preoperative hemoglobin was grouped as: 7 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, and 16 and over, and then included as a continuous variable. The estimated model was validated using the validation cohort (*i.e.*, data from other three hospitals). The probability of transfusion was calculated as:

$$\mathrm{P}(\text{Transfusion}) = 1/(1+\exp\left(-\begin{pmatrix} \mathrm{a}+\mathrm{b1}\times\mathrm{Hb}+\mathrm{b2}\times\text{total hip arthroplasty}+ \\ \mathrm{b3}\times\text{age65}+\mathrm{b4}\times\text{female}+\mathrm{b5}\times\text{age65}\#\text{female}\end{pmatrix}\right))$$

where a is the constant estimated using the derivation data set, b1 to b5 are coefficients estimated using the derivation data set for preoperative hemoglobin rounded down as described above, total hip arthroplasty flag (1 for total hip arthroplasty, 0 for total knee arthroplasty), age flag (0 for under 65, 1 for 65 and over), female flag (1 for female, 0 for male), and flag for females 65 yr and over (1 for 65 years old and older and female, 0 for others). A predictive model using an additional age category of 85 yr and older was also performed using the same methodology described above.

The model fit for derivation cohorts were examined using Pearson's goodness-of-fit test, and the area under the receiver operating curve was estimated for both the derivation cohort and the validation cohort. Relative risk reduction (RRR) was calculated as the difference in absolute risk reduction in transfusion need between two selected preoperative hemoglobin concentrations divided by the transfusion need for the lower of the two selected preoperative hemoglobin concentrations.

Results

Derivation Cohort

The OPMOD data listed 1,610 patients during the study period with figure 1 showing the number of patients excluded from the study and the reasons for exclusion. Of the 911 eligible patients, complete data were available for 737 patients. The median age of patients was 70 yr (interquartile rage [IQR] = 63 to 77) with 524 (71%) above the age of 65 yr. Of all the patients, 56% (415) were female, and 47% underwent total knee arthroplasty. Poor physical condition (ASA score III or IV) was diagnosed in 314 (43%), whereas an ASA score of I or II was diagnosed in 423 (57%). Patients excluded due to missing ASA status or preoperative hemoglobin data were statistically similar in age and gender but with a greater proportion undergoing total knee arthroplasty.

The median preoperative hemoglobin concentration levels for the different groups undergoing total hip arthroplasty and total knee arthroplasty are shown in table 1. In total, 19% of females and 22% of males were anemic. Univariate analysis showed that higher preoperative hemoglobin levels were found in patients who were male, younger, and had lower ASA scores; however, the absolute differences were small. There was no difference in preoperative hemoglobin concentrations levels between total hip arthroplasty and total knee arthroplasty patients.

A total of 184 (25%) of patients were transfused. Female patients, those undergoing total hip arthroplasty, and patients 65 yr and older with higher ASA scores had higher rates of transfusion (table 2). In addition, 55 and 38% of female and male anemic patients, respectively, were transfused, compared to 24 and 10% in nonanemic patients.

Logistic regression showed that the variables associated with erythrocyte transfusion were preoperative hemoglobin concentration (odds ratio [OR], 0.51; 95% CI, 0.43 to 0.59; $P < 0.001$ for each 1 g/dl increase) and primary total hip arthroplasty (OR, 3.56; 95% CI, 2.39 to 5.30; $P < 0.001$). ASA score was not significantly associated with transfusion and was thus excluded from the final model. There was a significant interaction between age and gender, with females 65 yr and older having a higher transfusion rate (OR, 3.37; 95% CI, 1.88 to 6.04; $P < 0.001$) compared to males 65 yr and older (OR, 1.01; 95% CI, 0.46 to 2.18; $P = 0.99$) or females less than 65 yr old (OR,

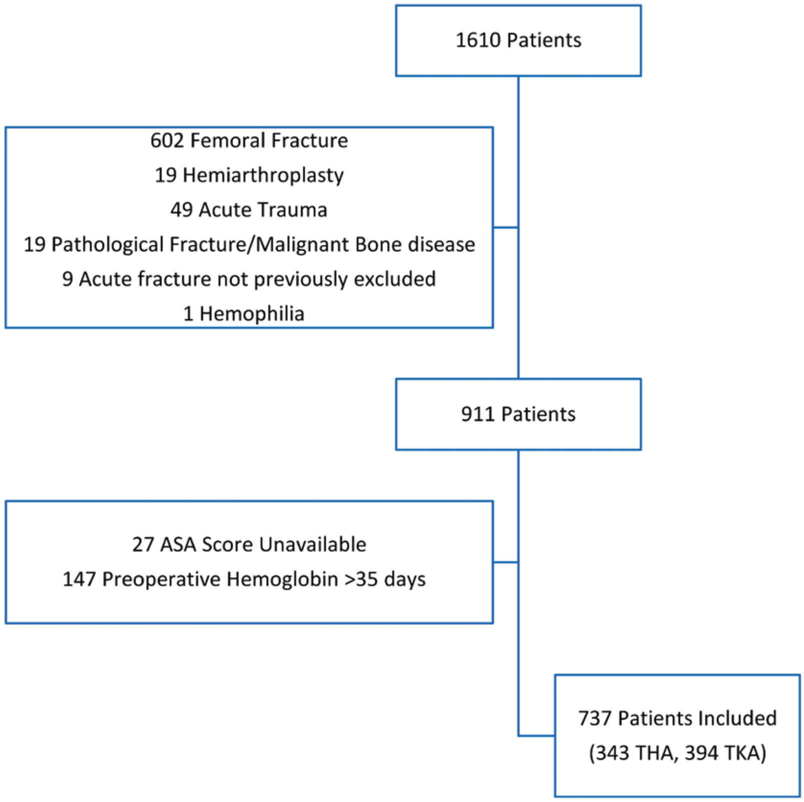


Fig. 1. Flow chart of patient selection in derivation group. ASA = American Society of Anesthesiologists; THA = total hip arthroplasty; TKA = total knee arthroplasty.

Table 1. Summary of Preoperative Hemoglobin by Age Category, Gender, Procedure, and ASA Status of the Derivation Cohort

	N	Median Preoperative Hemoglobin, g/dl (IQR)	*P* Value
All	737	13.6 (12.5–14.6)	
Male	322	14.4 (12.2–15.3)	< 0.001
Female	415	13.2 (12.2–14.0)	
THA	343	13.6 (12.3–14.6)	0.34
TKA	394	13.5 (12.7–14.6)	
ASA I	32	13.1 (12.4–14.5)	0.001
ASA II	391	13.7 (12.7–14.8)	
ASA III	302	13.4 (12.3–14.5)	
ASA IV	12	12.1 (11.3–14.0)	
< 65 yr	212	13.8 (12.7–15.0)	0.009
≥ 65 yr	525	13.5 (12.4–14.5)	

ASA = American Society of Anesthesiologists; IQR = interquartile range; THA = total hip arthroplasty; TKA = total knee arthroplasty.

0.64; 95% CI, 0.27 to 1.50; $P = 0.30$). Adding an additional category of 85 yr and older in age did not change the model.

Using the final model, figures 2 and 3 show that there is an inverse relationship between preoperative hemoglobin concentration and incidence of transfusion; patients with a lower preoperative hemoglobin have a higher probability of transfusion than patients with higher preoperative hemoglobin. Furthermore, the probability of transfusion is also influenced by sex and age combinations (females 65 yr and older, females less than 65 yr old, males 65 yr and older, and males less than 65 yr old) and procedure type. For both total hip arthroplasty and total knee arthroplasty, females 65 yr and older had the highest probability of transfusion followed by males, both less than 65 yr old and 65 yr and older, and females less than 65 yr old for any hemoglobin concentration.

Table 2. Summary of Derivation Patients Transfused by Age Category, Gender, Procedure, ASA Status, and Preoperative Hemoglobin

		Transfused	
	N	N (%)	*P* Value
All	737	184 (25)	
Male	322	52 (16)	< 0.001
Female	415	132 (32)	
THA	343	123 (36)	< 0.001
TKA	394	61 (14)	
ASA I	32	5 (16)	0.03
ASA II	391	84 (21)	
ASA III	302	91 (30)	
ASA IV	12	4 (33)	
<65 yr	212	16 (8)	< 0.001
≥65 yr	525	149 (28)	
Preoperative hemoglobin (g/dl)			
< 10	10	10 (100)	< 0.001
10–10.9	12	8 (67)	
11–11.9	88	42 (48)	
12–12.9	133	47 (35)	
13–13.9	192	50 (26)	
14–14.9	167	22 (13)	
15–15.9	87	4 (5)	
16+	48	1 (2)	

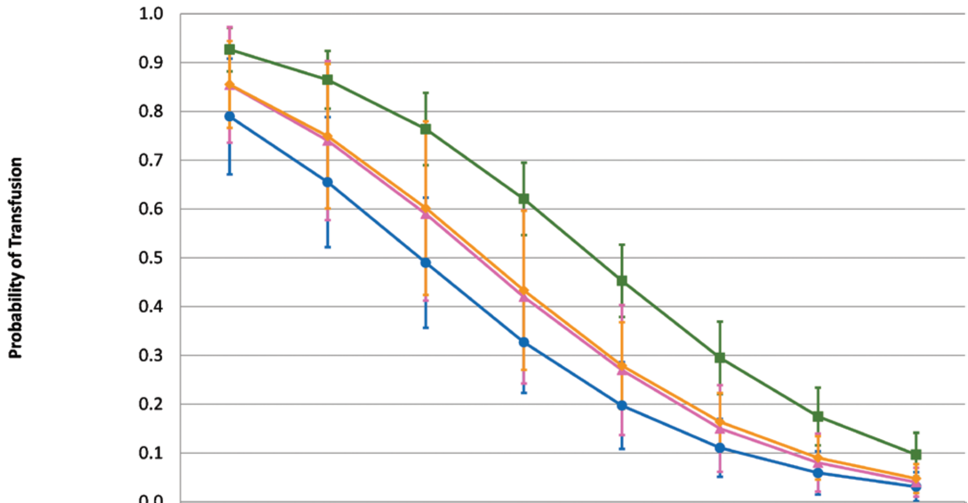
ASA = American Society of Anesthesiologists; THA = total hip arthroplasty; TKA = total knee arthroplasty.

The overall rate of transfusion in total knee arthroplasty patients was lower than in total hip arthroplasty. In females 65 yr and older undergoing total hip arthroplasty, there was a predicted RRR of 18% in transfusion requirement between patients with preoperative hemoglobin of 9 g/dl compared with patients with preoperative hemoglobin of 11 g/dl. This increased to 52% when compared with patients with preoperative hemoglobin of 13 g/dl. For females less than 65 yr old, the predicted RRR was 38 and 75% for a preoperative hemoglobin of 9 g/dl compared to 11 g/dl and 13 g/dl, respectively. In patients undergoing total knee arthroplasty, older females were also most likely to require transfusion, followed by younger and older males (same rate for both older and younger) and then younger females. The model predicts that even nonanemic patients require transfusion, and the RRR in transfusion requirements between female patients with preoperative hemoglobin of 13 g/dl compared to female patients with preoperative hemoglobin of 15 g/dl is 70% for those undergoing total hip arthroplasty and 68% for those undergoing total knee arthroplasty. The model also predicts that male patients undergoing total hip arthroplasty achieve a RRR of 68% if their preoperative hemoglobin is 15 g/dl compared to patients with a preoperative hemoglobin of 13 g/dl. This suggests that increasing preoperative hemoglobin within the normal range may still influence transfusion requirements.

Validation Cohort

The predictive erythrocyte transfusion model was applied on a validation series of 653 patients undergoing total hip arthroplasty or total knee arthroplasty surgery between July 2013 and June 2014. An additional 164 patients operated on during this period were excluded because preoperative hemoglobin concentration was not available. The patient characteristics were similar between derivation and validation series, except for a median age of 69 yr (IQR = 62 to 75) compared to 70 yr (IQR = 63 to 77, $P = 0.03$) (table 3). However, the diagnoses in this group were more diverse and included all patients undergoing total hip arthroplasty or total knee arthroplasty after trauma, revision of previous total hip arthroplasty or total knee arthroplasty, or for acute fracture management. A total of 97 (15%) patients were transfused, with more patients undergoing total hip arthroplasty transfused (70, 24%) compared to total knee arthroplasty patients (27, 8%). The excluded patients were statistically similar in age and gender, but with a lower proportion undergoing total hip arthroplasty and a lower proportion requiring transfusion.

Calibration of the model was acceptable with a well-fitted goodness-of-fit test with a Pearson chi-square test of



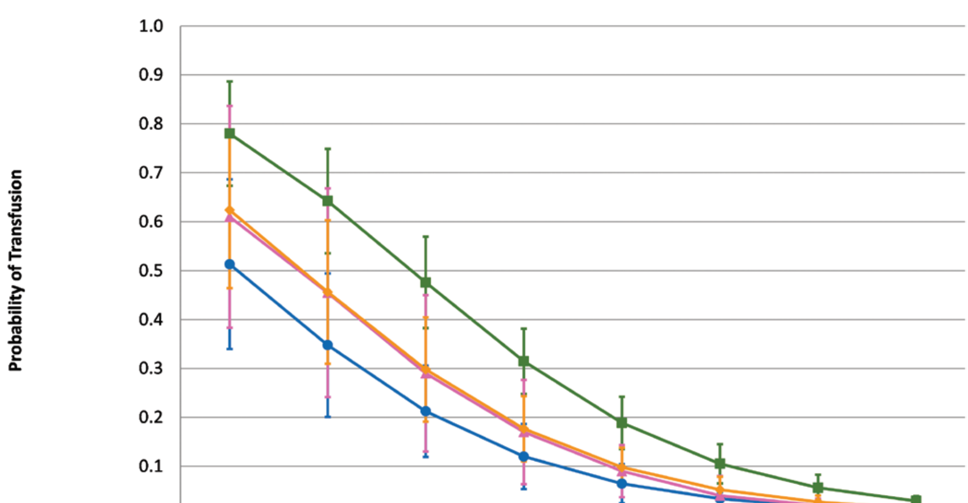
	9 g/dl	10 g/dl	11 g/dl	12 g/dl	13 g/dl	14 g/dl	15 g/dl	16 g/dl
Female <65 years	0.79	0.65	0.49	0.33	0.20	0.11	0.06	0.03
Female ≥65 years	0.93	0.86	0.76	0.62	0.45	0.30	0.17	0.10
Male <65 years	0.85	0.74	0.59	0.42	0.27	0.15	0.08	0.04
Male ≥65 years	0.86	0.75	0.60	0.43	0.28	0.16	0.09	0.05

Fig. 2. Probability of transfusion in four age and gender categories of total hip arthroplasty patients across preoperative hemoglobin concentrations.

33.40 (*df* = 51, *P* = 0.9731) for the derivation. The predictive power was slightly higher in the validation cohort than in the derivation cohort (area under the curve = 0.84 [0.79 to 0.88] *vs.* 0.80 [0.77 to 0.84]; fig. 4).Using the model with three age categories did not improve the sensitivity and specificity of the model (area under the curve = 0.84 [0.80 to 0.88] *vs.* 0.81 [0.77 to 0.84]; Supplemental Digital Content 1, http://links.lww.com/ALN/B467). The actual transfusion rates in the validation group according the identified predictors are comparable to the rates predicted by the model (Supplemental Digital Content 2, http://links.lww.com/ALN/B468).

Discussion

In this study, preoperative hemoglobin, type of procedure, and age above 65 yr in combination with female sex were identified as predictors of perioperative transfusion in patients undergoing elective arthroplasty. The validation series was external and temporally separate, increasing the



	9 g/dl	10 g/dl	11 g/dl	12 g/dl	13 g/dl	14 g/dl	15 g/dl	16 g/dl
Female <65 years	0.51	0.35	0.21	0.12	0.06	0.03	0.02	0.01
Female ≥65 years	0.78	0.64	0.48	0.31	0.19	0.11	0.06	0.03
Male <65 years	0.61	0.45	0.29	0.17	0.09	0.04	0.02	0.01
Male ≥65 years	0.62	0.46	0.30	0.18	0.10	0.05	0.03	0.01

Fig. 3. Probability of transfusion in four age and gender categories of total knee arthroplasty patients across preoperative hemoglobin concentrations.

Table 3. Comparison of Derivation and Validation Cohort Patients

	Derivation Cohort	Validation Cohort	*P* Value
N	737	653	
Median age, yr (IQR)	70 (63–77)	69 (62–75)	0.03
Male	322 (44%)	256 (39%)	0.09
≥65 yr	524 (71%)	440 (67.4%)	0.12
THA	343 (54%)	357 (45%)	0.1
TKA	394 (47%)	296 (55%)	

IQR = interquartile range; THA = total hip arthroplasty; TKA = total knee arthroplasty.

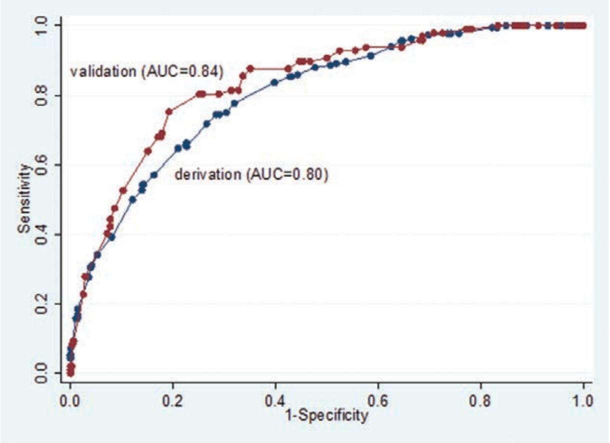


Fig. 4. Receiving operating characteristic with area under the curve (AUC) for derivation (*blue*) and validation (*red*) cohort.

strength of the model. The transfusion rates of 25 and 15% of the patients in the derivation and validation series, respectively, are comparable with the transfusion rates from other studies.[26–30] Specifically, the transfusion rates of the groups as identified by the model in the validation cohort was comparable to the predicted rates. The identified predictors are well known and generally accepted, but their incorporation into a model to predict transfusion for individual groups of patients is novel.

A previous study[31] found the likelihood of blood transfusion was lowest for those with preoperative hemoglobin greater than 13 g/dl, weight greater than 100 kg, undergoing unilateral total knee arthroplasty, and primary surgery. Although that study found that gender and age were not significant predictors on univariate analysis, our data showed that female gender and older age significantly increase need for transfusion when considered together. The results of this previous study would suggest that higher weight is protective, most likely as a surrogate measure of red cell mass. This was not included in our study but should be included in future prospective studies.

A further study[23] found that two readily available patient factors, ASA score and hemoglobin level, may help individualize the preoperative hemoglobin target in patients undergoing total knee arthroplasty who receive tranexamic acid. Poorer ASA status was associated with increased transfusion rates. Their univariate analysis also found age as a significant predictor; however, the reason for not including ASA status in their multivariate analysis is not clear, but it was not a significant predictor in our study. Their population of 784 patients was demographically similar to our derivation cohort but excluded some high surgical risk patients, which may also limit the applicability of their model. Our data showed that ASA status was only significant in univariate analysis and not in multivariate analysis. This suggests that ASA status may be a surrogate marker for other significant predictors such as hemoglobin concentration, age, gender, and type of procedure and therefore became less significant when multiple variates were included in the model.

Perioperative interventions such as tranexamic acid use and cell salvage were used at the discretion of the surgeons and anesthetists with variable use between clinicians and hospitals. These interventions were not recorded as variables in our retrospective study, but our model has been validated in a more diverse population, which strengthens its applicability. The hemoglobin transfusion trigger was not recorded, but the National Blood Authority guidelines were available at all sites combining clinical status with postoperative hemoglobin concentration in decision making.[32]

The need for transfusion increases with age, so older age is an accepted risk factor. A previous study[33] has demonstrated that age 65 yr and older is associated with a significantly higher need for transfusion, and hence this was used as the threshold for the model. Including an additional age category of greater than 85 yr in our model did not improve its specificity or sensitivity.

Avoiding and minimizing transfusion is a core aim of all PBM programs. For patients undergoing elective total hip arthroplasty or total knee arthroplasty, the only modifiable preoperative risk factor that is easily measured is low preoperative hemoglobin. Current PBM guidelines provide less advice on specific preoperative hemoglobin targets other than a normal hemoglobin for the individual patient, and our study demonstrates that transfusion requirement is a continuous risk, even for patients who are not anemic. According to this model, an older female with a preoperative hemoglobin of 11 g/dl undergoing total hip arthroplasty has a 76% chance of requiring a postoperative transfusion. The same older female undergoing total knee arthroplasty has a 48% chance of requiring transfusion. Although the patient would benefit from preoperative hemoglobin optimization regardless of procedure, there is greater need if she was undergoing total hip arthroplasty. Achieving a preoperative hemoglobin of 13 g/dl may reduce the need for transfusion to 45 and 19% for total hip arthroplasty and total knee arthroplasty, respectively. Therefore, even patients with a normal hemoglobin may still reduce their transfusion need with hemoglobin optimization.

Alternatively two different patients undergoing the same procedure may have different needs for transfusion, which may affect the desired preoperative hemoglobin. It is predicted that 49% of younger females undergoing total hip arthroplasty will require transfusion at 11 g/dl compared to 76% of older females. For the younger female, the transfusion need reduces to 20% if optimized to 13 g/dl, but this same reduced rate of transfusion in the older female would require a hemoglobin of nearly 15 g/dl.

Maximal optimization of preoperative hemoglobin concentration may not be possible or clinically appropriate based on factors not included in the model, *e.g.*, acute coronary syndromes or patients not willing to accept blood products, but this should not preclude attempts to optimize preoperative hemoglobin because these models suggest that gains can be made with relatively small increases in hemoglobin.

Not attempting to correct preoperative anemia is considered substandard care.[20,34] Therefore, identifying the cause of anemia guides the most appropriate intervention to improve preoperative hemoglobin concentration.[35] Patients with iron-deficiency anemia may require a combination of interventions including iron replacement and erythropoietin-stimulating agents[36–39] and more time to achieve normal hemoglobin levels before surgery. Treatment of underlying causes such as correction of bleeding or marrow-suppressive drugs is also often effective, but anemia of chronic disease is not always as responsive to interventions, and the success of hemoglobin correction may be limited.

Understanding the level of transfusion incidence will also help to inform other PBM measures that may be used to minimize transfusion including interventions at the time of surgery such as cell salvage and use of tranexamic acid. This early screening may increase preoperative costs, but these costs could be offset by decreased use of blood products. There is conflicting evidence about the effect on other transfusion risks such as risk of infection and increased length of stay. A study currently underway may better inform our understanding of this with its healthcare utilization and cost analysis.[40]

The retrospective nature of this study results in a number of limitations. All procedures in this study were performed in tertiary teaching hospitals, and the procedures were performed by different surgeons. A number of factors influencing transfusion could not be controlled: preoperative interventions to optimize hemoglobin use of tranexamic acid, intraoperative cell salvage, transfusion triggers, and specific clinical decisions. The different data collection and extraction methods used for the two cohorts mean that patients in the validation cohort potentially represent a more diverse group of patients. In fact, the model performed better in the validation group than the derivation group and suggests that the model could be applied in more diverse patient populations.

Prospective studies are required to confirm the accuracy of this predictive model particularly to confirm the actual decrease in transfusion with preoperative hemoglobin optimization and whether this translates to improvements in important patient outcomes. A clinical score could also be developed to guide clinical practice in the preoperative period. Further studies are required to validate this model in other patient groups such as emergency orthopedic surgery or other surgical procedures.

Our model not only predicts the transfusion need and demonstrates differences in transfusion needs between patients undergoing the same procedure, as well as patients with the same preoperative hemoglobin undergoing different procedures, but also provides guidance as to a hemoglobin target to decrease transfusion. Use of universal hemoglobin targets regardless of patient characteristics or procedure does not allow for these differences and may limit the opportunities to minimize transfusion exposure in the postoperative period. Used in conjunction with other PBM initiatives, the model empowers clinicians to target patients most likely to benefit from improved preoperative hemoglobin and reserve the use of donated blood, which is a limited resource, for when the benefits clearly outweigh the risks.

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Competing Interests

The authors declare no competing interests.

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References

1. Shander A: Preoperative anemia and its management. Transfus Apher Sci 2014; 50:13–5
2. Jans Ø, Jørgensen C, Kehlet H, Johansson PI; Lundbeck Foundation Centre for Fast-track Hip and Knee Replacement Collaborative Group: Role of preoperative anemia for risk of transfusion and postoperative morbidity in fast-track hip and knee arthroplasty. Transfusion 2014; 54:717–26
3. Musallam KM, Tamim HM, Richards T, Spahn DR, Rosendaal FR, Habbal A, Khreiss M, Dahdaleh FS, Khavandi K, Sfeir PM, Soweid A, Hoballah JJ, Taher AT, Jamali FR: Preoperative

anaemia and postoperative outcomes in non-cardiac surgery: A retrospective cohort study. Lancet 2011; 378:1396–407
4. Beattie WS, Karkouti K, Wijeysundera DN, Tait G: Risk associated with preoperative anemia in noncardiac surgery: A single-center cohort study. Anesthesiology 2009; 110:574–81
5. Bierbaum BE, Callaghan JJ, Galante JO, Rubash HE, Tooms RE, Welch RB: An analysis of blood management in patients having a total hip or knee arthroplasty. J Bone Joint Surg Am 1999; 81:2–10
6. Spahn DR: Anemia and patient blood management in hip and knee surgery: A systematic review of the literature. Anesthesiology 2010; 113:482–95
7. Vamvakas EC, Blajchman MA: Transfusion-related mortality: The ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. Blood 2009; 113:3406–17
8. Ponnusamy KE, Kim TJ, Khanuja HS: Perioperative blood transfusions in orthopaedic surgery. J Bone Joint Surg Am 2014; 96:1836–44
9. So-Osman C, Nelissen R, Brand R, Faber F, Slaa RT, Stiggelbout A, Brand A: The impact of a restrictive transfusion trigger on post-operative complication rate and well-being following elective orthopaedic surgery: A post-hoc analysis of a randomised study. Blood Transfus 2013; 11:289–95
10. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, Rhoads GG, Nemo G, Dragert K, Beaupre L, Hildebrand K, Macaulay W, Lewis C, Cook DR, Dobbin G, Zakriya KJ, Apple FS, Horney RA, Magaziner J; FOCUS Investigators: Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med 2011; 365:2453–62
11. Carson JL, Carless PA, Hebert PC: Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database of Systematic Reviews 2012; 4:CD002042
12. Loftus TJ, Spratling L, Stone BA, Xiao L, Jacofsky DJ: A patient blood management program in prosthetic joint arthroplasty decreases blood use and improves outcomes. J Arthroplasty 2016; 31:11–4
13. Muñoz M, Leal-Noval SR: Restrictive transfusion triggers in major orthopaedic surgery: Effective and safe? Blood Transfus 2013; 11:169–71
14. Goodnough LT, Maniatis A, Earnshaw P, Benoni G, Beris P, Bisbe E, Fergusson DA, Gombotz H, Habler O, Monk TG, Ozier Y, Slappendel R, Szpalski M: Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. Br J Anaesth 2011; 106:13–22
15. Salpeter SR, Buckley JS, Chatterjee S: Impact of more restrictive blood transfusion strategies on clinical outcomes: A meta-analysis and systematic review. Am J Med 2014; 127:124–131.e3
16. Wong S, Tang H, de Steiger R: Blood management in total hip replacement: An analysis of factors associated with allogenic blood transfusion. ANZ J Surg 2015; 85:461–5
17. Kotzé A, Harris A, Baker C, Iqbal T, Lavies N, Richards T, Ryan K, Taylor C, Thomas D: British Committee for Standards in Haematology Guidelines on the Identification and Management of Pre-Operative Anaemia. Br J Haematol 2015; 171:322–31
18. Evans S, O'Loughlin E, Bruce J: Retrospective audit of blood transfusion and comparison with haemoglobin concentration in patients undergoing elective primary and revision lower limb arthroplasty. Anaesth Intensive Care 2011; 39:480–5
19. Rosencher N, Kerkkamp HE, Macheras G, Munuera LM, Menichella G, Barton DM, Cremers S, Abraham IL; OSTHEO Investigation: Orthopedic Surgery Transfusion Hemoglobin European Overview (OSTHEO) study: Blood management in elective knee and hip arthroplasty in Europe. Transfusion 2003; 43:459–69
20. Muñoz M, Gómez-Ramírez S, Kozek-Langeneker S, Shander A, Richards T, Pavía J, Kehlet H, Acheson AG, Evans C, Raobaikady R, Javidroozi M, Auerbach M: "Fit to fly": Overcoming barriers to preoperative haemoglobin optimization in surgical patients. Br J Anaesth 2015; 115:15–24
21. Holt JB, Miller BJ, Callaghan JJ, Clark CR, Willenborg MD, Noiseux NO: Minimizing blood transfusion in total hip and knee arthroplasty through a multimodal approach. J Arthroplasty 2016; 31:378–82
22. Cheung WY, Zimmermann C: Pharmacologic management of cancer-related pain, dyspnea, and nausea. Semin Oncol 2011; 38:450–9
23. Basora M, Tió M, Martin N, Lozano L, Salazar F, Sánchez-Etayo G, Raquel B, Pereira A: Should all patients be optimized to the same preoperative hemoglobin level to avoid transfusion in primary knee arthroplasty? Vox Sang 2014; 107:148–52
24. Rashiq S, Shah M, Chow AK, O'Connor PJ, Finegan BA: Predicting allogeneic blood transfusion use in total joint arthroplasty. Anesth Analg 2004; 99:1239–44
25. Husted H, Holm G, Jacobsen S: Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: Fast-track experience in 712 patients. Acta Orthop 2008; 79:168–73
26. Aderinto J, Brenkel IJ: Pre-operative predictors of the requirement for blood transfusion following total hip replacement. J Bone Joint Surg Br 2004; 86:970–3
27. Pedersen AB, Mehnert F, Overgaard S, Johnsen SP: Allogeneic blood transfusion and prognosis following total hip replacement: A population-based follow up study. BMC Musculoskelet Disord 2009; 10:167
28. Browne JA, Adib F, Brown TE, Novicoff WM: Transfusion rates are increasing following total hip arthroplasty: Risk factors and outcomes. J Arthroplasty 2013; 28(8 Suppl):34–7
29. Rashiq S, Shah M, Chow AK, O'Connor PJ, Finegan BA: Predicting allogeneic blood transfusion use in total joint arthroplasty. Anesth Analg 2004; 99:1239–44
30. Theusinger OM, Kind SL, Seifert B, Borgeat L, Gerber C, Spahn DR: Patient blood management in orthopaedic surgery: A four-year follow-up of transfusion requirements and blood loss from 2008 to 2011 at the Balgrist University Hospital in Zurich, Switzerland. Blood Transfus 2014; 12:195–203
31. Larocque BJ, Gilbert K, Brien WF: A point score system for predicting the likelihood of blood transfusion after hip or knee arthroplasty. Transfusion 1997; 37:463–7
32. National Blood Authority: Patient Blood Management Guideline: Module 2. Perioperative, The National Blood Authority, 2012
33. Yoshihara H, Yoneoka D: Predictors of allogeneic blood transfusion in total hip and knee arthroplasty in the United States, 2000–2009. J Arthroplasty 2014; 29:1736–40
34. Spahn DR, Zacharowski K: Non-treatment of preoperative anaemia is substandard clinical practice. Br J Anaesth 2015; 115:1–3
35. Kearney B, To J, Southam K, Howie D, To B: Anaemia in elective orthopaedic surgery—Royal Adelaide Hospital, Australia. Intern Med J 2016; 46:96–101
36. Bisbe E: Role of iron replacement in the management of preoperative anemia. Transfusion Alternatives in Transfusion Medicine 2012; 12: 150–6
37. So-Osman C, Nelissen RG, Koopman-van Gemert AW, Kluyver E, Pöll RG, Onstenk R, Van Hilten JA, Jansen-Werkhoven TM, van den Hout WB, Brand R, Brand A: Patient blood management in elective total hip- and knee-replacement surgery (Part 1): A randomized controlled trial on erythropoietin and blood salvage as transfusion alternatives using a restrictive transfusion policy in erythropoietin-eligible patients. Anesthesiology 2014; 120:839–51

38. Ralley FE: Erythropoietin and intravenous iron in PBM. Transfus Apher Sci 2014; 50:16–9
39. Muñoz M, Gómez-Ramírez S, Cuenca J, García-Erce JA, Iglesias-Aparicio D, Haman-Alcober S, Ariza D, Naveira E: Very-short-term perioperative intravenous iron administration and postoperative outcome in major orthopedic surgery: A pooled analysis of observational data from 2547 patients. Transfusion 2014; 54:289–99
40. Richards T, Clevenger B, Keidan J, Collier T, Klein AA, Anker SD, Kelly JD: PREVENTT: Preoperative intravenous iron to treat anaemia in major surgery: Study protocol for a randomised controlled trial. Trials 2015; 16:254

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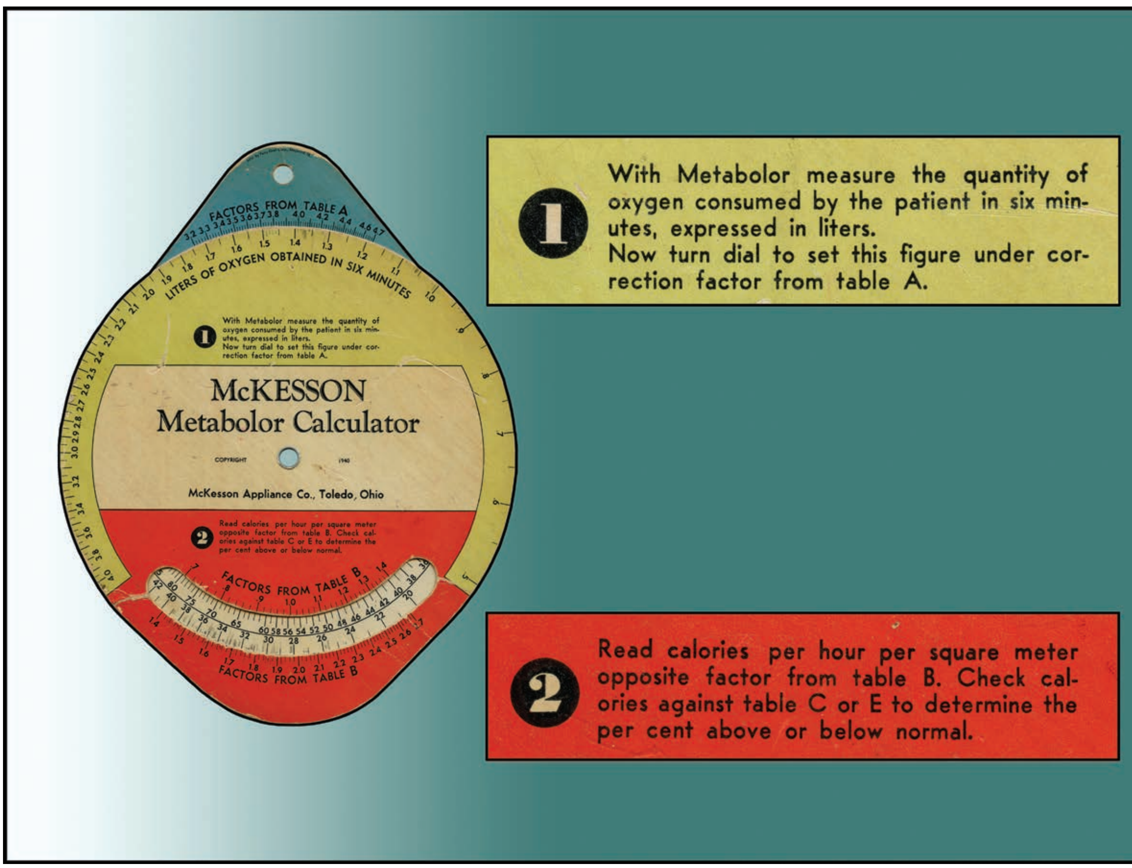
The McKesson Metabolor Calculator



After filing the patent design for his "Basal Metabolism Factor" in May of 1925, physician-anesthetist Elmer Isaac "Ira" McKesson, M.D. (1881 to 1935), was granted U.S. Patent No. 1863929 in June of 1932. Just over 2 yr later, he copyrighted his circular slide rule for estimating basal metabolism, his "McKesson Metabolor Calculator" (*left*). Before using the calculator, McKesson would use his invention, the Metabolor, to measure the number of liters of oxygen consumed by a patient in 6 min. In using the Calculator, the first step (*upper right*) involved positioning that measured number of liters of consumed oxygen on the yellow scale under the blue scale's "correction factor from table A." In the second step (*lower right*), "calories per hour per meter squared" on the white scale could be read opposite the red scale "factors of table B." McKesson's patent and copyright on his Metabolor and its Calculator, respectively, underscored his reputation as a physiologist. Consequently, many physician-anesthetists blindly trusted his hypoxic method of "secondary saturation" with nitrous oxide (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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