

# Development and Validation of a Generalizable Model for Predicting Major Transfusion During Spine Fusion Surgery

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**Background:** Surgery for posterior spine instrumentation often requires major transfusion. The aim of this study was to develop and test the validity of a model for predicting intraoperative major transfusion (> 4U total red blood cells), based on preoperative patient and surgical variables, that was applicable to adult patients undergoing cervical, thoracic, and/or lumbar spine deformity surgery with and without osteotomies.

**Materials and Methods:** The perioperative data from 548 patients who underwent  $\geq 3$  levels of posterior spinal fusion with instrumentation between January 1, 2003 and May 30, 2009, were retrospectively collected to create a model for predicting major blood transfusion. The validity of the model was retrospectively tested with a separate data set of 95 patients who underwent surgery from June 1, 2009 through September 30, 2010.

**Results:** There was a 59.5% incidence of major transfusion in the derivation set of patients. Independent predictors of major transfusion were operation duration, number of posterior levels instrumented, surgical complexity score, and preincision hemoglobin. This model was able to predict major transfusion significantly better than a previously published model (ROC<sub>AUC</sub> = 0.89; 99% confidence interval, 0.80-0.90;  $P < 0.001$ ).

**Conclusions:** Our model has an increased accuracy for predicting the probability of major transfusion compared with a previously published model. In addition, our model is applicable to all types of spine fusion surgery and accounts for the complexity of

surgical instrumentation, the number of levels instrumented, and the predicted duration of surgery as independent variables.

**Key Words:** spine, lumbar fusion, major transfusion, preoperative assessment

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Complex spine instrumentation can be associated with long operative times and estimated blood loss ranging between 25% and 230% of a patient's estimated blood volume.<sup>1–3</sup> Accordingly, certain patients will require intraoperative transfusion of multiple units of red blood cells (RBCs). Although administration of even a single unit of RBCs is associated with adverse reactions and immunomodulatory effects, transfusion-related morbidity and mortality after surgery increases with the number of units transfused.<sup>4–6</sup> Numerous strategies may be used to decrease blood transfusion requirements (eg, acute normovolemic hemodilution, antifibrinolytics, lower transfusion triggers, staging complex reconstructive procedures, etc.). However, these techniques are not without their own risks and cannot eliminate the overall requirement for transfusion in major spine fusion surgery. Therefore, it is necessary to understand which patients will require multiple units of RBCs to accurately determine the perioperative risk of patients undergoing complex spine fusion surgery and to plan appropriately for the necessary intraoperative management with respect to intravenous access, invasive hemodynamic monitoring, and blood product resourcing.

The only quantitative model that can predict the need for blood transfusion during spine surgery in the literature is the Predictive Model of Transfusion in Spine Surgery (PMTSS) developed by Lenoir and colleagues (Table 1). This model uses preoperative variables to predict the risk of transfusion of a single unit of RBCs over a 5-day period in adult patients undergoing thoracolumbar posterior spine fusion.<sup>7</sup> Although a PMTSS score of more than 2 is highly predictive of transfusion of 1 U RBCs in the *perioperative* period, this scoring system may not have the ability to determine which patients will have major intraoperative blood loss (>40% blood volume) and require major transfusion (ie, >4 U of RBCs, including cell salvage blood) in the *intraoperative* period.

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**TABLE 1.** Description of Predictive Model of Transfusion in Spine Surgery

	PMTSS Points		
	0	1	
Age (y)	≤ 50	> 50	
Lumbar levels fused	1-2 0	> 2 1	2
Initial hemoglobin (g/dL)	< 12 0	12-14 4	> 14
Transpedicular osteotomy	No	Yes	

\*The PMTSS score is the sum of the points assigned. Patients with a score of 3 or 4 have a 64% or 88% probability of receiving a single unit of red blood cells in the initial 5-day perioperative period, respectively.

The aim of this study was to develop and test the validity of a model for predicting intraoperative major transfusion (> 4 U RBCs, including allogeneic transfusion and returned cell salvage), based on preoperative patient and surgical variables, that is generalizable to adult patients undergoing complex cervical, thoracic, and/or lumbar spine deformity surgery. The secondary aim of

this study was to determine the ability of the PMTSS to predict intraoperative major transfusion in adult spine deformity patients.

**MATERIALS AND METHODS**

**Study Design**

This retrospective observational cohort study was conducted after approval for waiver of written informed consent from the local Institutional Review Board. Patients were identified by the current procedural terminology codes for arthrodesis of spine deformity (22,800, 22,802, 22,804, 22,810, 22,812, and 22,819), spinal instrumentation (22,842, 22,843, 22,844, 22,846, and 22,847), and osteotomy of the spine (22,208, 22,216, and 22,226). The model derivation data were obtained from patients who had surgery at our hospital between January 1, 2003 and May 31, 2009 (derivation data set) and the validity of the model was tested with data extracted from patients who had surgery at our hospital between June 1, 2009 and September 30, 2010 (validation data set). The PMTSS model performance was tested with the model validation data set.

**TABLE 2.** Development Data Set Patient Demographics, Preoperative Coexisting Disease and Medications, and Surgical Variables Stratified by Red Cell Units Transfused\*

	≤ 4U RBC Transfusion	> 4U RBC Transfusion	Difference (99% CI)†	P
Number	222	326		
Sex (female:male)	127 (57.2%):95 (42.8%)	205 (62.9%):121 (37.1%)		0.183
Age (y)	54.9 ± 14.7	58.1 ± 15.0	- 3.1 (- 6.5 to 0.2)	0.016
Weight (kg)	78.5 ± 18.7	77.3 ± 19.5	1.2 (- 3.1 to 5.6)	0.456
Body mass index (kg/m <sup>2</sup> )	27.7 ± 6.0	27.7 ± 6.3	0 (- 1.4 to 1.3)	0.925
ASA physical status (n [%])				
1	17 (7.7)	12 (3.6)		
2	103 (46.4)	152 (46.6)		0.228
3	97 (43.6)	154 (47.2)		
4	5 (2.2)	8 (2.5)		
Smoking history (n [%])	86 (38.7)	107 (32.8)		0.172
History of coronary artery disease (n [%])	26 (11.7)	32 (9.8)		0.483
Preoperative anticoagulant use (n [%])	49 (22.1)	89 (27.3)		0.193
Aspirin (n [%])	43 (19.4)	67 (20.6)		0.746
Warfarin (n [%])	6 (2.7)	15 (4.6)		0.365
Clopidogrel (n [%])	7 (3.2)	8 (2.5)		0.607
Low molecular weight heparin (n [%])	2 (0.9)	7 (2.2)		0.324
Infection (n [%])	6 (2.7)	12 (3.7)		0.630
Tumor (n [%])	21 (9.5)	10 (3.1)		0.002
No. posterior levels instrumented (0-20)	5 (0-17)	10 (0-20)	- 4 (- 5 to - 3)	< 0.001
Surgical category (0-3)‡ (n [%])				
0	8 (3.6)	4 (1.2)		
1	73 (32.9)	20 (6.1)		< 0.001
2	123 (55.5)	221 (67.8)		
3	18 (8.1)	81 (24.8)		
Revision surgery (n [%])	75 (33.8)	142 (43.6)		0.118
Pre-incision hemoglobin (g/dL)	11.80 ± 1.56	11.35 ± 1.64	0.44 (0.08 to 0.81)	0.002
Operation duration (min)	527 ± 162	716 ± 140	- 189 (- 222 to - 155)	< 0.001

\*Data are mean ± SD, median (range), or number of patients (%). Shaded variables were all included in the initial multivariate analysis. Light gray-shaded variables—P < 0.01; Dark gray-shaded variables—P < 0.2.

†Differences not calculated for categorical data.

‡The surgical categories were classified as follows: 0, any exclusively anterior spine surgery with or without anterior cervical corpectomies (excluding Anterior Lumbar Interbody Fusions); 1, any posterior cervical or thoracic instrumentation with or without anterior cervical corpectomies; 2, any surgery with lumbar posterior instrumentation with or without Smith Peterson osteotomies; 3, any surgery with any combination of posterior corpectomies, pedicle subtraction osteotomies, or vertebral column resections.

ASA Physical Status indicates American Society of Anesthesiologists Physical Status; CI, confidence interval.

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**TABLE 3.** Intraoperative Fluids, Blood Products, and Systemic Hemostatic Medications Stratified by Total Red Blood Cell Units Transfused\*

	≤ 4 U RBC Transfusion (n = 222)	> 4 U RBC Transfusion (n = 326)	Difference (99% CI)†	P
<b>Red blood cell transfusion</b>				
Total red blood cells (U)	2.0 (0-4.0)	9.9 (4.1-55.0)	-8.0 (-9.0 to -7.3)	< 0.0001
Packed red blood cells (U)	1 (0-4)	7 (0-33)	-5 (-6 to -5)	< 0.0001
Cell salvage (mL)	0 (0-883)	795 (0-8110)	-736 (-869 to -681)	< 0.0001
Cell salvage (U)	0 (0-2.94)	2.65 (0-27.0)	-1.33 (-1.67 to 0)	< 0.001
Postoperative hemoglobin (g/dL)	10.4 (8.5-12.9)	11.1 (8.6-13.8)	-0.8 (-1.1 to -0.4)	< 0.001
<b>Nonblood products</b>				
Crystalloid (mL)	4000 (800-11500)	7125 (1000-25000)	-3000 (-3600 to -2200)	< 0.0001
Hetastarch (mL)	125 (0-1500)	0 (0-2000)	0 (0 to 0)	0.219
Human albumin 5% (mL)	500 (0-3000)	1000 (0-6000)	-500 (-1000 to -500)	< 0.0001
<b>Non-red cell blood products</b>				
Fresh frozen plasma	22 (9.9%)	163 (50%)		< 0.0001
Fresh frozen plasma (U)	0 (0-4)	0.5 (0-28)	0 (-2 to 0)	< 0.0001
Cryoprecipitate	14 (6.3%)	116 (35.6%)		< 0.0001
Cryoprecipitate (U)	0 (0-2)	0 (0-5)	0 (0-0)	< 0.0001
Platelets (U)	0 (0-2)	0 (0-8)	0 (0-0)	< 0.0001
DDAVP‡	11 (5.0%)	53 (16.3%)		< 0.0001
Recombinant factor VIIa	1 (0.5%)	13 (4.0%)		0.011
<b>Intraoperative physiological variables</b>				
Estimated blood loss (mL)	1100 (50-5500)	3800 (850-15750)	-2700 (-3000 to -2300)	< 0.0001
Minimum intraoperative temperature (°C)	35.1 ± 0.7	34.8 ± 0.8	0.4 (0.2-0.5)	< 0.001
Urine output (mL)	1000 (155-7000)	1562.5 (150-8000)	-515 (300-690)	< 0.0001

\*Data are mean ± SD, median (range), or number of patients (%).

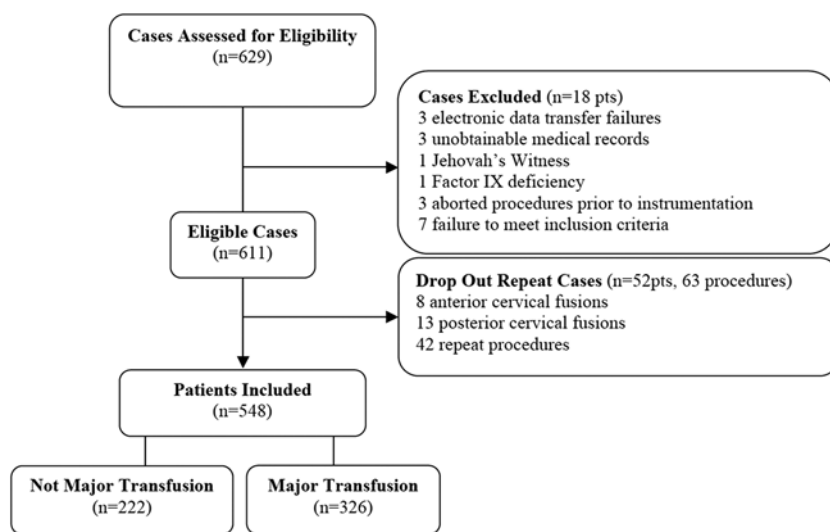
†Differences not calculated for categorical data.

‡Deamino-8-D-arginine vasopressin.

CI indicates confidence interval.

Patients with preexisting bleeding disorders and patients who abstained from receiving blood products due to religious beliefs were excluded from the study. To avoid the possible confounding influence of multiple procedures on the same patient, we included only 1 surgical procedure for each patient who may have had multiple eligible spine operations throughout the 8-year study period. This was

done using a priori sequential dropout rules, created to preferentially include the surgical procedure that most closely resembled the majority of the patients in the data set—posterior lumbar spine fusion. Therefore, anterior operations were excluded first, posterior cervical operations were excluded next, and if multiple operations remained, the earliest eligible surgical procedure was included.



**FIGURE 1.** The CONSORT (Consolidated Standards of Reporting Trials) flow diagram for the model development data set delineating patient enrollment, inclusion/exclusion, drop out, and final group allocation for patients with and without major transfusion.

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**TABLE 4.** Final Model for Prediction of a Transfusion of > 4 U of Total Red Blood Cells\*

Variables	Regression Coefficient (SE)	Odds Ratio (95% CI)†	P
Constant	-3.93 (1.02)	—	0.0001
Operation duration (min)	0.00688 (0.00086)	1.007 (1.005-1.009)	< 0.0001
No. posterior levels instrumented (0-20)	0.245 (0.034)	1.28 (1.17-1.42)	< 0.0001
Surgical category (0-3)	0.685 (0.208)	1.98 (1.14-3.86)	0.001
Pre-incision hemoglobin (g/dL)	-0.278 (0.075)	0.76 (0.63-0.91)	0.0002

\*Logit  $P = -3.93 + 0.00688 \times \text{operation duration in minutes} + 0.245 \times \text{number of posterior levels instrumented} + 0.685 \times \text{surgical category} - 0.278 \times \text{pre-incision hemoglobin (g/dL)}$ . The likelihood ratio test statistic was 269.13,  $P < 0.0001$ .

†Bias-corrected by bootstrapping.

Perioperative management of hemodynamics and blood product administration was at the discretion of the attending anesthesiologists and surgeons. Cell salvage was used for noninfected and noncancer patients. Preoperative autologous blood donation, acute normovolemic hemodilution, deliberate moderate hypotension, and antifibrinolytic agents were not used for any patient. Data were extracted from the clinical charts of the patients. The variables collected included patient demographics, preoperative coexisting diseases, preoperative medications, duration of surgery, intraoperative fluids and blood

products, estimated blood loss, lowest recorded temperature, perioperative laboratory values, and details of the surgical procedure. To simplify the types of operations, we reclassified the surgical procedure using a surgical category variable (Table 2) related to the rank order of the estimated blood loss reported in the literature.<sup>8</sup>

### Statistical Methods

The primary outcome was the total number of units of red blood cells (total RBCs) transfused. The total RBCs transfused was the sum of the units of allogeneic

**TABLE 5.** Validation Data Set Patient Demographics, Preoperative Coexisting Disease and Medications, and Surgical Variables Stratified by Red Cell Units Transfused\*

	≤ 4U RBC Transfusion	> 4U RBC Transfusion	Difference (99% CI)†	P
Number	34	61		
Sex (female:male)	16 (47.1%):18 (52.9%)	38 (62.3%):23 (37.7%)		0.151
Age (y)	48.9 ± 15.8	56.9 ± 13.8	-8.0 (-16.1 to 0.2)	0.0119
Weight (kg)	79.4 ± 23.4	80.2 ± 21.9	-0.8 (-13.5 to 11.8)	0.859
Body mass index (kg/m <sup>2</sup> )	27.1 ± 7.1	28.8 ± 7.8	-1.7 (-5.9 to 2.6)	0.321
ASA physical status (n [%])				
1	1 (2.9)	1 (1.6)		
2	17 (50.0)	30 (49.2)		0.537
3	14 (41.2)	29 (47.5)		
4	1 (2.9)	0 (0)		
Smoking history (n [%])	13 (41.9)	26 (42.6)		0.677
History of coronary artery disease (n [%])	2 (5.9)	3 (4.9)		0.844
Preoperative anticoagulant use (n [%])	6 (17.6)	15 (24.6)		0.434
Aspirin (n [%])	4 (11.8)	13 (21.3)		0.245
Warfarin (n [%])	0 (0)	1 (1.6)		0.453
Clopidogrel (n [%])	1 (2.9)	3 (4.9)		0.646
Low molecular weight heparin (n [%])	1 (2.9)	1 (1.6)		0.672
Infection (n [%])	2 (5.9)	3 (4.9)		0.844
Tumor (n [%])	5 (14.7)	4 (6.6)		0.194
No. posterior levels instrumented (0-20)	5.5 (0-13)	10.0 (3-18)	-4 (-7 to -2)	< 0.001
Surgical category (0-3)‡ (n [%])				
0	4 (11.8)	0 (0)		
1	5 (14.7)	2 (3.2)		0.004
2	16 (47.1)	44 (72.1)		
3	9 (26.5)	15 (24.6)		
Revision Surgery	10 (29.4)	30 (49.2)		0.061
Pre-incision hemoglobin (g/dL)	11.0 ± 1.7	11.3 ± 1.8	-0.3 (-1.1 to 0.5)	0.313
Operation duration (min)	470 ± 131	667 ± 118	-193 (-266 to 128)	< 0.001

\*Data are mean ± SD, median (range), or number of patients (%).

†Differences not calculated for categorical data.

‡The surgical categories were classified as follows: 0, any exclusively anterior spine surgery with or without anterior cervical corpectomies (excluding anterior lumbar interbody fusions); 1, any posterior cervical or thoracic instrumentation with or without anterior cervical corpectomies; 2, any surgery with lumbar posterior instrumentation with or without Smith Peterson osteotomies; 3, any surgery with any combination of posterior corpectomies, pedicle subtraction osteotomies, or vertebral column resections.

ASA Physical Status indicates American Society of Anesthesiologists Physical Status; CI, confidence interval.

**TABLE 6.** Validation Data Set Intraoperative Fluids, Blood Products, and Systemic Hemostatic Medications Stratified by Total Red Blood Cell Units Transfused\*

	≤ 4 U RBC Transfusion (n = 222)	> 4 U RBC Transfusion (n = 326)	Difference (99% CI)†	P
<b>Red blood cell transfusion</b>				
Total red blood cells (U)	1.9 (0-4)	9 (4.1-40.8)	-7.2 (-9.2 to -5.5)	< 0.001
Packed red blood cells (U)	1 (0-4)	5 (1-29)	-5 (-6 to -3)	< 0.001
Cell salvage (mL)	0 (0-767)	1150 (0-6264)	-965 (-1335 to -529)	< 0.001
Cell salvage (U)	0 (0-2.6)	3.8 (0-20.1)	-3.2 (-4.5 to -1.7)	< 0.001
Postoperative hemoglobin (g/dL)	10.5 ± 1.0	11.1 ± 1.3	-0.6 (-1.3 to -0.01)	0.009
<b>Nonblood products</b>				
Crystalloid (mL)	2100 (1200-5400)	2900 (1000-5300)	-500 (-1000 to 0)	0.021
Hetastarch (mL)	1000 (0-1500)	1000 (0-1500)	0 (0-0)	0.272
Human albumin 5% (mL)	1000 (0-3000)	3000 (1000-8000)	-2250 (-3000 to -1500)	< 0.001
<b>Nonred cell blood products</b>				
Fresh-frozen plasma (U)	0 (0-0)	0 (0-0)	0 (0-0)	1.00
Cryoprecipitate (U)	0 (0-2)	2 (0-9)	-1 (-2 to -1)	< 0.001
Platelets (U)	0 (0-2)	1 (0-10)	-1 (-2 to -1)	< 0.001
DDAVP‡ (n [%])	3 (9.7)	26 (42.6)		< 0.001
Recombinant factor VIIa (n [%])	0 (0)	3 (4.9)		0.631
<b>Intraoperative physiological variables</b>				
Estimated blood loss (mL)	1100 (50-650)	3500 (50-13000)	-2200 (-3150 to -1600)	< 0.001
Minimum intraoperative temperature (°C)	35.3 ± 0.8	35.2 ± 0.7	0.1 (-0.3 to 0.5)	0.485
Urine output (mL)	1000 (70-3100)	1300 (280-14810)	-300 (-785 to 125)	0.068

\*Data are mean ± SD, median (range), or number of patients (%).

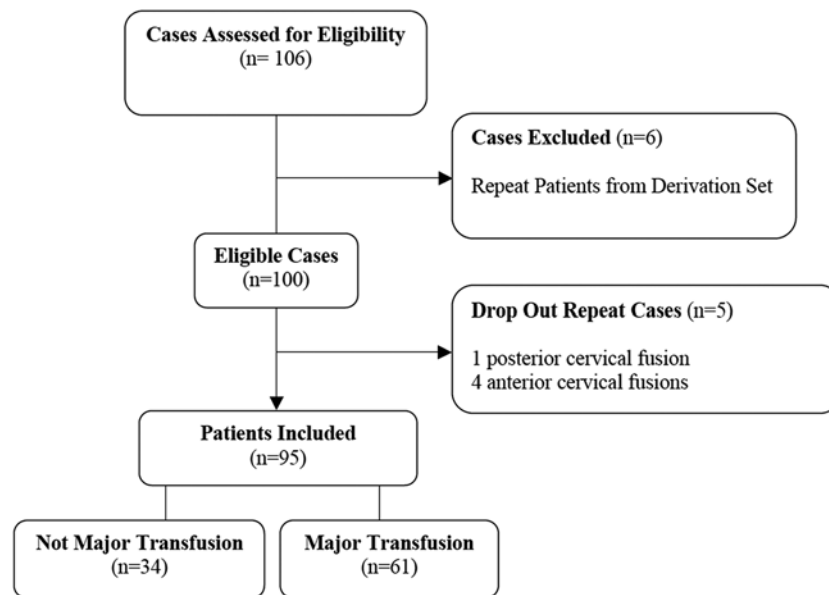
†Differences not calculated for categorical data.

‡Deamino-8-D-arginine vasopressin.

CI indicates confidence interval.

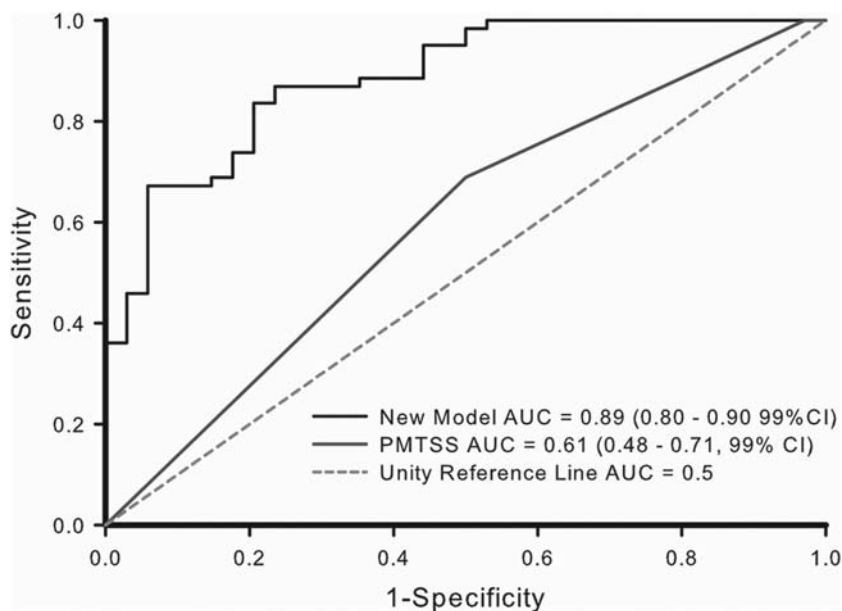
packed red blood cells (PRBCs) administered and the reinfused units of cell salvage RBCs, assuming the volume of a unit of cell salvage RBCs was 300 mL. The need to transfuse > 4 U of total RBCs (ie, major transfusion) was chosen as a dichotomous outcome for the predictive model, because this represents an estimated blood loss of more than 40% of a patient's blood volume when the starting hemoglobin is >13 g/dL.

Statistical analysis was performed using StatsDirect statistical software (version 2.6.5, StatsDirect Ltd., Cheshire, UK). Discrete data were compared using the Fisher exact test or  $\chi^2$  test. Ordinal data and continuous data that were not normally distributed were compared between groups using the Mann-Whitney *U* test. Normally distributed continuous data were compared using the unpaired *t* test. Given the large number of compar-



**FIGURE 2.** The CONSORT (Consolidated Standards of Reporting Trials) flow diagram for the model validation data set delineating patient enrollment, inclusion/exclusion, drop out, and final group allocation for patients with and without major transfusion.

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**FIGURE 3.** The empiric receiver operator characteristic (ROC) curves demonstrating that our model (solid black line) performed better at predicting the probability of major transfusion than the Predictive Model for Transfusion in Spine Surgery (PMTSS; grey solid line, difference  $ROC_{AUC} = -0.25$ ; 99% CI,  $-0.40$  to  $-0.10$ ;  $P < 0.001$  PMTSS vs. our model). Of note, the PMTSS ( $ROC_{AUC}$  median 0.60; 99% CI, 0.48-0.71) did not perform better than chance ( $P = 0.07$ , dotted black line). CI indicates confidence interval;  $ROC_{AUC}$ , area under the ROC curve.

isions being made, to help reduce the chance of a type I error, the criterion for rejection of the null hypothesis established a priori was  $P < 0.01$ .

### Predictive Model Derivation

Multiple logistic regression analysis was performed to determine the predictors of  $>4$  U of RBCs transfused. Variables included in the initial multiple logistic regression analysis were those variables identified in the univariate analyses as having a  $P < 0.20$  (Tables 1, 2). In the final analyses, variables with higher  $P$ -values were removed from the model one at a time and were excluded from the final model if their removal either did not diminish the fit of the model or actually improved it, as determined by the Pearson  $\chi^2$  statistic, the likelihood ratio test statistic, the Hosmer-Lemshow statistic, and the correct prediction of both positive and reference responses. Bias-corrected confidence intervals for the odds ratios derived from the final fitted logistic model were determined by bootstrapping (1000 samples, with replacement).

### Predictive Model Validation

The validity of the model was tested in an independent set of patients. To adequately validate the 4-variable predictive model for major transfusion in a population with an estimated major transfusion rate of 40% to 50%, the data from 72 to 100 patients undergoing complex spine fusion surgery are required.<sup>9,10</sup> The sensitivity and specificity of the new predictive model and the area under the receiver operating characteristic (ROC) curve were calculated from the model-predicted reference, the model-predicted positive responses (using the default

threshold probability for positive classification of 0.5), and the actual reference and actual positive responses. The performance of the new predictive model compared with random chance (ie, a random classifier, area under the ROC curves [ $ROC_{AUC}$ ] = 0.5) was determined using the  $\chi^2$  statistic, with  $P < 0.05$  considered significant.<sup>11</sup> The ability of the PMTSS to correctly predict major transfusion was similarly calculated for scores of 1.5, 2.5, and 3.5. The performance of the 2 models was evaluated by comparing the  $ROC_{AUC}$  using the  $\chi^2$  statistic, with  $P < 0.05$  considered significant.<sup>11</sup>

## RESULTS

Major transfusion, which occurred in 326 of the 548 patients (59.5%, Table 3) was more likely in patients who underwent more extensive posterior spine fusions ( $P < 0.001$ ), had posterior lumbar instrumentation with or without major osteotomies ( $P < 0.001$ ), had longer operations ( $P < 0.001$ ), or had surgery to debulk spinal metastases ( $P = 0.002$ ) (Fig. 1 and Table 2). In addition, these patients had lower preincision hemoglobin concentrations ( $P = 0.002$ ). Variables included in the final multiple logistic regression model as predictors of major transfusion were operation duration, number of posterior levels instrumented, surgical category, and preincision hemoglobin concentration (Table 4). The sensitivity of the logistic model was 86.2%, the specificity was 74.9%, and the  $ROC_{AUC}$  was 0.88.

The demographic and surgical variables for the cohort of patients in the validation data set are provided in Tables 5 and 6. Sixty-one of the 95 patients (64.2%) in

**TABLE 7.** Patient Demographics and Perioperative Variables Stratified by Red Cell Units Transfused Model Validation Data Set\*

	≤4 U RBC Transfusion	>4 U RBC Transfusion	Difference (99% CI)†	P
Number	34	61		
Estimated blood loss (mL)	1100 (50-650)	3500 (500-13000)	-2200 (1600-3150)	< 0.001
Total red blood cell units transfused (U)	1.9 (0-4)	9 (4.1-40.8)	-7.2 (-5.5 to -9.2)	< 0.001
<i>New model parameters</i>				
Age (y)	48.9 ± 15.8	56.9 ± 13.8	-8 (-0.2 to 16.1)	0.012
No. posterior levels instrumented (0-20)	5.5 (0-13)	10 (3-18)	-4 (-2 to -7)	< 0.001
<i>Surgical category (n [%])</i>				
0	4 (11.8)	0 (0)		
1	5 (14.7)	2 (3.3)		0.004
2	16 (47.1)	44 (72.1)		
3	9 (26.5)	15 (24.6)		
Pre-incision hemoglobin (g/dL)	11.0 ± 1.7	11.3 ± 1.3	-0.3 (-0.5 to 1.1)	0.313
Operation duration (min)	470 ± 131	667 ± 118	-193 (-266 to 128)	< 0.001
Model predicted probability	0.33 ± 0.25	0.73 ± 0.22	-0.4 (-0.53 to -0.28)	< 0.001
<i>PMTSS components (n [%])</i>				
Age > 50	17 (50)	48 (68.7)		0.002
<i>Pre-incision hemoglobin score</i>				
0	3 (8.8)	1 (1.6)		
1	5 (14.7)	18 (29.5)		0.089
2	26 (76.5)	42 (68.9)		
> 2 lumbar levels fused	30 (88.2)	61 (100)		< 0.001
Transpedicular osteotomy	9 (26.5)	15 (24.6)		0.841
<i>PMTSS score (n [%])</i>				
1	2 (5.9)	1 (1.6)		
2	9 (26.5)	7 (11.5)		0.066
3	9 (26.5)	14 (23.0)		
≥ 4	14 (41.2)	39 (63.9)		

\*Data are mean ± SD, median (range), or number of patients (%). Pre-incision hemoglobin score: > 14 g/dL = 0; ≤ 14 g/dL but ≥ 12 g/dL = 1; < 12 g/dL = 2.  
 †Differences not calculated for categorical data.  
 CI indicates confidence interval; PMTSS, predictive model of transfusion in spine surgery.

the validation data set had a major transfusion (Fig. 2). Major transfusion was more likely in patients who underwent more extensive posterior spine fusions ( $P < 0.001$ ) and had longer operations ( $P < 0.001$ ) (Table 5). The present model was able to predict the occurrence of major transfusion using preoperative variables (ROCAUC = 0.89; 99% confidence interval [CI], 0.80-0.90;  $P < 0.001$  compared with random chance, Fig. 3).

The specific variables that comprise the PMTSS and our new model are presented in Table 7 for the validation data set. The distribution of the PMTSS scores was not different between groups ( $P = 0.066$ , Table 7), and there was no optimal cutoff PMTSS score to predict major transfusion. Using a cutoff of a PMTSS score  $\geq 4$ , the ROCAUC was 0.60 (99% CI, 0.48-0.71, Fig. 3), which was not better than chance ( $P = 0.07$  compared with random chance). Our new model performed better than the PMTSS in predicting major transfusion (difference ROCAUC = -0.25; 99% CI, -0.40 to -0.10;  $P < 0.001$  PMTSS vs. our model).

### DISCUSSION

We developed and tested the validity of a quantitative model based on preoperative patient and surgical variables that can accurately predict the probability of major transfusion in a cohort of adults undergoing

complex spine surgery (Table 5). Although not all of these variables can be independently manipulated, all of these variables can be accurately determined preoperatively and therefore used to optimize the timing of the operations and the perioperative management of these patients. Our model performed significantly better than the PMTSS, which was derived to determine a different level of transfusion, the probability of receiving 1 U of PRBCs anytime throughout the initial 5 perioperative days, rather than >4 U RBCs in the intraoperative period (Fig. 3). Our model can be used to identify which patients may benefit from strategies to increase preoperative hemoglobin concentration with iron supplementation and, possibly, erythropoietin (Figs. 4-6). Furthermore, because perioperative blood conservation strategies, such as acute normovolemic hemodilution, preoperative autologous donation, or perioperative administration of anti-fibrinolytics, have been found to be useful only when the estimated blood loss exceeds 1000 mL, our model can help predict when the benefits associated with these interventions outweigh the risks. Finally, our model can provide an objective basis for rational allocation of resources required for anticipated major blood loss, such as appropriate invasive hemodynamic monitoring, large caliber intravenous access, adequate resourcing of blood products, including cell salvage, and the possible need for postoperative ventilation and intensive care management.

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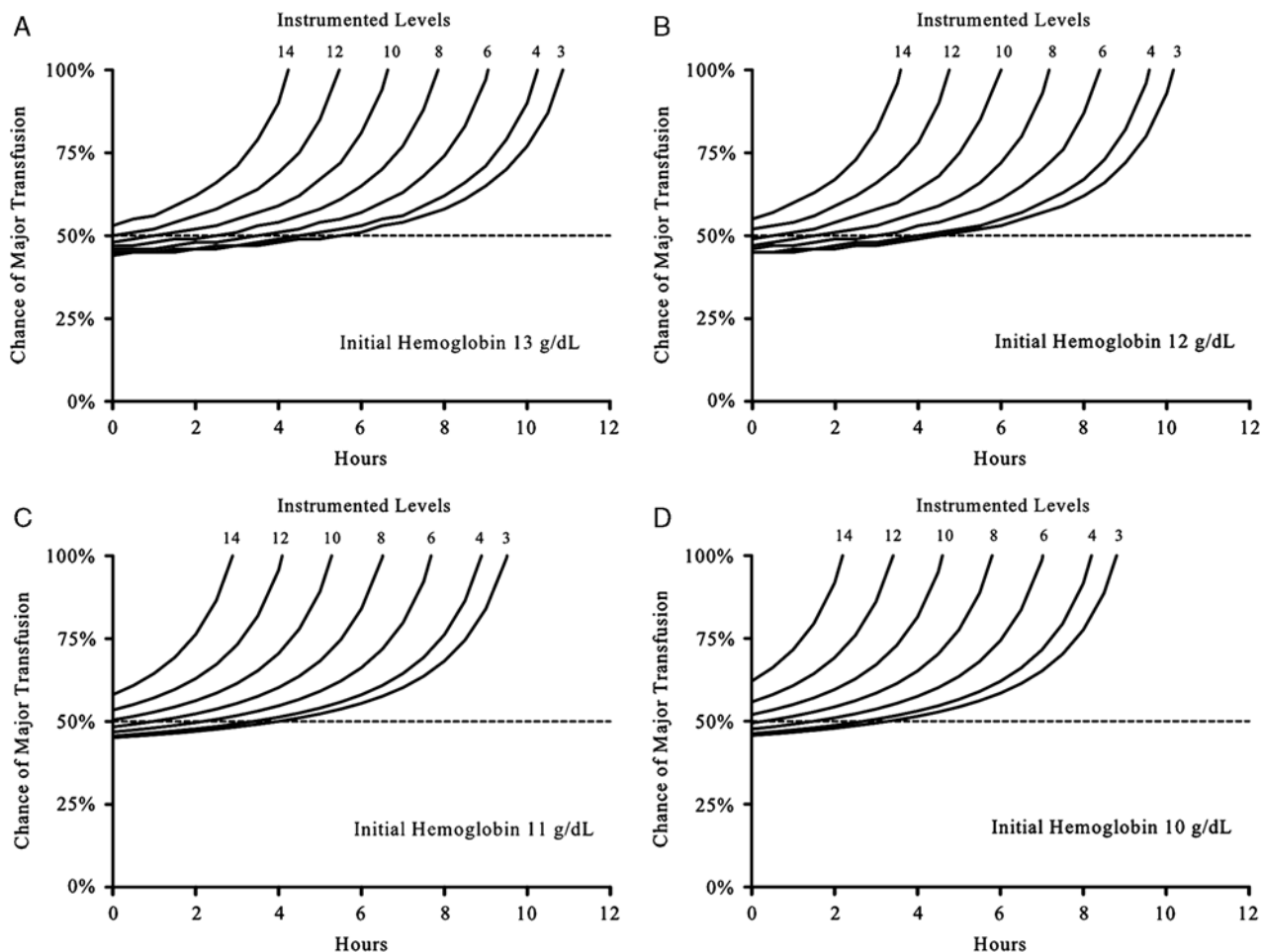
Therefore, this model may be of great value in the preoperative evaluation of patients undergoing adult deformity spine fusion surgery.

**Limitations**

The first limitation of this study is that because the validation data set patients had surgery after the patients that comprised the model derivation data set, there is the possibility that learning effects and other uncontrolled and often unmeasured changes related to the surgical date would limit the generalizability of these data. We attempted to minimize the contribution of temporality by only including surgeons that had an extensive history (>3y) of caring for patients undergoing complex adult spine surgery as the majority (>90%) of their surgical cases. In addition, we found no relationship between the date of the surgery and the duration of the operation uncorrected and corrected for the number of posterior

levels instrumented or surgical category, or the incidence of major transfusion ( $P > 0.9$ , data not shown).

The second limitation of these data are the lack of a formal transfusion trigger. The patients who received major transfusions were found to have an initial postoperative hemoglobin concentrations approximately 0.8g/dL higher than the group who received  $\leq 4$ U of RBCs. This difference is  $< 1$ g/dL, which is typically considered to be the expected increase in hemoglobin concentration after administration of 1 U of PRBCs. As PRBCs are not typically fractionated to  $< 1$  U in adults, the difference is not surprising and probably clinically insignificant. Because the median difference in the number of RBCs transfused was 5 U (99% CI, 5-6 U), it is unlikely that the statistically higher initial postoperative hemoglobin concentrations is due to the erroneous administration of  $< 1$  U of RBCs. Hypothermia may have contributed to this difference, although its effect is difficult to quantify. Furthermore, there was no statistical



**FIGURE 4.** The influence of the hemoglobin concentration, ranging from 10 to 13 g/dL (A–D), the number of posterior instrumented levels (individual curves), and the duration of surgery (x-axis) on the probability of major transfusion (>4U of red blood cell transfusion) in posterior spine fusion involving lumbar segments (surgical category 2). In this model, increasing the duration of surgery (x-axis) increases the probability of major transfusion (y-axis) as does increasing the number of levels instrumented and decreasing the hemoglobin concentration (A–D).

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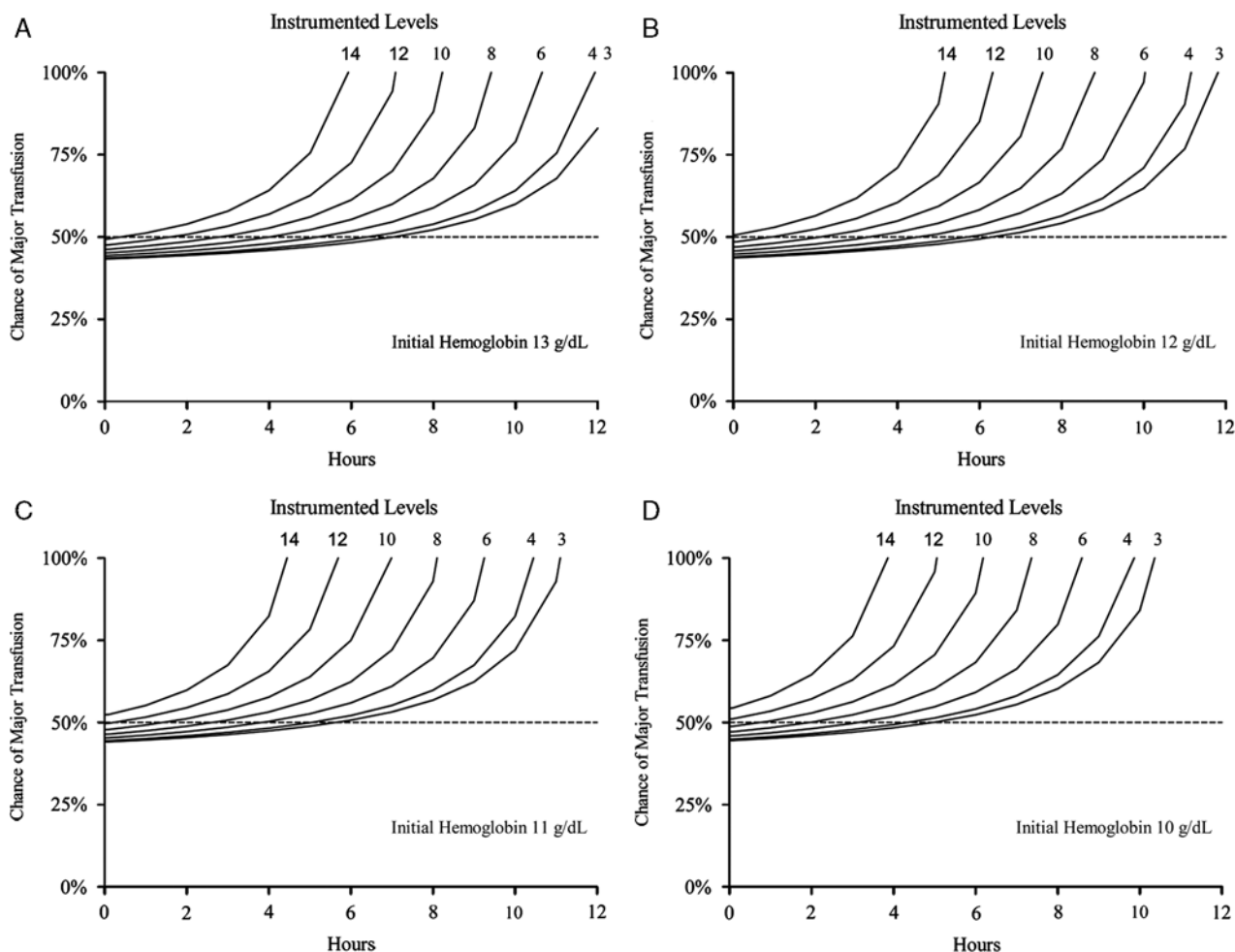
difference in the postoperative hemoglobin concentration for the patients in the derivation cohort ( $10.9 \pm 1.5$  g/dL) when compared with the patients in the validation cohort corrected ( $10.9 \pm 1.1$  g/dL) (99% CI of the difference in the means,  $-0.4$  to  $0.41$  g/dL,  $P = 0.969$ ).

### Interdependence of Variables Associated With Blood Loss

Our model identified some of the same major predictors identified in other predictive models—preincision hemoglobin concentration and number of posterior levels instrumented.<sup>7,12–15</sup> Other models, based on mainly posterior spine fusion without major osteotomies, found a strong correlation between the duration of surgery and the number of levels. In contrast, we demonstrated that surgical duration and the number of surgical levels are each independent determinants of major transfusion that were not tightly correlated.<sup>16</sup> This may be because 18.1% of our

population had procedures that may not have had as many levels operated on but had time-consuming vertebral osteotomies for major angular correction (ie, surgical category 3). We included the more routinely performed lumbar Smith Peterson osteotomies with lumbar fusion surgeries into a single category (ie, surgical category 2), whereas the less commonly performed transpedicular wedge osteotomies (ie, vertebral column resection or pedicle subtraction osteotomies) were categorized separately (surgical category 3).<sup>17,18</sup> The current study extends the findings of Lenoir et al<sup>7</sup> by discretely examining the levels of surgery and the extent of “routine” versus major osteotomies separately. Because this model can account for variability in the different speeds of surgeons, the number of levels instrumented, and the use of more complex osteotomies, this model may be generalizable to other centers.

Although other models have included age, weight, or a history of pulmonary disease as predictors of major



**FIGURE 5.** The influence of the hemoglobin concentration, ranging from 10 to 13 g/dL, (A–D), the number of posterior instrumented levels (individual curves), and the duration of surgery (*x*-axis) on the probability of major transfusion (>4U of red blood cell transfusion) in posterior spine fusion involving cervical and/or thoracic segments (surgical category 1). In this model, increasing the duration of surgery (*x*-axis) increases the probability of major transfusion (*y*-axis) as does increasing the number of levels instrumented and decreasing the hemoglobin concentration (A–D).

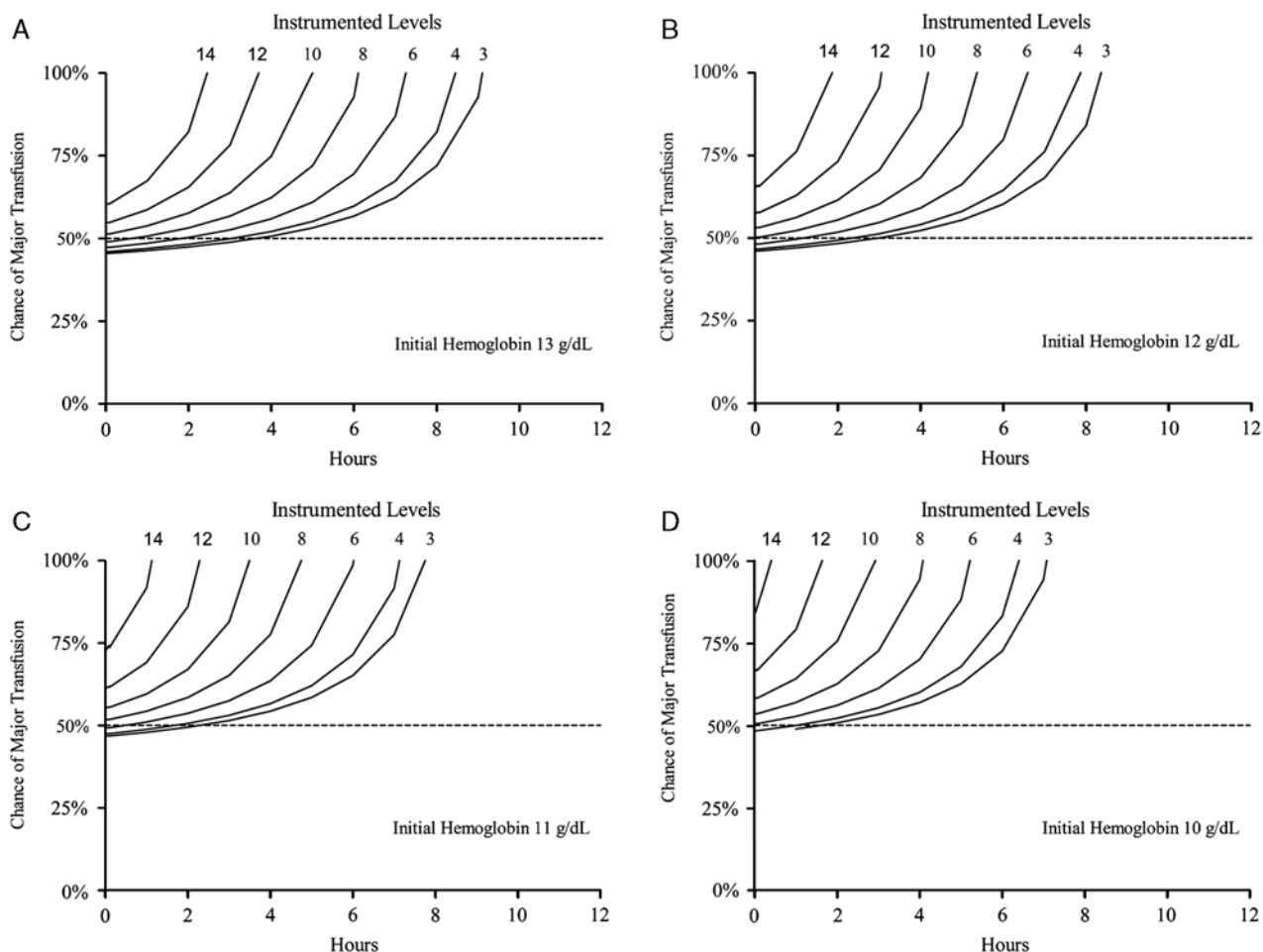
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transfusion, these variables were not specific predictors in our model.<sup>7,12-15</sup> The models that found weight or body mass index strongly predictive of blood transfusion requirements performed surgery on the Relton-Hall or Wilson frames.<sup>14,15</sup> The Jackson table further decreases the risk of blood transfusion by further reducing abdominal pressure compared with other positioning devices, thereby decreasing venous bleeding.<sup>12,19</sup> Because we perform all of our procedures on the Jackson table, it is possible that body weight or body mass index were not important predictors of major transfusion in the “optimally” positioned patient.

### Preoperative Optimization of Patients at Risk for Major Transfusion

Models capable of identifying patients most likely to require major transfusion can serve several important preoperative functions.<sup>1,7,20</sup> We currently use the model

described above in our adult spine deformity practice in several ways. First, and most obviously, this model helps the perioperative team decide if an individual patient will be at risk for major blood loss and transfusion. By providing a discrete probability of requiring a major transfusion, this model offers additional information on the risks versus benefits compared with other models that provided only a “yes” or “no” based on predetermined cutoff values (thresholds). Patients with significant coexisting diseases that may result in worse morbidity or mortality may instead be managed by conservative therapies.<sup>21</sup> Next, for patients predicted to have a high probability of major transfusion, the elective surgical procedure may be postponed to complete preoperative evaluation and optimization in an attempt to improve the patient’s ability to tolerate high-risk surgery or to collect enough compatible blood if the patient has antibodies that require compatible PRBCs that are difficult to



**FIGURE 6.** The influence of the hemoglobin concentration, ranging from 10 to 13 g/dL, (A–D), the number of posterior instrumented levels (individual curves), and the duration of surgery (x-axis) on the probability of major transfusion (>4 U of red blood cell transfusion) in posterior spine fusion that includes any combination of posterior corpectomies, pedicle subtraction osteotomies, or vertebral column resections (surgical category 3). In this model, increasing the duration of surgery (x-axis) increases the probability of major transfusion (y-axis) as does increasing the number of levels instrumented and decreasing the hemoglobin concentration (A–D).

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obtain.<sup>22</sup> Furthermore, we individualize RBC transfusion triggers based on each patient's risk for cardiovascular morbidity.<sup>1</sup> Finally the anesthesiologist can use these predictive models to determine the appropriate invasive hemodynamic monitoring and vascular access, and the need to incorporate strategies to minimize blood loss, such as intraoperative use of cell salvage or antifibrinolytics.<sup>16,23</sup> Because antifibrinolytic agents are costly and may not be indicated in patients at low risk to receive transfusion of multiple units of PRBC, we currently weigh this cost versus the benefit of decreasing transfusion requirements and administer tranexamic acid only if our model predicts major transfusion as highly likely (>80% probability).<sup>24,25</sup>

## CONCLUSIONS

We developed and tested the validity of a generalizable model based on preoperatively available clinical variables that quantitatively predicts the probability of requiring major transfusion in a cohort of adults undergoing complex spine surgery for deformity correction. This model, and the plots demonstrating the interdependence of these variables, can assist the perioperative care team in making decisions regarding which patients can tolerate the large perioperative stress associated with major transfusion. Furthermore, our model can help guide the decisions on when the benefits may outweigh the risks associated with perioperative strategies that could either decrease perioperative bleeding (eg, antifibrinolytics) or blood bank resource utilization (eg, cell salvage, acute normovolemic hemodilution, preoperative autologous donation, etc.). Therefore, this model may be of great value in the preoperative preparation of patients undergoing adult deformity spine fusion surgery.

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