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Clinical Study

The pattern of blood loss in adolescent idiopathic scoliosis

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Abstract

*Background context*Previous studies have shown that modern intraoperative blood-saving techniques dramatically reduce the allogeneic transfusion requirements in surgery for adolescent idiopathic scoliosis (AIS). No studies have looked at the pattern of postoperative hemoglobin (Hb) in AIS patients undergoing corrective spinal surgery and correlated this with the timing of allogeneic transfusion.

Purpose To describe the pattern of perioperative blood loss in instrumented surgery for AIS. We look at the recommendations regarding an ideal preoperative Hb, the need for preoperative cross-matching, and the timing of postoperative Hb analysis.

Study design This was a retrospective case series. Surgeries were performed by one of four substantive pediatric spinal surgeons within a single regional center over a 3-year period.

Patient sample A consecutive series of 86 patients who underwent posterior instrumented fusion for AIS were included: 10 males and 76 females. Mean age was 14 years (range 10–17 years). All patients had posterior instrumented fusion using various blood-saving techniques (eg, cell-saver). All patients were cross-matched preoperatively, and our transfusion trigger value (TTV) was 7 g/dL.

Outcome measures Hemoglobin level was the outcome measure. Hemoglobin readings were obtained preoperatively, within 2 hours of surgery, and daily up to 5 days after surgery. This physiologic measure was assessed using routine blood sampling techniques and standardized laboratory processing.

Methods Patient predictor variables (demographic and surgical) were assessed for association with Hb levels in a hierarchical model, with repeated Hb readings at the lower level being clustered within an individual patient at the upper level of the structure. The variation of Hb levels within individuals was compared with mean levels in different individuals via the variance partition coefficient of the model structure.

Results No patients required intraoperative allogeneic transfusion. Only four patients (4.65%) received allogeneic transfusion, all within 2 days of surgery. A clinically important drop in Hb occurred within the first 2 postoperative days, rising thereafter. The average

postoperative drop in Hb was 4.1 g/dL. Young males had lower postoperative Hb values. Neither the preoperative curve magnitude (Cobb angle of major curve) nor the number of vertebrae/levels fused significantly affected the blood loss.

Conclusions We recommend setting a minimum preoperative Hb value that is 5 g/dL higher than your TTV. Because no patients required an intraoperative transfusion when using modern blood-saving techniques, preoperative cross-matching is unnecessary and potentially wasteful of blood reserves. Hemoglobin analysis beyond the second postoperative day is unnecessary unless clinically indicated.

Keywords: Scoliosis; Adolescent; Hemoglobin; Blood loss; Transfusion

Introduction

Corrective surgery for adolescent idiopathic scoliosis (AIS) puts the patient at a risk of allogeneic transfusion because of the extent of exposure, complexity of the surgery, and longer operative times [1–4]. Bowen et al. [3] found pediatric idiopathic scoliosis patients twice as likely to require transfusion, with a surgical time of more than 6 hours. Allogeneic transfusion carries the risks of sensitization, transfusion reactions, disease transmission, and surgical site infection [5,6]. The rate of hospital-acquired infection rose from 3% to 20% when patients received allogeneic blood [7].

Historically, a high percentage of patients received allogeneic blood to replace surgical blood loss [8]. With the use of modern blood conserving techniques, blood loss and the use of allogeneic blood for transfusion have reduced significantly [8–10]. Various blood conserving methods have been adopted in spinal surgery.

Tranexamic acid (TXA) has shown a definite benefit in both arthroplasty and spinal surgery at reducing blood loss and the need for a transfusion [4,11–17]. A placebo-controlled study in pediatric patients undergoing scoliosis surgery found that TXA reduced blood loss by 41% [15]. Cell salvage has been shown to reduce allogeneic transfusion rates in spinal surgery [3,18,19], but recent review articles show little evidence to support its routine use [12,14]. A nonrandomized study has even showed increased blood loss in the cell-saver group [20]. Preoperative autologous blood donation has had mixed reports in the literature [21–25].

Corrective surgery for AIS is performed on a regular basis at our institution. Our blood-saving protocol uses a combination of techniques, such as TXA infusion, cell-salvage, meticulous hemostasis with electrocautery, controlled hypotension (mean blood pressure of 50–60 mmHg), and warmed fluids and warming blanket (avoiding hypothermia). Our institution has low allogeneic transfusion rates because of these techniques [9]. Despite our low allogeneic transfusion rate, all patients are preoperatively cross-matched for 1 to 2 adult units (1unit≈270 mL) of blood.

Our patients are managed postoperatively according to a documented protocol that dictates a minimum of 2 days high dependency care, standardized fluid supplementation to maintain mean blood pressure above 60 mmHg, and daily blood analysis. Our documented transfusion trigger value (TTV) is 7 g/dL. Low TTVs have been shown to safely lower allogeneic transfusion rates [8,9,26].

This study was aimed at answering a number of questions:

1.

What is the pattern of postoperative blood loss in corrective surgery for AIS?

2.

What is an acceptable preoperative hemoglobin (Hb) level in corrective surgery for AIS?

3.

Is preoperative cross-matching necessary?

4.

When should postoperative Hb analysis occur?

5.

Is our view of the need for transfusion absolute, when perhaps it should be relative?

Methods

This was a retrospective review of consecutive children undergoing instrumented posterior spinal fusion for AIS at our institution. Theater records were used to identify 86 children between May 2008 and September 2011. Most children had a preoperative magnetic resonance imaging scan that confirmed idiopathic scoliosis.

Surgeries were performed by four substantive pediatric spinal surgeons. Segmental fixation was used in all cases. One wound drain was routinely placed superficial to the deep fascia during wound closure. Anesthesia was provided by four substantive pediatric anesthetists using a standardized technique. No child was excluded from the study or lost to follow-up. There has not been any conflict of interest.

For each case the following information was recorded: gender, curve type, blood-saving methods (ie, TXA, cell-saver, monopolar dissection, hypotensive anesthesia, and warming blanket), whether or not chemical prophylaxis (enoxaparin) was administered during the perioperative period, age at surgery, Cobb angle [27] before and after surgery, number of vertebrae included in fixation, reinfused blood cell-saver volume, crystalloid and colloid volume given during surgery, drain volume, and preoperative Hb level. Curve types were classified according to Lenke et al. [28] and grouped into whether the major curve was thoracic or thoracolumbar/lumbar.

During the perioperative period, Hb level is routinely used to measure the functional blood volume (in respect of oxygen carrying capacity) and, indirectly, the blood loss. Therefore the outcome measure recorded was Hb level. This physiologic measure was assessed using routine blood sampling techniques and standardized laboratory processing. For each patient, a number of readings of this measure were made, taken within 2 hours of surgery and daily up to 5 days after surgery. Not all measurements were taken from each patient on every measurement occasion: while almost all patients supplied at least three readings, only a minority of patients supplied four or five readings. No patient supplied more than five readings. Intrapatient changes in Hb levels from baseline were recorded for each set of readings.

Modeling strategy and model specification

Patient predictor variables were assessed for inclusion in a hierarchical model, with repeated Hb measurements of a particular patient at the lower level (Level 1) being clustered within an individual patient at the upper level (Level 2) of the structure.

Following a screening procedure, in which any variable found not to be associated with the outcome measure in an uncontrolled model was eliminated from further consideration, a subset of predictors was derived, based on the considerations of model fit measured by changes in the likelihood ratio statistic. Parameter estimates and standard errors, with associated p values, were reported for each included parameter in a final parsimonious two-level multiple regression model. All variables were assessed for collinearity before entry into any model, and an adequate ratio of cases to variables was maintained in all models.

The assessment of the patient data structure was facilitated by the determination of the variance partition coefficient. This is a measure of the extent to which repeated Hb readings from specific individuals vary compared with mean levels in different individuals.

All analysis was undertaken using the multilevel modeling software MLwiN(version 2.25) (Centre for Multilevel Modelling), using the iterated general least squares procedure for parameter estimation. The sample size of 86 was assessed for adequacy to detect a difference in the outcomes for a multiple regression study of this design with a medium or large effect size. The ratio of fitted variables in the final multiple model to sample size was controlled to ensure the stability of parameter estimates.

Results
Descriptive summary of data

Ten males and 76 females were included in the analysis, aged between 10 and 17 years. There was no significant difference in mean age between males and females (p=.122). All demographic and studied data, where available, are summarized in Table 1.

Variables corresponding to the number of blood-saving methods used during surgery and the type of curve were found not to discriminate sufficiently between patients. These variables were not included in subsequent analyses.

Table 1 Summary of individual-level health/demographic variables

Individual-level categorical variables	Frequency (valid %)
Gender	
Male	10 (11.6)
Female	76 (88.4)
Curve type	
Thoracic (left or right)	78 (91)
Thoracolumbar/lumbar (left or right)	8 (9)
Tranexamic acid given during surgery	
Yes	83 (97.6)
No	2 (2.4)
Cell-saver used during surgery	
Yes	67 (80.7)
No	16 (19.3)
Monopolar dissection used during surgery	
Yes	83 (100.0)
No	0 (0.0)
Hypotensive anesthesia used during surgery	
Yes	83 (100.0)
No	0 (0.0)
Warming blanket used during surgery	
Yes	83 (100.0)
No	0 (0.0)

Individual-level categorical variables	Frequency (valid %)
Enoxaparin administered postoperatively	
Yes	23 (28.0)
No	59 (72.0)
Individual-level numerical variables	Mean (SD)
Age (y)	14.0 (1.57)
Age (males), y	14.6 (1.17)
Age (females), y	13.8 (1.57)
Cobb angle before surgery (°)	64.4 (13.8)
Cobb angle after surgery (°)	21.0 (7.61)
Number of vertebrae included in fixation	10.2 (2.23)
Reinfused blood cell-saver volume (mL)	197 (177)
Crystalloid volume given during surgery (mL)	1,636 (648)
Colloid volume given during surgery (mL)	694 (502)
Drain volume (mL)	73.2 (101)
Preoperative hemoglobin value (g/dL)	13.4 (1.09)
Hemoglobin value within 2 h of surgery	10.7 (1.07)
Hemoglobin value 1 d after surgery (g/dL)	9.91 (1.26)
Hemoglobin value 2 d after surgery (g/dL)	9.24 (1.22)
Hemoglobin value 3 d after surgery (g/dL)	9.36 (1.54)
Hemoglobin value 4 d after surgery (g/dL)	9.37 (1.23)
Hemoglobin value 5 d after surgery (g/dL)	10.2 (1.40)

SD, standard deviation.

Our sample is typical of the population to which we wish to generalize our results: in age, diagnosis, and surgical procedure. All children had normal pre- and postoperative coagulation (platelets and prothrombin/ activated partial thromboplastin times)

and renal function. For reasons unknown, estimated blood loss was not recorded in enough patients to be included in the study. Four children were transfused allogeneic blood in the postoperative period (one child on Day 1 and three children on Day 2). Two of them were transfused despite an Hb level above our AIS specific TTV.

Table 2 summarizes the intrapatient changes in Hb levels at all measured time points from baseline. Although a drop in Hb levels from preoperative levels to levels recorded within 2 hours of surgery may be observed, there was no monotonic trend in Hb levels over the 5-day postoperative period. Mean Hb levels (plus associated confidence intervals) over a period spanning from preoperative to 4 days after surgery are illustrated in Fig. 1. An insufficient number of readings were taken on Day 5 to be included in the figure. The wide confidence intervals associated with readings taken on Day 3 and 4 reflect the relatively low numbers of patients from whom readings were taken on those days.

Table 2 Intrapatient reduction in Hb levels from baseline

Time	Mean	SD
2 h	2.64	0.88
1 d	3.46	0.95
2 d	4.10	1.02
3 d	4.04	1.23
4 d	3.97	1.14
5 d	3.10	2.26

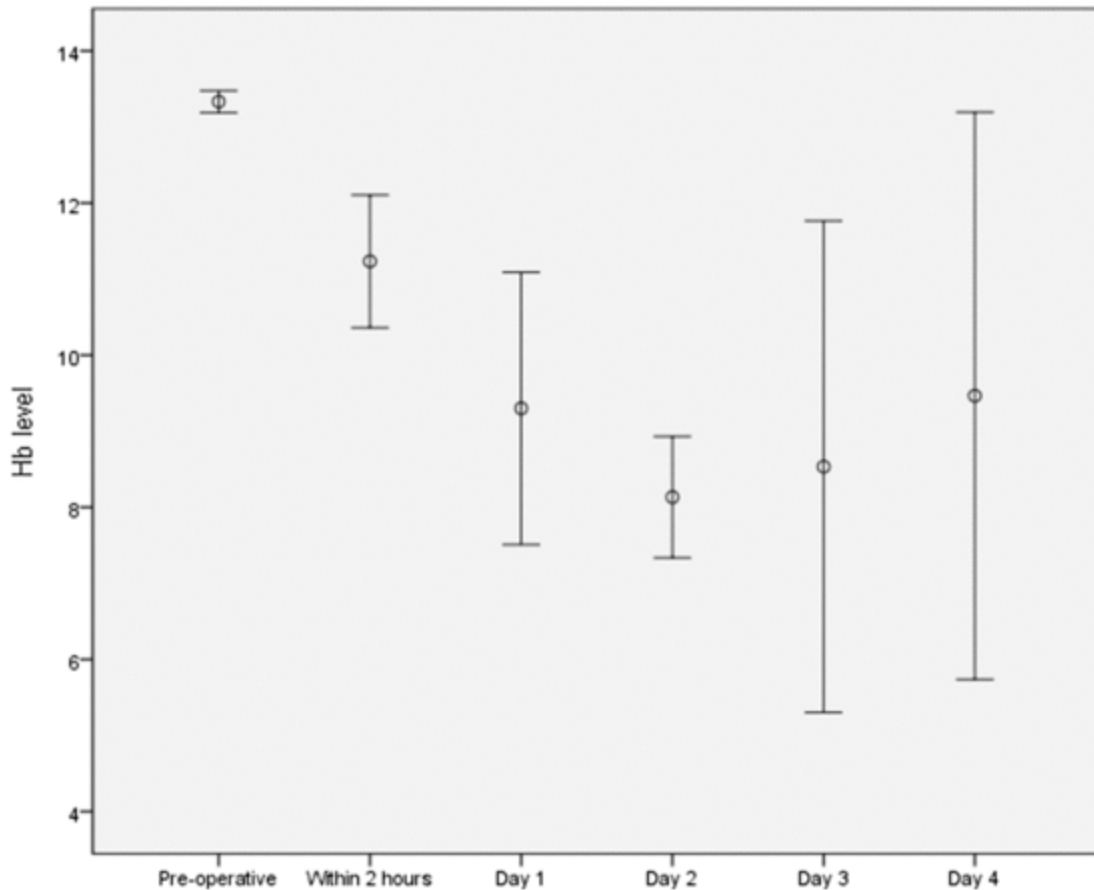Hb, hemoglobin; SD, standard deviation.

Fig. 1 Mean Hb levels (and associated 95% confidence intervals): preoperative to 4 days after surgery. Hb, hemoglobin.

Changes in Hb levels for individual patients over time are illustrated inFig. 2, for male and female patients separately, and Fig. 3, for patients with high ($\geq$13 g/dL) and low ($<$13 g/dL) preoperative Hb levels. For both males and females, minimum Hb levels appear to occur in general around Day 2 and 3. For patients with high preoperative Hb levels, the trend in subsequent Hb levels is unclear. For patients with low preoperative Hb levels, minimum Hb levels appear to occur in general around Day 2 and 3. A small number of patients in this subgroup experienced oscillation of levels between the surgery and Day 2.
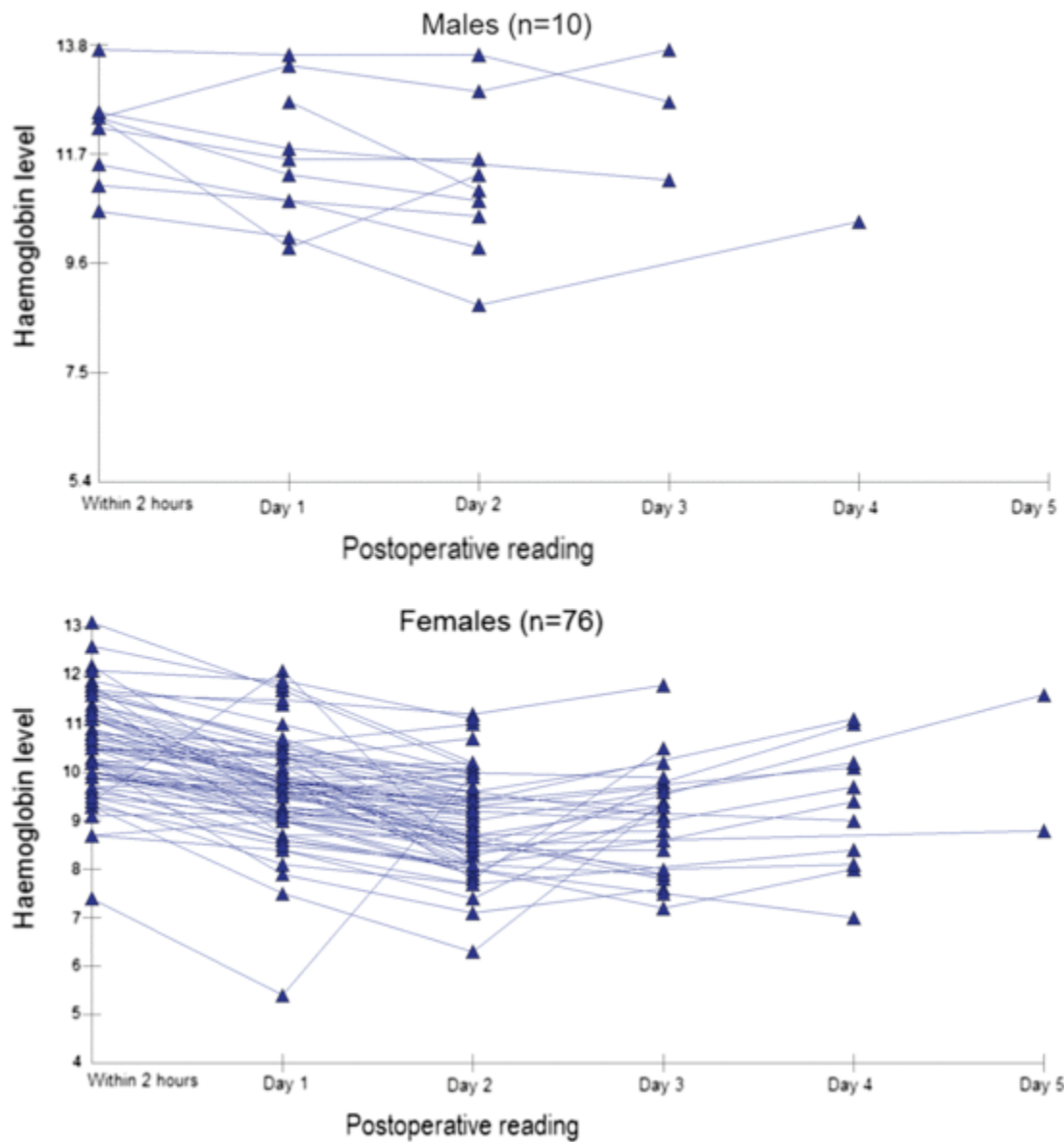
Fig. 2 (Top and Bottom) Hb levels for individual patients at each measured time point (data partitioned by gender). Hb, hemoglobin.
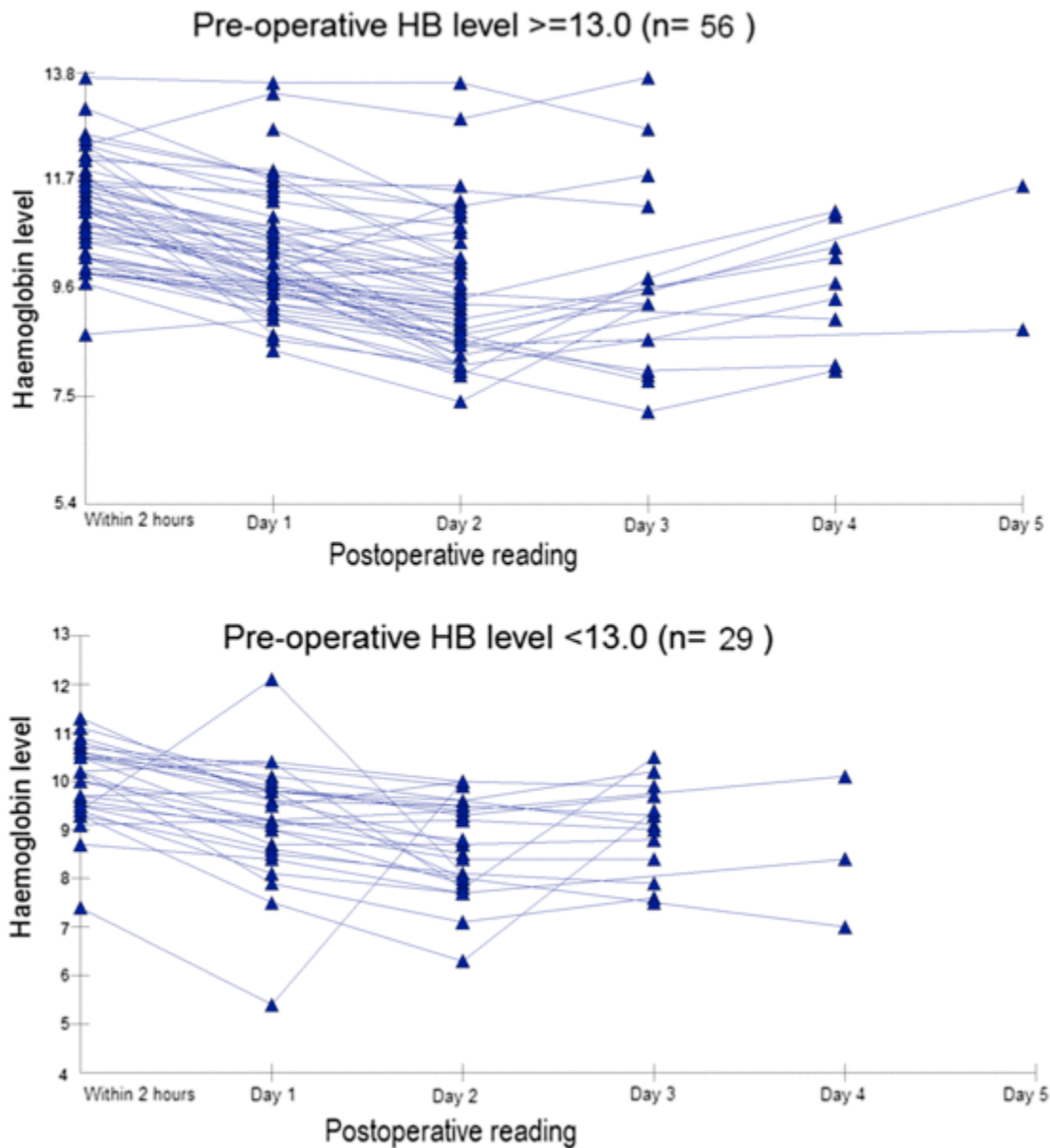
Fig. 3 (Top and Bottom) Hb levels for individual patients at each measured time point (data partitioned by preoperative Hb levels). Hb, hemoglobin.

Uncontrolled regression models

Comparison of likelihood ratio statistics associated with a two-level null model and a simple multilevel regression model indicated that inclusion of all patient-level factors and covariates with the exception of the *vertebrae* covariate resulted in a significantly better model fit. These variables were thus carried

forward to the further stages of the modeling process. Output from this series of models is summarized in Table 3.

Table 3 Partial regression coefficients, likelihood ratio statistics, and p values: uncontrolled multilevel regression models

Variable	Estimate	Standard error	LRS	ΔLRS*	p
Gender (M=0)	−1.95	0.299	871.599	34.363	<.001
Age (y)	0.223	0.0699	896.347	9.615	.002
Cobb (°)	0.013	0.015	897.934	8.028	.005
Vertebrae	−0.091	0.050	902.706	3.256	.071
Cell-saver	−0.00131	0.00066	879.000	26.962	<.001
Crystalloid	−0.000012	0.000201	817.909	88.053	<.001
Colloid	0.000030	0.000260	806.514	99.448	<.001
Enoxaparin (no enoxaparin=0)	−0.277	0.266	875.113	30.849	<.001
Drain (mL)	−0.001	0.001	834.996	70.966	<.001
Preop Hb	0.684	0.0799	843.648	62.314	<.001

M, male; preop, preoperative; Hb, hemoglobin.

*From an LRS of 905.962 for a multilevel null model.

Multiple regression models

Collinearity diagnostics did not indicate evidence for collinearity between any variables carried forward from the univariate analyses for consideration in a multiple regression model. Comparison of likelihood ratio statistics associated with a two-level model including all qualifying variables and a corresponding model with each variable deleted in turn indicated that in the presence of other variables, neither *Cobb*, *cell-saver* volume, or *crystalloid* volume significantly improved the model fit. Remaining variables (*gender, age, colloid* volume, *enoxaparin, drain* volume, and *preoperative*

Hb level) were carried forward for inclusion in a final parsimonious multilevel multiple regression model. Output from this model is summarized in Table 4. The number of variables remaining in the final parsimonious model [6] is not excessive for an observational study with 86 cases and should have no implications for stability of parameter estimates.

Table 4 Partial regression coefficients, likelihood ratio statistics, and p values: parsimonious multiple multilevel regression model

Variable	Estimate	Standard error	LRS	ΔLRS*	p
Constant	0.191	1.404	—	—	—
Gender (M=0)	1.07	0.282	704.802	13.11	<.001
Age (y)	0.182	0.059	700.479	8.79	.003
Colloid	−0.00033	0.00016	746.410	54.72	<.001
Enoxaparin (no enoxaparin=0)	−0.078	0.207	697.794	6.10	.014
Drain (mL)	0.00004	0.00082	727.045	35.35	<.001
Preop Hb	0.541	0.088	721.349	29.66	<.001

M, male; preop, preoperative; Hb, hemoglobin.

*Compared with a model including all the above factors and covariates for which an LRS of 691.693 was obtained.

Variance partitioning

The variance partition coefficient for the multilevel regression model was calculated to be 0.157, with the implication that daily variation in Hb levels between patients is relatively large in comparison with the magnitude of the variation between patients, with about 84% of data variability occurring between Hb readings within individuals and about 16% of data variability occurring between individual patients.

Discussion

Statistical model

Casting the data into a hierarchical model structure has many advantages. Parameter standard errors accurately reflect the clustering of Hb readings within individuals. A standard single-level regression model structure would not be able to account for the dependencies between readings taken from the same individual, leading to overestimates of precision of estimates, and possible spurious inferences of significance. The multilevel structure also enables the identification of sources of variation in the data (between patients or between readings within patients) and allows an assessment of the effect of patient-level factors and covariates. Furthermore, in models where readings are cast as the lowest level of a hierarchical structure, it is not necessary to have an equal number of readings associated with each individual, as would be the case, for example, in a treatment based around repeated measures analysis of variance. The method of approach is, hence, appropriate in the present context, where many readings are missing in the later stages of the analysis period. There is no evidence that data in this study are not missing at random.

Conclusions

Our analysis appears to indicate that gender and preoperative Hb level are the factors that most affect postoperative Hb, followed by age and use of enoxaparin. Highest postoperative Hb levels are recorded in older girls for whom enoxaparin was not used. We should, therefore, be mindful of young boys who are more likely to have low postoperative Hb levels: our study found that boys had, on average, 1.07 g/dL lower Hb levels than girls of the same age and that younger children had, on average, lower levels than older children, with mean levels increasing by about 0.18 g/dL with

each year of advancing age. Enoxaparin was associated with an average reduction of only 0.078 g/dL of Hb. However, the use of chemical thromboprophylaxis remains a decision based on local venous thromboembolic guidelines.

A surprising but nonetheless noteworthy finding was that the extent of surgery (the number of vertebrae/levels exposed and included in the fusion) did not have a significant effect on blood loss. A number of studies have shown increasing levels to be associated with increased blood loss and/or transfusion[1,4,29–33], although this result was found in shorter fusions (eg, comparing two-level fusions and more). The number of vertebrae fused in our study ranged from 5 to 14. Although Hassan et al. [34] analyzed a similar number of fused levels, they showed increased blood loss with higher number of levels fused. Our finding contradicts this and would suggest that a more selective fusion does not have a blood-saving advantage. Although statistically significant, the effects of colloid volume and the use of enoxaparin and drains are not clinically important. There is, therefore, no clinically important dilution of red blood cells through either crystalloid or colloid supplementation. Our results would also suggest that cell-saver has no influence on postoperative Hb. This may reflect low volumes reinfused, which is as a result of attention to the other blood-saving techniques used.

Many authors have looked at the predictors of transfusion in spinal surgery. It is only logical that a low preoperative Hb carries a higher risk for transfusion [1,29,31,32,35]. We recommend that every institution set a minimum preoperative Hb level. Because we have shown an average postoperative drop in Hb of 4.1 g/dL, the minimum preoperative Hb level for an AIS patient undergoing

corrective surgery should be at least 4 g/dL higher than the TTV set by an institution. Preoperative Hb in our study ranged from 10.9 to 17.4 g/dL. Within this range, it was shown that every 1.0 g/dL increase in the preoperative Hb was associated with a 0.54 g/dL increase in the postoperative Hb: a statistically significant effect of substantive importance. This would suggest that there is a disproportionate relationship between preoperative and postoperative Hb levels. If this is true, then it cannot be assumed that all patients have the same drop in Hb, a statement that seems sensible in itself. Given the association inferred by our data and the variance within our patient sample, we suggest to aim for a preoperative Hb of 5 g/dL higher than the TTV.

Jones et al. [36] recommended cross-matching three blood units for instrumented spinal surgery, and our current practice is 1 to 2 units. Using modern blood-saving techniques, no child in our study required intraoperative allogeneic blood transfusion. Although it is contrary to longstanding practice, we, therefore, consider preoperative cross-matching unnecessary and potentially wasteful of allogeneic blood reserves. However, we still recommend preoperative typing (group and save) in the event that allogeneic blood is required during the perioperative period.

The trigger to transfuse allogeneic blood in our patient sample occurred on either the first or second postoperative day. No transfusion occurred beyond the second postoperative day, despite continued Hb analysis. According to our observation, the lowest Hb levels occurred around 2 to 3 days postoperatively and began to rise thereafter. The difference in Hb levels between Days 2 and 3 was not clinically important. Hemoglobin analysis beyond the second (and certainly the third) postoperative day is therefore considered

unnecessary unless clinically indicated (eg, hemodynamic instability).

The lowest mean Hb was on the second postoperative day, and therefore, the most likely to trigger transfusion. Because no patient in our study was transfused beyond the second postoperative day, the Day 2 Hb level is considered essential. The mean drop in Hb from shortly after surgery (blood sample taken in theater recovery) to the second postoperative day is 1.46 g/dL. Thus, if the Hb shortly after surgery is 2 g/dL higher than the TTV, we consider that Hb analysis is only required again on the second postoperative day (assuming the patient is well).

Despite setting a TTV of 7 g/dL, two of the patients in our cohort were transfused for Hb values above the TTV (7.4 g/dL and 7.9 g/dL). This was in response to an Hb reading of less than the generally accepted TTV of 8 g/dL. We challenge what was an almost automated response to an Hb value below a certain TTV. According to our observation, a patient with an Hb level of 6.9 g/dL the day after surgery has a greater need for transfusion than a patient with an Hb level of 6.9 g/dL on the third postoperative day. We suggest considering an Hb result in relation to time, previous results and predicted future results, all within the limits of safe medical practice (eg, hemodynamic status of the patient). However, we do not deny the need for an absolute. We simply agree with other authors that the decision to transfuse be based on clinical judgment [37,38].

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