ORIGINAL ARTICLE

Prediction of Hidden Blood Loss During Posterior Spinal Surgery

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Objective Identification of the risk factors for extraordinary hidden blood loss (HBL) could clarify the underlying causes and provide more appropriate management. This study aims to identify the predictors of HBL in spinal surgery.

Methods Medical records were retrospectively retrieved to collect the data of patients who undergoing posterior thoracic and lumbar fusion surgery or scoliosis surgery. Demographic information, perioperative visible blood loss volume, as well as laboratory results were recorded. The patients receiving fusion surgery or scoliosis surgery were further divided into the HBL positive subgroup and the HBL negative subgroup. Differences in the variables between the groups were then analyzed. Binary logistic regression analysis was performed to determine independent risk factors associated with HBL.

Results For patients undergoing posterior spinal surgery, the independent risk factors associated with HBL were autologous transfusion (for fusion surgery $P=0.011$, $OR: 2.627$, $95\%CI: 1.574-2.782$; for scoliosis surgery $P<0.001$, $OR: 2.268$, $95\%CI: 2.143-2.504$) and allogeneic transfusion (for fusion surgery $P<0.001$, $OR: 6.487$, $95\%CI: 2.349-17.915$; for scoliosis surgery $P<0.001$, $OR: 3.636$, $95\%CI: 2.389-5.231$).

Conclusion Intraoperative blood transfusion might be an early-warning indicator for perioperative HBL.

POSTOPERATIVE hemoglobin (Hb) level is one of the important reference indexes to calculate postoperative blood loss, however, in clinical practice Hb level drop is usually inconsistent with volume of visible blood loss. The

dramatic decrease of Hb level might be attributed to hidden blood loss (HBL). Perioperative total blood loss usually refers to visible intraoperative blood loss plus postoperative drainage volume, however, HBL due to blood extravasating from trauma into the surrounding tissue spaces or hemolysis is frequently ignored by clinical physicians.^[1-2] Although the formula described by Se-hat *et al.* has been used to determine HBL volume, the calculated results reported by different studies varied greatly.^[3-4] Up to now, there are few reports focusing on

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possible reasons for HBL after spinal surgery. In this retrospective study, we explored the risk factors that might increase HBL of cases with spinal surgery, and expected to provide appropriate management to reduce HBL.

PATIENTS AND METHODS

Data collection

We retrospectively collected the data of patients undergoing posterior thoracic and lumbar fusion surgery or scoliosis surgery in the Peking Union Medical College Hospital between May 2012 and August 2013. The exclusive criteria were as follows: patients with perioperative infection or severe coagulation disorders, hematological diseases; those who exhibited intraoperative or postoperative serious blood loss that did not match the calculated blood loss volume with Gross equation;^[5] those whose clinical data were incomplete.

Data were collected from all patients including: age; gender; height (m); weight (kg); body mass index ($BMI = \text{weight}/\text{height}^2$); preoperative and the 1st to 3rd day postoperative Hb, hematocrit (Hct), platelet count, white blood cell count, preoperative Cobb angle; type of surgery (whether the patients underwent osteotomy); intraoperative blood loss and postoperative drainage volume; perioperative blood transfusion volume; operation duration.

Calculation of HBL

The blood volume was calculated based on the formula described by Gross.^[5] The calculated blood volume (PBV) (L) = $k_1 \times h + k_2 \times w + k_3$, where h = height (m); w = weight (kg); for male $k_1 = 0.13669$, $k_2 = 0.103219$, $k_3 = 0.16041$; for female $k_1 = 0.13561$, $k_2 = 0.103308$, $k_3 = 0.11833$.

HBL (L) was calculated as follows, $HBL (L) = PBV \times (\text{preoperative Hct} - \text{Hct on the 3rd day postoperatively}) - \text{visible blood loss (intraoperative visible blood loss volume} + \text{postoperative drainage volume)} + \text{blood transfusion (autologous} + \text{allogeneic blood transfusion volume)}$.^[6-7]

In clinical practice, blood loss volume of 400 ml is of a threshold for maintaining cardiovascular stabilization, therefore patients with blood loss volume less than 400 ml do not need transfusion. Based on the above fact HBL was defined as the calculated volume in excess of 400 ml. According to this standard patients undergoing thoracic and lumbar fusion surgery or scoliosis surgery were allocated to the HBL positive

subgroup and HBL negative subgroup respectively.

Statistical analysis

Data were analyzed with Statistical Package for Social Science (version 20.0; SPSS, Inc., Chicago, IL, USA). Categorical variables were expressed as frequencies and intergroup comparison was performed with Chi-square test. Normally distributing continuous variables were expressed as means and standard deviations and t -test was used to assay intergroup difference, and non-normally distributing data were expressed as medians and 25th and 75th percentiles and compared by using Wilcoxon rank-sum test. A value of $P < 0.05$ was considered statistically significant.

Statistically significant continuous variables were transformed into categorical variables by their cutoff points. Binary logistic regression analysis was performed to determine the independent risk factors associated with HBL and to calculate odds ratio (OR) and 95% confidence intervals (95%CI).

RESULTS

General characteristics

During the study period, 614 patients underwent posterior spinal surgery. And 53 cases were excluded including 27 for incomplete data and 25 for perioperative blood loss volume $> 50\%$ of total blood volume, and 1 for postoperatively severe hemothorax. Finally, a total of 561 patients were enrolled in the study, where 292 underwent thoracic and lumbar fusion surgery and 269 with scoliosis surgery. Patients' general characteristics are shown in **Table 1**.

Comparisons of perioperative blood loss between the two groups

The blood loss of patients with thoracolumbar spine fusion surgery was significantly lower than that with scoliosis surgery, which included total blood loss volume (842 ± 611 vs. 1580 ± 1315 ml, $t = -8.6$, $P < 0.01$), visible blood loss volume (346 ± 251 vs. 732 ± 597 ml, $t = -10.1$, $P < 0.01$), HBL volume (496 ± 353 vs. 852 ± 506 ml, $t = -9.7$, $P < 0.01$), and ratio of HBL to estimated blood volume (8% of body weight) (8.1 ± 6.5 vs. 10.0 ± 6.9 , $t = -3.4$, $P < 0.01$).

Risk factors associated with HBL in patients undergoing thoracic and lumbar fusion surgery

During the study period we included all the patients

Table 1. General characteristics of the thoracolumbar spine fusion surgery and scoliosis surgery groups

Variables	Thoracolumbar spine fusion surgery (n=292)	Scoliosis surgery (n=269)	Statistic	P-value
Male [n (%)]	132 (45.2)	100 (37.2)	3.39	0.06
Female [n (%)]	160 (54.8)	169 (62.8)	3.39	0.06
Age [§] (yrs)	54.6±15.6	15.6±9.1	35.77	0.00
Height [§] (m)	1.64±0.11	1.49±0.18	12.01	0.00
Weight [§] (kg)	68.9±13.4	44.1±14.3	21.19	0.00
Body mass index [§] (kg/m ²)	25.4±3.8	19.1±3.5	20.37	0.00
Surgical duration (min)	174.2±55.0	213.6±80.1	-6.83	0.00
Autologous blood transfusion [n (%)]	105 (35.9)	164 (60.9)	34.08	0.00
Allogeneic blood transfusion [n (%)]	24 (8.2)	66 (24.5)	26.47	0.00

§: Plus-minus values are means±SD.

who met the inclusion criteria into the analysis, so a power analysis with the maximum available sample size of 292 receiving thoracic and lumbar fusion surgery and 269 receiving scoliosis surgery was conducted. Before this study, we hypothesized that allogeneic blood transfusion was the most important predictor of HBL for both fusion surgery and scoliosis surgery. In fusion surgery, there were 174 patients with HBL negative. In these patients, the proportion receiving allogeneic blood transfusion was 2.9%. We used a 2-side probability of 0.05 and 0.2 for type I and II error respectively and found a sample size of 292 was enough to detect an OR equal to or larger than 4.65. The actual ORs from the univariate and multivariate analyses were 6.49. Therefore, the sample size was enough for the analyses in fusion surgery. Based on a similar rationale, the sample size of 269 was enough to detect an OR equal to or larger than 3.31 for scoliosis surgery, which was enough to detect the actual ORs of 14.36 and 3.63 in the univariate and multivariate analyses respectively.

As illustrated in **Table 2**, for cases with thoracic and lumbar fusion surgery, variables including age, height, weight, number of segments, surgical time, intraoperative transfusion of autologous blood and allogeneic blood showed significant differences between the HBL positive and negative groups (all $P < 0.05$). These variables were further analyzed by using binary logistic regression analysis and results showed that the independent risk factors for HBL were intraoperative autologous blood transfusion ($P = 0.011$, OR: 2.627, 95%CI: 1.574–2.782) and intraoperative allogeneic blood transfusion ($P < 0.001$, OR: 6.487, 95%CI: 2.349–17.915) (**Table 3**).

Risk factors associated with HBL in patients undergoing scoliosis surgery

Variables including cases receiving osteotomy, preoperative Cobb angle, operation duration, intraoperative infusion of colloids, and intraoperative transfusion of autologous blood, allogeneic blood, and frozen plasma had significant differences between the positive and negative groups (all $P < 0.05$, **Table 4**). These variables were then analyzed using binary logistic regression analysis. The results revealed that the independent risk factors for HBL were intraoperative autologous blood transfusion ($P < 0.001$, OR: 2.268, 95%CI: 2.143–2.504) and intraoperative allogeneic blood transfusion ($P < 0.001$, OR: 3.636, 95%CI: 2.389–5.231) (**Table 5**).

DISCUSSION

Intraoperative visible blood loss plus postoperative drainage are usually measured and recorded as perioperative blood loss.^[8–9] Intraoperative HBL causing by hemolysis as well as by surgical trauma hemorrhage oozing into tissue spaces is frequently underestimated.^[1] Smorgick *et al.*^[1] found that 42% of total blood loss was HBL in patients undergoing primary decompression and posterior fusion surgery, and 39% in those with revision posterior spinal fusion surgery. Our study showed that the average volume of HBL for thoracic and lumbar fusion surgery patients was 496 ml, accounting for 58.9% of total blood loss, while for scoliosis surgery patients the mean HBL was 852 ml, accounting for 53.9% of the total blood loss. These results indicated HBL is commonly occurred in the perioperative period of posterior spinal

Table 2. Comparisons of general characteristics between the hidden blood loss positive and negative groups for patients undergoing thoracic and lumbar fusion surgery

Variables	Hidden blood loss positive (n=118)	Hidden blood loss negative (n=174)	P-value
Gender			0.490
Male [n (%)]	40 (33.9)	73 (41.9)	
Female [n (%)]	78 (65.5)	101 (58.0)	
Age [§] (yr)	56.3±14.1	51.8±16.3	0.015
Height [§] (m)	1.58±0.09	1.68±0.11	<0.001
Weight [§] (kg)	64.6±11.7	71.6±13.8	<0.001
Body mass index [§] (kg/m ²)	25.6±3.9	25.2±3.7	0.328
Number of segments [§]	2.27±1.89	1.86±1.05	0.026
Surgical duration [§] (min)	182.2±61.5	168.4±49.6	0.036
Visible blood loss [§] (ml)	797.5±692.3	775.2±601.6	0.688
Intraoperative infusion of crystalloids [§] (ml)	1518.3±998.2	1514.9±907.6	0.657
Intraoperative infusion of colloids [ml, M (QR)]	500 (500, 1000)	500 (500, 1000)	0.135
Intraoperative autologous blood transfusion [n (%)]			
Yes	73 (61.8)	40 (23.0)	<0.001
No	45 (38.2)	134 (77.0)	
Intraoperative allogeneic blood transfusion [n (%)]			
Yes	19 (16.2)	5 (2.9)	<0.001
No	99 (83.8)	169 (97.1)	
Intraoperative frozen plasma infusion [n (%)]			
Yes	8 (6.7)	4 (2.3)	0.074
No	110 (93.3)	170 (97.7)	

§: Plus-minus values are means ± SD.

M: median; QR: quartile range.

Table 3. Results of binary logistic regression analysis for variables in the hidden blood loss positive patients who undergoing thoracic and lumbar fusion surgery

Variables	β	SE	P	OR	95%CI
Age > 60 yrs	0.448	0.840	0.594	1.564	0.302–8.111
Height < 1.60 m	0.321	0.508	0.527	1.379	0.509–3.731
Weight < 65 kg	-0.019	0.383	0.961	0.981	0.463–2.080
Number of segments > 2	0.253	0.356	0.477	0.477	0.386–1.559
Surgical duration > 180 min	0.286	0.299	0.338	0.751	0.418–1.349
Autologous blood transfusion	2.019	0.537	0.011	2.627	1.574–2.782
Allogeneic blood transfusion	1.870	0.518	<0.001	6.487	2.349–17.915

SE: standard error; OR: odds ratio; 95%CI: 95% confidence interval.

surgery, therefore surgeons and anesthesiologists should closely check for physiological disturbance HBL leads to.

The underlying mechanism for HBL remains elusive.^[10-12] To our knowledge, there are many reports about the mechanisms of HBL only focusing on joint surgery, but few reports have mentioned spinal surgery. Therefore, we carried out this study to investi-

gate the potential risk factors for HBL involved spinal surgery patients. The results revealed that both intraoperative autologous and allogeneic blood transfusions were the independent risk factors for HBL in patients either with thoracic and lumbar fusion surgery or scoliosis surgery. The main reason for HBL is hematocoele formed by intra-articular or tissue bleeding, having been proven by experiments using labeled red blood

Table 4. Comparisons of general characteristics between the hidden blood loss positive and negative patients undergoing scoliosis surgery

Variables	Hidden blood loss positive (n=100)	Hidden blood loss negative (n=169)	P-value
Gender			0.888
Male [n (%)]	37 (37.0)	60 (35.5)	
Female [n (%)]	63 (63.0)	109 (64.5)	
Age [§] (yr)	17.6±9.9	16.4±8.6	0.272
Corrected height [§] (m)	1.53±0.19	1.52±0.18	0.826
Weight [§] (kg)	43.6±13.9	44.2±14.6	0.718
Body mass index [§] (kg/m ²)	19.0±3.55	19.1±3.51	0.819
Number of segments [§]	9.9±3.8	9.0±3.5	0.120
Osteotomy [n (%)]			
Yes	41 (41.0)	44 (26.0)	0.011
No	59 (59.0)	125 (73.9)	
Preoperative Cobb angle [§] (°)	66.23±26.7	58.65±23.1	0.022
Operation duration [§] (min)	254.6±72.6	217.9±81.6	<0.001
Visible blood loss [§] (ml)	1336±947.1	1175±811.2	0.131
Intraoperative infusion of crystalloids [§] (ml)	1524.8±892.2	1480.2±728.2	0.566
Intraoperative infusion of colloids (ml)	1000 (500, 1000)	500 (500, 1000)	0.004
Intraoperative autologous blood transfusion [n (%)]			
Yes	93 (93)	121 (71.6)	<0.001
No	7 (7.0)	48 (28.4)	
Intraoperative allogeneic blood transfusion [n (%)]			
Yes	50 (50.0)	11 (6.5)	<0.001
No	50 (50.0)	158 (93.5)	
Intraoperative frozen plasma infusion [n (%)]			
Yes	36 (36.0)	13 (7.7)	<0.001
No	64 (64.0)	156 (92.3)	

§: Plus-minus values are means±SD.

Table 5. Results of binary logistic regression analysis for variables in the hidden blood loss positive patients undergoing scoliosis surgery

Variables	β	SE	P	OR	95%CI
Osteotomy	0.035	0.258	0.819	1.036	0.625-1.716
Preoperative Cobb angle>60°	0.378	0.306	0.217	1.460	0.801-2.661
Operation duration>240 min	0.446	0.283	0.115	0.640	0.368-1.114
Colloids infusion>800 ml	1.102	0.240	0.536	1.233	0.636-2.389
Autologous blood transfusion	0.121	0.361	<0.001	2.268	2.143-2.504
Allogeneic blood transfusion	0.209	0.338	<0.001	3.636	2.389-5.231
Frozen plasma	-1.315	0.321	0.051	0.268	0.143-0.504

cells.^[13-16] This may play a crucial role in the process of HBL of joint surgery and in our opinion this would not be suitable in the case of spinal surgery, because the spine has no articular cavity like the joint. Autologous hemolysis is another possible cause for HBL.^[17-18]

Thereby we speculated that rapid lysis of red blood cells in the circulation induced by autologous blood or allogeneic blood transfusion might be responsible for HBL happened in patients with spinal surgery. Further prospective investigations are needed to clarify the un-

derlying mechanisms involved HBL.

Meanwhile we found no matter what kind of spine surgery the patients received, the risk of HBL occurring after allogeneic blood transfusion was higher than that after autologous blood transfusion. It is likely due to recipients' elimination responses to donor cells after the transfusion of allogeneic blood products. In addition, red blood cells are easily damaged or destroyed when stored for a long time.^[19-20] Each of these considerations could explain the high risk of HBL associated with allogeneic blood transfusion. Autologous transplants have the advantage of lower risk of rejection, so autologous blood cells are preferred for transfusion. However, autologous blood cells may have a shorter life span because of the injuries arising from washing and centrifugation process by Cellsaver machine,^[20-21] which might be a potential cause of increased risk of HBL after autologous blood transfusion.

When comparing the two surgeries (Table 2), we found that the total blood loss, visible blood loss, and HBL volumes in patients with thoracic and lumbar fusion surgery were all less than those with scoliosis surgery, but the incidence of HBL of thoracic and lumbar fusion surgery cases was greater than that of scoliosis patients, which was consistent with Smorgick *et al*'s research,^[1] suggesting that surgical method to treat spine diseases might have an impact on HBL.

Perioperative blood transfusion, which is required for the management of surgical patients experiencing blood loss, possibly results in immune suppression, transfusion-related acute lung injury, circulatory overload, and transfusion-transmitted infection.^[13, 20] Therefore a precise estimate of transfusion risk and application of strict blood recipient selection will be helpful in keeping the patients' safety and allocating limited blood resources. For example, patients with Hb > 10 g/L as well as stable circulation should be strictly evaluated before receiving blood transfusion.

Our study has several limitations. First, the study was performed in a single centre with the relatively small case numbers; Second, this is a retrospective study that would be apt to cause bias; Finally, we could not rule out the influence of racial differences because most patients are native population in China. Therefore a perspective study with a larger sample size and multi-center should be performed.

In brief, intraoperative blood transfusion might be an early-warning indicator for perioperative HBL.

Conflict of interest statement

The authors have no conflict of interest to disclose.

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