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Original Article

Predictive factors for massive transfusion in patients with non-idiopathic scoliosis undergoing corrective surgery

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Abstract: Non-idiopathic scoliosis can be divided into congenital and secondary (neuromuscular disease, syndrome/genetic disorder, trauma) scoliosis. Spinal deformity surgery for scoliosis causes considerable blood loss and may require blood transfusion. This study investigated risk factors for massive transfusion following spinal surgery in non-idiopathic scoliosis and the influence of the etiology on the rate of postoperative complication between 2008 and 2015. Multivariable logistic regression analysis was performed to assess the predictive factors for massive transfusion, which was defined as transfusion of ≥ 10 red blood cell units for adults or ≥ 100% estimated total body volume within 24 h for children. We compared the incidence of postoperative complications according to whether massive transfusion occurred and each etiology of non-idiopathic scoliosis. Of 170 patients, 25 (14.7%) received massive transfusion. In multivariable analysis, body mass index (odds ratio [OR], 0.742; 95% confidence interval [CI], 0.615-0.895; $P = 0.002$), maximal standing Cobb angle (OR, 1.056; 95% CI, 1.030-1.083; $P < 0.001$), and operation time (OR, 1.011; 95% CI, 1.003-1.020; $P = 0.006$) were independent factors for massive transfusion. The massive transfusion group had higher postoperative cardiopulmonary complication rates, greater need of intensive care, and longer hospital stays compared to those without massive transfusion. Compared with secondary scoliosis, congenital scoliosis exhibited significantly lower complications. In patients with non-idiopathic scoliosis undergoing corrective surgery, a lower body mass index, greater Cobb angle, and longer operation time were predictive factors for massive transfusion. Massive transfusion negatively impacted the postoperative course. The etiology of non-idiopathic scoliosis was also an important risk factor for predicting postoperative hemorrhage and related complications.

Keywords: Non-idiopathic scoliosis, massive transfusion, etiology of scoliosis

Introduction

Scoliosis in children and young adults has been classified as idiopathic and non-idiopathic. Non-idiopathic scoliosis in pediatric populations is further categorized into congenital and secondary scoliosis, which occurs secondary to primary medical conditions, such as neuromuscular diseases, neurofibromatosis, mesenchymal diseases, or trauma [1]. The process of surgical correction of scoliosis includes multiple-level fusion and screw instrumentation that can be associated with major blood loss and intraoperative hemodynamic instability. Patients with comorbidities such as neuromuscular diseases exhibit greater blood loss compared with patients with idiopathic scoliosis [2]. A mean blood loss of up to 4500 mL has been documented in the literature [3], with a subsequent need for massive blood transfusions. However, transfusion may induce several complications such as allergic reactions, infections, immunological effects, and metabolic complications [4]. Pediatric surgical candidates can be particularly vulnerable to these negative effects [4]. Thus, anesthetic management of patients with non-idiopathic scoliosis, especially in pediatric patients, requires special attention. Understanding the predictive factors for massive transfusion during scoliosis surgery may influence the administration of adequate transfusion therapy during the operation and

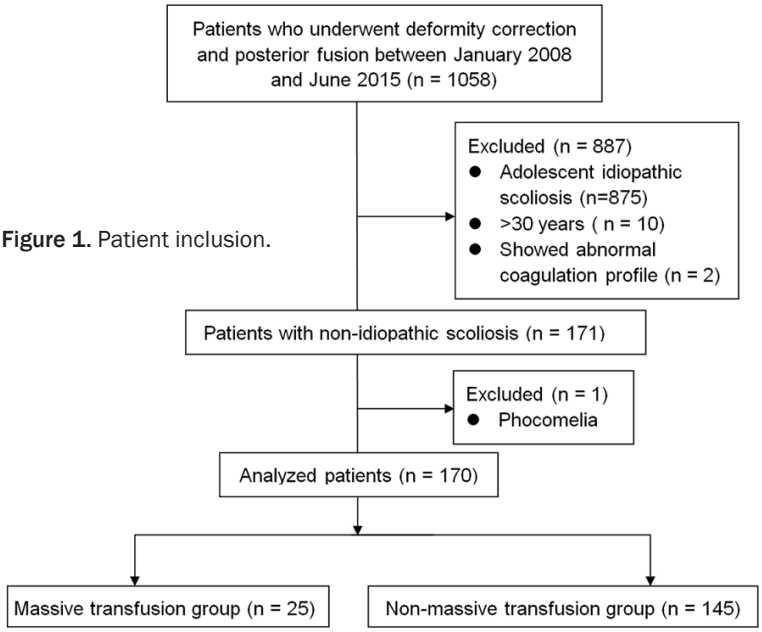

Figure 1. Patient inclusion.

postoperative period. It can also improve perioperative anesthetic management and postoperative prognosis. The aim of this study was to investigate the incidence, outcomes, and factors associated with massive blood transfusion following spinal surgery in children and young adults with non-idiopathic scoliosis.

Materials and methods

Study population

We performed a retrospective chart review of patients with non-idiopathic (congenital and secondary) scoliosis who underwent deformity correction surgery at our institute from January 2008 to June 2015. A total of 1058 pediatric and adult patients underwent scoliosis surgery during this period. Among them, patients with idiopathic scoliosis, age over 30 years, and abnormal coagulation profile were excluded. The Institutional Review Board of our institution approved this study after an expedited review. The need for informed consent was waived considering the retrospective nature of the study, and this manuscript complied with the EQUATOR recommendations. All surgeries were performed at our institute. A total of 171 patients were identified, but one patient with phocomelia was excluded. Thus, 170 patients were included in the analysis (**Figure 1**).

These patients were further distributed into four groups according to the etiology of non-idiopathic scoliosis [1]. Patients with congenital vertebral abnormalities were classified into the congenital scoliosis group, and patients with secondary scoliosis were divided into neuromuscular, syndrome/genetic-related, and trauma-related scoliosis groups. The neuromuscular scoliosis group included patients with neuromuscular diseases such as cerebral palsy, Duchenne muscular dystrophy, syringomyelia, spinal muscular atrophy (Kugelberg-Welander syndrome), and central motor pathologies. The syndrome/genetic-related scoliosis group included patients with systemic diseases such as congenital heart disease, neurofibromatosis, mesenchymal disorders, and other genetic syndromes or diseases. Patients with scoliosis due to a post-traumatic history such as laminectomy and/or thoracotomy were classified into the trauma group.

Anesthetic management

Standardized anesthetic and surgical protocols were used [5]. Total intravenous anesthesia with propofol and remifentanil was administered to most patients (91%) using a programmed target concentration infusion device. Somatosensory evoked potential and motor evoked potential monitoring were performed during the surgery; thus, muscle relaxation was partially or completely reversed under train-of-four monitoring. Standard monitoring was provided, including a noninvasive blood pressure monitor, pulse oximeter, three-lead electrocardiographic monitor, and bispectral index monitor. Invasive arterial pressure was measured, and a central venous catheter was inserted for continuous central venous pressure monitoring and stable infusion of the anesthetic drug.

A balanced salt solution was used as the main crystalloid solution, and hetastarch was used as the main colloid solution. Frequent blood sampling and analysis via the arterial cannula was conducted to assess the intraoperative hemoglobin (Hb) levels and for further blood gas analysis. Allogeneic red blood cells (RBCs) were transfused according to a liberal transfu-

sion Hb trigger (Hb ≥ 8-9 g/dL intraoperatively or Hb ≥ 8 g/dL postoperatively) [6, 7] or when clinical assessment indicated hemodynamic instability despite adequate crystalloid administration, with an increasing requirement of vasopressors.

Clinical data

Patients' demographics and laboratory data were collected through electronic medical chart reviews. The assessed comorbidities included pulmonary abnormalities on pulmonary function tests, cardiac diseases including congenital heart diseases, and others such as seizures and presence of mental retardation. The collected laboratory data included Hb levels, platelet counts, activated partial thromboplastin time, prothrombin time, and serum albumin and creatinine levels. Perioperative data included the volume of transfusion (packed RBCs), total administered volume of crystalloid and colloids, urine output, postoperative blood loss, requirement for intensive care unit (ICU) treatment, and postoperative complications. However, we excluded 'intraoperative estimated blood loss (EBL)' from the analysis because of inaccurate measurement methods and substantial loss of data. Postoperative blood loss was determined by measuring the amount of blood collected from wound drains. Surgical factor-related data included the number of fused vertebral levels, presence of osteotomy, and maximal standing Cobb angle.

Definition of outcomes

Massive transfusion was defined as transfusion of ≥ 10 RBC units, which was approximately equal to the total blood volume (TBV) of an average adult patient, within 24 h in adults or the transfusion of > 100% of the estimated TBV within 24 h in children [8]. According to these definitions, we examined the volume of transfusion within 24 h in the intraoperative and postoperative periods. The estimated TBV for adults was calculated based on Gilcher's rule of five for blood volume. In the pediatric population, TBV estimation was performed based on the body weight and age as follows: young child (10-24 kg) with 75 mL/kg body weight and older child (25-49 kg) with 70 mL/kg body weight.

Postoperative complications were defined as those requiring any medical or surgical intervention according to Clavien-Dindo classification score of ≥ 2 [9]. Complications were divided into the following categories: 1) cardiopulmonary, including hypotension and arrhythmia, pulmonary edema, postoperative intubated state, pneumonia, pleural effusion, and pneumothorax; 2) postoperative hemorrhage or hematoma requiring allogeneic transfusion; 3) postoperative conditions requiring revision surgery or endoscopic or radiologic intervention; 4) gastrointestinal complications, including moderate-to-severe ileus, liver insufficiency, and acute gastritis; 5) neurologic complications, including significant sensory or motor changes; 6) renal complications, including acute kidney injury; and 7) other complications requiring pharmacologic treatment or intervention. Postoperative fever was defined as a body temperature of > 38°C during seven postoperative days. Postoperative complications requiring surgical, endoscopic, or radiologic intervention or those that were life-threatening (Clavien-Dindo classification score of 3 or 4) [9] were considered major complications.

Statistical analysis

Continuous variables with normal distributions were expressed as mean ± standard deviation, and variables with skewed distributions were expressed as medians with ranges (25^{th} and 75^{th}). Univariable and multivariable logistic regression analyses were used to assess risk factors for massive transfusion. Associated factors identified as being significant to $P < 0.1$ were selected into backward elimination with logistic regression analysis. The results of each analysis were expressed as odds ratio (OR) with the 95% confidence interval (CI) and the *P*-value. We compared the incidence of postoperative complications, rate of postoperative ICU admission, and length of hospital stay according to whether massive transfusion occurred and each etiology of scoliosis. Continuous variables were tested with Kruskal-Wallis test, and the categorical variables were examined using the chi-squared test or the Fisher's exact test. Receiver operator characteristic (ROC) curves were calculated to predict the cut-off value of the risk factors. For all analyses, the reported *P*-values were two-sided, and *P*-values ≤ 0.05 were considered statisti-

Table 1. Characteristics, preoperative, intraoperative and postoperative data of patients who were and were not massive transfusion recipients

	Non-massive transfusion n = 145	Massive transfusion n = 25	*P*
Sex, Female (%)	75 (81.5)	17 (18.5)	0.136
Age (years)	14.4 ± 4.1	13.9 ± 4.6	0.633
Body mass index (kg/m^2)	20.1 ± 3.9	16.8 ± 2.5	< 0.001
Etiology of scoliosis			
Congenital	55 (90.2)	6 (9.8)	0.152
Neuromuscular	40 (88.9)	5 (11.1)	0.832
Syndrome, genetic	41 (75.9)	13 (24.1)	0.046
Trauma	9 (90.0)	1 (10.0)	0.987
ASA grade 1, 2	134 (92.4)	22 (20.4)	0.728
ASA grade 3	11 (7.6)	3 (21.4)	0.176
Comorbidities			
Cardiac disease	23 (15.9)	5 (20)	0.607
Pulmonary disease	18 (12.4)	5 (20)	0.311
Other disease	46 (31.7)	10 (40)	0.560
Preoperative laboratory values			
Hemoglobin (g/dL)	13.8 ± 1.3	13.5 ± 1.8	0.315
Platelet (×10^9/uL)	269 ± 61.5	271.8 ± 69.3	0.854
Prothrombin time (INR)	1.03 ± 0.1	1.06 ± 0.1	0.1
aPTT (sec)	29.9 ± 2.3	30.3 ± 2.9	0.513
Albumin (g/dL)	4.4 ± 0.3	4.2 ± 0.4	0.032
Fused level (number)	9.8 ± 2.7	12 ± 2.5	< 0.001
Osteotomy	14 (77.8)	4 (22.2)	0.380
Cobb angle (°)	62.0 ± 16.3	88.8 ± 28.3	< 0.001
Anesthesia time (min)	302 ± 67	384 ± 101	< 0.001
Operation time (min)	228 ± 64	292 ± 93	< 0.001
Crystalloid (mL)	2519 ± 1419	4082 ± 2320	< 0.001
Colloid (mL)	864 ± 378	916 ± 377	< 0.001
Intraoperative transfusion	n = 138	n = 25	
RBC (units)	3.5 ± 2.4	9.0 ± 5.0	< 0.001
RBC (ml)	1223.8 ± 846.4	3133.2 ± 1745.1	< 0.001
RBC (ml/kg)	26.1 ± 16.0	89.2 ± 39.7	< 0.001
24-h transfusion (ml)	1474.8 ± 830.8	3530.8 ± 1629.5	< 0.001
Wound drainage*	875.0 ± 324.7	1067.4 ± 474.7	0.005
Postoperative ICU† care	14 (9.7)	14 (56)	< 0.001

Data are expressed as mean ± standard deviation or number (%). ASA: American Society of Anesthesiologists Score; aPTT: activated partial thromboplastin time; RBC: red blood cell; *Postoperative wound drainage, n = 104; †intensive care unit.

cally significant. All statistical analyses were performed using IBM SPSS Statistics software (version 22; SPSS Inc., Chicago, IL, USA) and MedCalc version 13.1.1 (MedCalc Software, Mariakerke, Belgium).

Results

The baseline demographic data are listed in **Table 1**. Twenty-two of 170 patients were aged > 19 years, and the remaining patients were in the pediatric age group (3-18 years). Most patients (157, 92.4%) underwent posterior approach spinal surgery. Four patients underwent staged surgery via an anterior approach followed by posterior fusion, and five patients had revision surgery via a posterior approach.

During the perioperative period, almost all patients received allogeneic transfusion within

Table 2. Comparison of complications between massive- and non-massive transfusion

Complications	n	Non-massive transfusion n = 145	Massive transfusion n = 25	*P*
Cardiopulmonary	14	7 (4.8)	7 (28)	0.001
Hemorrhage requiring transfusion	102	81 (55.9)	21 (84)	0.008
Intervention/reoperation	3	2 (1.4)	1 (4)	0.381
Gastrointestinal*	16	14 (9.7)	2 (8)	> 0.999
Neurology injury	2	2 (1.4)	0	> 0.999
Acute kidney injury†	4	4 (2.8)	0	> 0.999
Clavien-Dindo classification ≥ 3	11	6 (4.1)	5 (20)	0.012
Fever	74	63 (43.4)	11 (44)	0.959
Postoperative ICU care	28	14 (9.7)	14 (56)	< 0.001
POD Discharge (day)		7 (7, 9)	8 (7, 10.5)	0.041

Data are expressed as number (%) or median (interquartile range). *Gastrointestinal: nausea, vomiting, ileus, liver insufficiency, acute gastritis; †Acute kidney injury definition by KDIGO (kidney disease improving global outcomes) criteria; ICU, intensive care unit; POD, postoperative day.

Table 3. Logistic regression analysis of risk factors associated with massive transfusion during non-idiopathic scoliosis surgery

Variables	Univariate analysis			Multivariable analysis		
	OR*	95% CI†	*P*	OR	95% CI	*P*
Body mass index	0.715	0.601-0.851	< 0.001	0.651	0.532-0.799	< 0.001
Operation time	1.011	1.005-1.017	< 0.001	1.011	1.003-1.020	0.006
Etiology of scoliosis						
Congenital	1		0.152			
Neuromuscular	1.146	0.327-4.018	0.832			
Syndrome, genetic	2.907	1.019-8.293	0.046			
Trauma	1.019	0.109-9.484	0.987			
Fused levels	1.524	1.195-1.943	0.001			
Cobb angle	1.060	1.035-1.086	< 0.001	1.034	1.006-1.063	0.019
Preoperative albumin	0.261	0.077-0.889				

*OR: odds ratio; †CI: Confidence interval of odds ratio.

24 h. Among them, 25 patients received massive transfusion, and they showed a significantly higher incidence of postoperative cardiopulmonary complications and a greater need for postoperative ICU care (**Table 2**).

Multiple parameters as risk factors

Multivariable regression analysis revealed that lower body mass index (BMI), greater maximal standing Cobb angle, and longer operation time were risk factors associated with massive transfusion (**Table 3**). The clinical cut-off points for each variable defined using ROC curves (**Figure 2**) were as follows: 18.0 kg/m^2 for BMI (OR, 0.742; 95% CI, 0.615-0.895) with sensitivity of 72% and specificity of 77.9%, 68.5° for the Cobb angle (OR, 1.056; 95% CI, 1.030-1.083) with sensitivity of 68.0% and specificity of 74%, and 248.5 min for the operation time (OR, 1.011; 95% CI, 1.003-1.020) with sensitivity of 64.0% and specificity of 70.3% (*P* = 0.002, *P* < 0.001, and *P* = 0.006, respectively).

Complications and the etiology of non-idiopathic scoliosis

The comparison among patients with different etiologies of non-idiopathic scoliosis in terms of the postoperative wound drainage per body weight demonstrated a significant difference between patients with congenital scoliosis and those with neuromuscular scoliosis and syndrome-related scoliosis (*P* = 0.006 and *P* = 0.02, respectively).

When the correlation between the etiology of non-idiopathic scoliosis and postoperative

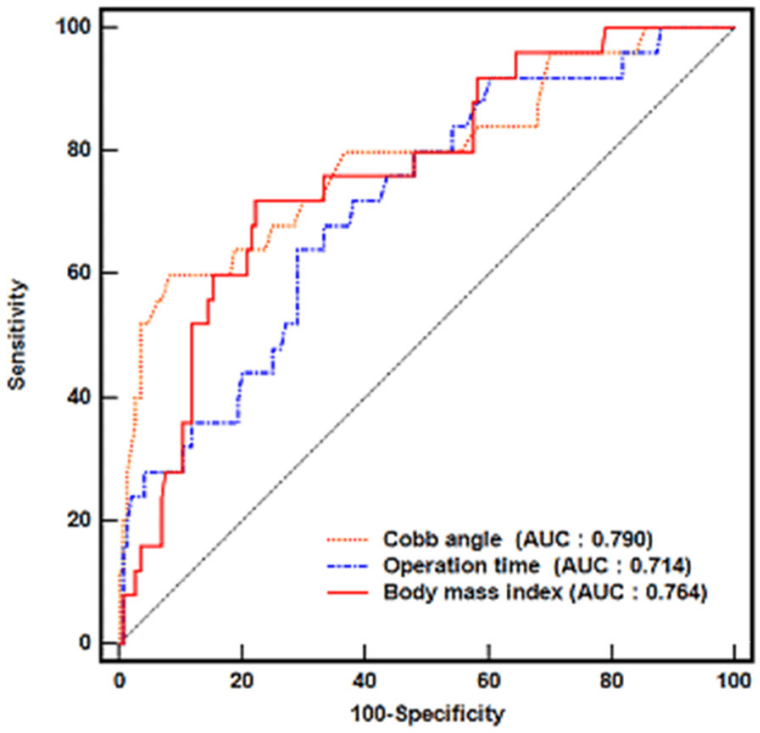

Figure 2. Receiver operating characteristic curves used to assess the cut-off values of Cobb angle (> 68.5°), operation time (> 248.5 min), and body mass index (BMI; > 18.0 kg/m^2) to predict the need for massive transfusion. AUC, area under the curve.

complications was evaluated, congenital scoliosis was associated with a lower overall rate of complications, including cardiopulmonary and major complications, compared with other types of scoliosis. There was also a difference in the rate of ICU admission and length of hospital stay, which indicated favorable findings in the congenital scoliosis group compared with the other groups (**Table 4**).

Discussion

The current study demonstrated that lower BMI, larger Cobb angles, and longer operation time were independent risk factors for massive transfusion in patients with non-idiopathic scoliosis undergoing corrective spinal surgery. Although several studies [10-12] have discussed risk factors for intraoperative bleeding or transfusion in pediatric patients with scoliosis, most reports have only assessed an adolescent idiopathic scoliosis group or mixed non-idiopathic and idiopathic scoliosis groups. Only a few previous studies have discussed surgeries in patients with non-idiopathic scoliosis and the associated blood loss.

We previously reported that lower BMI was a predictive factor for massive transfusion in patients with adolescent idiopathic scoliosis [5]. The current analysis demonstrated that a BMI of < 18.0 kg/m^2 was associated with massive transfusion, regardless of the etiology of non-idiopathic scoliosis. This result is consistent with previous studies [10, 13]. A low BMI is related to lower estimated blood volume, which suggests that smaller patients lose a greater proportion of their circulating TBV during surgery, regardless of the diagnosis [14].

Another related factor for massive transfusion was a maximal standing Cobb angle. The Cobb angle was found to be correlated with total blood loss and transfusion, regardless of the type of scoliosis [11]. The Cobb angle reflected the severity of the curvature, which determined the need for extensive surgical procedures. The third factor associated with massive transfusion was the duration of the operation time, because surgical and anesthesia times were related to surgical invasiveness and complexity. This finding is consistent with that of other reports on perioperative transfusion [10, 15].

The etiology of non-idiopathic scoliosis is known to be a strong determinant of intraoperative blood loss. Typically, patients with neuromuscular disease have a greater extent of blood loss and need for allogeneic blood transfusion [3, 10, 11, 13, 16]. On the other hand, the congenital scoliosis group in the current study has a lower rate of complications and less postoperative blood loss compared with the secondary scoliosis groups. This may be because the congenital group has less surgical invasiveness-related elements than the secondary groups. The congenital scoliosis group has a lower Cobb angle (57.6° ± 20.7° vs. 70.0° ± 20.5°) and number of fused vertebrae (8.4 ± 3.2 vs. 10.9 ± 2.4) compared with the other groups. These factors may have influ-

Table 4. Comparison among the etiologies of non-idiopathic scoliosis with respect to the postoperative complication

	Congenital (n = 61)	Neuromuscular (n = 45)	Syndrome, genetic (n = 54)	Trauma (n = 10)	*P*
	n (%)	n (%)	n (%)	n (%)	
Cardiopulmonary	0 (0)	6 (13.3)	6 (11.1)	2 (20.0)	< 0.001
Hemorrhage requiring transfusion	33 (54.1)	30 (66.7)	34 (63.0)	5 (50.0)	0.11
Intervention	0 (0)	0 (0)	3 (5.6)	0 (0)	0.132
Gastrointestinal*	4 (6.6)	4 (8.9)	8 (13.0)	0 (0)	0.244
Neurology deficit	1 (1.6)	0 (0)	1 (1.9)	0 (0)	> 0.999
Acute kidney injury†	1 (1.6)	3 (6.7)	0 (0)	0 (0)	0.261
Clavien-Dindo classification ≥ 3	0 (0)	4 (8.9)	5 (9.3)	2 (20.0)	< 0.001
Fever	24 (39.3)	24 (53.3)	25 (46.3)	1 (10.0)	0.180
Postoperative ICU care	4 (4.4)	7 (46.7)	15 (27.8)	2 (20.0)	< 0.001
POD discharge (Day)	7 (7, 8)	8 (7, 10)	8 (7, 9)	8 (7, 9.5)	0.237

*Gastrointestinal: nausea, vomiting, ileus, liver insufficiency, acute gastritis; †Acute kidney injury definition by KDIGO (kidney disease improving global outcomes) criteria; ICU, intensive care unit; POD, postoperative day.

enced the low rates of massive transfusion and postoperative complications in the congenital scoliosis group.

In the present study, the overall intraoperative RBC transfusion volume was higher than that reported in other studies. A previous report [17] that only assessed patients with neuromuscular scoliosis administered RBCs at a rate of 26.1 (19.2-34.3) mL/kg to the massive EBL group. A study of patients with cerebral palsy [18] reported a blood loss of 1333 ± 878 mL without anti-fibrinolytics. The reasons for high transfusion volumes in our data are as follows. First, our study included 20 children aged < 10 years. These young and smaller patients may have lost a greater proportion of their circulating TBV during surgery compared with adolescents [14]. Second, the current study population had a greater mean preoperative Cobb angle than that reported in other study populations. Moreover, even mean Cobb angle of the massive blood loss groups in other studies (64.4° ± 23.1° [17] and 70.3° ± 28.0° [19]) was similar to that in the current study. Furthermore, our massive transfusion group had an extremely high preoperative Cobb angle.

There are some limitations of this study. First, this study is a retrospective study with a relatively small sample size for each etiology of scoliosis. However, non-idiopathic scoliosis in children is not common and other studies [10, 17, 19, 20] investigating non-idiopathic scoliosis surgeries and the related blood loss did not include large numbers of patients. Second, we exclude EBL from the data analysis because the method of estimating intraoperative blood loss is inaccurate and there is a considerable loss of data. Third, our anesthesiologists and orthopedic surgeons applied a liberal transfusion strategy. These may be confounding factors for higher rates of transfusion and higher incidence of massive transfusion in this study.

Conclusions

The predictive factors of massive transfusion in non-idiopathic scoliosis were BMI < 18.0 kg/m^2, Cobb angle > 68.5°, and operation time > 248.5 min. The etiology of non-idiopathic scoliosis was an important risk factor to predict postoperative blood loss and surgery-related complications. The occurrence of massive transfusion affected the need for longer ICU care and hospital stay in the postoperative period, with increased postoperative complications. Considering these risk factors, meticulous pre-anesthetic planning is needed to decrease the rate of massive transfusion and the incidence of complications in patients with non-idiopathic scoliosis who are having spine surgery.

Disclosure of conflict of interest

None.

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