Factors Associated with Postoperative Respiratory Complications following Posterior Spinal Instrumentation in Children with Early-onset Scoliosis

Ying Zhang, MD, Yingsong Wang, MD, Jingming Xie, MD, Ni Bi, MD, Zhi Zhao, MD, Tao Li, MD, Zhiyue Shi, MD, Tianyi Huang, MD, Bing Gao, MD, Kaiven Gu, MD, Wuyao Li, MD

Department of Orthopaedics, The 2nd Affiliated Hospital of Kunming Medical University, Kunming, China

Objective: To investigate the incidence and risk factors of postoperative respiratory complications (PRCs) in children with early-onset scoliosis (EOS) following posterior spine deformity surgery (PSDS) based on growth-friendly techniques, so as to help improve the safety of surgery.

Methods: A retrospective study of children with EOS admitted for PSDS based on growth-friendly techniques from October 2013 to October 2018 was reviewed at a single center. There were 73 children (30 boys, 43 girls) who fulfilled the criteria in this research. The mean age of the patients was 7.6 ± 6.2 years. Patients were divided into the groups with and without PRCs. Variables that might affect the PRCs during the perioperative period, including general factors, radiographic factors, laboratory factors and surgical factors, were analyzed using univariate analysis to evaluate the potential risk factors. The variables that were significantly different were further analyzed by binary logistic regression analysis to identify the independent factors of PRCs.

Results: All the 73 children included 42 idiopathic scoliosis (57.5%), 12 congenital scoliosis (16.4%), 10 syndromic scoliosis (13.7%) and nine neuromuscular scoliosis (12.3%). PRCs were detected in 16 children (21.9%) with nine different PRCs. The total frequency of detected PRCs was 54, including pleural effusion (25.9%), postoperative pneumonia (20.4%), hypoxemia (18.5%), atelectasis (14.8%), prolonged intubation with mechanical positive pressure ventilatory support (PIMPPVS) (7.4%), bronchospasm (3.7%), reintubation (3.7%), delayed extubation (3.7%) and pneumothorax (1.9%). Results of univariate testing demonstrated that the following six variables were statistically different (P < 0.05): nonidiopathic scoliosis, combined with pulmonary comorbidities, pretransferrin < 200 mg/dL, prealbumin < 3.5 g/dL, anesthesia time ≥ 300 min and blood loss to total blood volume ratio (BL/TBV) ≥ 15%. Binary logistic regression analysis confirmed that BL/TBV ≥ 15% (odd ratio OR = 29.188, P = 0.010), combined with pulmonary comorbidities (OR = 19.216, P = 0.012), pretransferrin < 200 mg/dL (OR = 11.503, p = 0.024), and nonidiopathic scoliosis (OR = 7.632, P = 0.046) were positively linear correlated with PRCs in children with EOS following PSDS.

Conclusion: PRCs has a higher incidence in children with EOS following PSDS. BL/TBV ≥ 15%, combined with pulmonary comorbidities, pre-transferrin < 200 mg/dL, and nonidiopathic scoliosis play an important role for the development of PRCs in this population.

Key words: Complication; Early-onset scoliosis; Respiratory; Spinal deformity; Surgery
Introduction

According to both the Scoliosis Research Society and the Pediatric Orthopedic Society of North America, early-onset scoliosis (EOS) is referred to as curvature of the spine ≥10° in the coronal plane with onset before age 10 years regardless of etiology. Early diagnosis and appropriate treatment are of utmost importance because spine, thoracic cage, and lung development in this age group occur rapidly, placing children with EOS at significant risk for rapid deformity progression and thoracic constraints, ultimately leading to impaired pulmonary function. In addition, children with EOS may also be associated with cardiopulmonary and/or gastrointestinal pathological anomalies, which can exacerbate pulmonary insufficiency. Thus, compared with adolescent idiopathic scoliosis, children with EOS demonstrate higher mortality and lower quality of life.

Previous studies have shown that bracing and casting may slow the progression of spinal deformity, but up to a one-third of conservatively managed children with EOS eventually undergo surgery. Therefore, children with severe progressive EOS require early surgical intervention to prolong their life and maintain a better quality of life. When treating children with EOS who do not respond to brace or cast treatments, the surgery based on growth-friendly techniques is preferable to fusion surgery because it has less interference with the normal development of the children’s spine, thoracic cage, and lung.

Although remarkable advances have been made in growth-friendly techniques and implants over the past decades, most of which are posterior procedures due to their fewer adverse effects on postoperative respiratory function, the treatment of EOS remains a challenge. Initial reports of these growth-friendly techniques have demonstrated superior deformity correction and predicted growth maintenance during the treatment period. However, postoperative complication rates remain high (29%–58%). Among these, postoperative respiratory complications (PRCs) are the most common postoperative nonneurological complications following posterior spine deformity surgery (PSDS) for treating EOS. PRCs are generally defined as any adverse event that affects the respiratory system during the intraoperative or postoperative period. PRCs can lead to an increased length of hospitalization, worsened patient outcomes, and higher hospital and postoperative costs. Therefore, it is important to determine the various factors that put children with EOS at increased risk of PRCs after PSDS. This will allow for an optimized perioperative management strategy, improved allocation of clinical resources, and better patient experience. However, there is a paucity of studies correlating PRCs with the characteristics of children diagnosed with EOS. In addition, there is no standardized definition of PRCs in the existing literature, which makes the clinical research results lack any clinical guidance significance.

The current study analyzed the data of children with EOS undergoing PSDS at a single institution in the past 5 years with a minimum of 2 years of follow-up with the objective of: (i) determining the incidence of PRCs; (ii) cataloging the kinds and frequency of PRCs; and (iii) identifying the risk factors for PRCs. We believe that our data could help spine surgeons to guide perioperative management and surgical planning, thus reducing the probability of PRCs after PSDS.

Materials and Method

Patient Cohort

Institutional Review Board approval (No. PJ-2021-37) was obtained by the Scientific and Research Ethics Committee of the Second Affiliated Hospital of Kunming Medical University before the start of this retrospective study. Written consent was obtained from the children’s guardians. Inclusion criteria: (i) children with EOS; (ii) the deformity continues to progress and the coronal Cobb angle of the main curve ≥40° after regular conservative treatment or deformities that are predicted to have a high risk for progression; (iii) underwent PSDS based on growth-friendly techniques (including various posterior approach growth-friendly techniques); (iv) children with complete preoperative and postoperative imaging and clinical data; and (v) a minimum of 2 year of follow-up after the initial PSDS. Exclusion criteria: final arthrodesis surgery.

The databases at our center, including general factors, radiographic factors, laboratory factors and surgical factors, were reviewed, and 10 variables were selected to compare the differences between the groups with and without PRCs in children with EOS who had undergone PSDS between October 2013 and October 2018 at our center. The presence or absence of PRCs was determined by two respiratory physicians using an independent double-blind method.

Surgical Techniques

All PSDSs were generally categorized into two types according to the type of correction technique applied: distraction-based and other techniques (including compression-based, growth-guidance and hybrid techniques).

All surgeries were performed under general anesthesia in the prone position. Neurophysiological monitoring of somatosensory evoked potentials and MEPs were performed routinely. Two to three small incisions for a minimally invasive posterior approach to the spine were utilized in the determined spine levels for the upper, lower instrumented vertebra and apex vertebrae. Pedicle screw insertion with the freehand technique for proximal, apex and distal anchors were performed according to the preoperative plan. The rods, which were contoured for maximal curve correction as well as the establishment of appropriate lumbar lordosis and thoracic kyphosis, were placed submuscularly from proximal to distal. Then, proper correction maneuvers were applied to the spinal curvature to restore the trunk balance. When distraction-based techniques were performed, the lengthening interval mostly ranged from 6 to 12 months before the final arthrodesis surgery.
General Factors
The general information included gender, etiology and pulmonary comorbidities. We used the C-EOS classification to describe the etiological characteristics of the children with EOS in this study. Scoliosis with identified reasons was defined as nonidiopathic scoliosis, and the remaining cases were defined as idiopathic scoliosis. Therefore, the etiology was divided into two broad groups: nonidiopathic and idiopathic scoliosis. The assessment of comorbidity requires a multidisciplinary involvement. All of the children were divided into two broad groups: combined with pulmonary comorbidities or not.

Radiographic Factors
The radiographic information included coronal major curve angle and sagittal kyphosis angle. We used two variables of C-EOS classification to describe the radiographic characteristics of the children with EOS. In the C-EOS classification, four groups were defined according to the coronal major curve subgrouping: coronal major curves of <20°, 20° to 50°, 51° to 90° and >90°. Accordingly, in this study, the coronal major curve angle was divided into two broad groups: coronal major curve angle greater than 50° or not. Regarding kyphosis, the C-EOS classification defined a normokyphotic (N) range of 20° to 50°. Kyphosis lower or higher than this extent was defined as hypokyphotic (−) or hyperkyphotic (+). Therefore, kyphosis was also divided into two groups: normokyphotic (N) and abnormokyphotic.

Laboratory Factors
To analyze the relationship between preoperative nutritional status and PRCs, we selected blood loss to total blood volume ratio (BL/TBV ≥15%) and preoperative albumin (prealbumin < 3.5 g/dL) as markers from the preoperative laboratory test results.

Surgical Factors
Anesthesia time ≥ 300 min, types of PSDS and blood loss to total blood volume ratio (BL/TBV ≥15%) were selected as surgical factors that might affect the PRCs following PSDS. Anesthesia time was defined as the time elapsed from intubation under general anesthesia until the patient was removed from the operating room following surgery. All surgeries were posterior-only approach with various growth-friendly techniques, including distraction-based techniques, compression-based techniques, growth-guidance techniques and hybrid techniques. Among them, the distraction-based technique predominated. Therefore, the types of PSDS were divided into two groups: the distraction-based technique group and the other techniques group. Additionally, in view of the different physiological characteristics between children and adults, BL/TBV was selected to evaluate the intraoperative blood loss.

TABLE 1 General information and clinical data

| Parameter Data | Data |
|----------------|------|
| Age at initial PSDS (years) | 7 ± 6.2 |
| Gender, n (%) | | |
| Boys | 30 (41.1) |
| Girls | 43 (58.9) |
| BMI (kg/m²) | 24.05 ± 2.52 |
| Etiology, n (%) | | |
| Idiopathic scoliosis | 42 (57.5) |
| Congenital scoliosis | 12 (16.4) |
| Syndromic scoliosis | 10 (13.7) |
| Neuromuscular scoliosis | 9 (12.3) |
| Initial surgery (initial/none) | 58/15 |
| Coronal main curve magnitude (°) | | |
| Initial | 72.16 ± 20.21 |
| Last follow-up | 30.28 ± 18.67 |
| Sagittal maximum angle of kyphosis (°) | | |
| Initial | 54.26 ± 13.33 |
| Last follow-up | 44.58 ± 16.53 |
| Type of PSDS (distraction-based/other techniques) | 28/45 |

Abbreviations: BMI, body mass index; PSDS, posterior spine deformity surgery based on growth-friendly techniques.

Observation Index
PRCs
PRCs are generally considered to be comprised of any adverse event that causes a clinically relevant and identifiable pulmonary alteration that affects the respiratory system in either the intraoperative or the postoperative period, including postoperative pneumonia, pleural effusion, hypoxemia, atelectasis, bronchospasm, pneumothorax, reintubation, delayed extubation and prolonged intubation with mechanical positive pressure ventilatory support (PIMPPVS). We used standardized definitions to determine PRCs following PSDS in children with EOS, which were those described in the statement from the ESA-ESICM joint taskforce on perioperative outcome measures. The presence of any perioperative respiratory symptoms or physical findings was recorded. Chest radiographs and/or thoracic ultrasound images were obtained from patients with abnormal cardiopulmonary symptoms and signs to determine the presence of PRCs when necessary:

1. Postoperative pneumonia was considered if two or more serial chest radiographs after surgery with at least one of the following (one radiograph is sufficient for patients with no underlying pulmonary or cardiac disease): (i) new or progressive and persistent infiltrates; (ii) consolidation; (iii) cavitation; and at least one of the following: (a) fever (>38 °C) with no other recognized cause; and (b) abnormal leucocyte count (<4000 or > 12,000/mm³); and at least two of the following: (a) new onset of purulent sputum or a change in the characteristic of the sputum, or increased respiratory secretions, or increased suctioning requirements; (b) new onset or worsening cough, or dyspnea, or tachypnea; (c) bronchial breath sounds; or...
(d) worsening gas exchange (hypoxemia, increased oxygen requirement, increased ventilator demand).

2. Pleural effusion was considered if chest radiograph demonstrated blunting of the costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in the upright position, evidence of displacement of the adjacent anatomical structures or (in the supine position) a hazy opacity in one hemithorax with preserved vascular shadows, regardless of the need for treatment.

3. Hypoxemia was considered if arterial blood gas analysis indicated a deficient exchange of oxygen (PO$_2$ < 60 mmHg), regardless of the need for treatment.

4. Atelectasis was considered if lung opacification occurred with a shift of the mediastinum, hilum or hemidiaphragm toward the affected area with compensatory overinflation in the adjacent nonatelectatic lung on chest radiograph, regardless of the need for treatment.

5. Bronchospasm: Bronchospasm was considered if any episode of wheezing was associated with acute respiratory symptoms and was relieved by bronchodilators.

6. Pneumothorax was considered if air was present in the pleural space with no vascular bed surrounding the visceral pleura on chest radiograph, regardless of the need for treatment.

7. Delayed extubation, reintubation or prolonged intubation with mechanical positive pressure ventilatory support (PIMPPVS) was defined as a continuation of postoperative ventilation beyond 24 hours in line with the previous literature. Reintubation was defined as a need for reintubation within 24 hours of extubation. Prolonged intubation with mechanical positive pressure ventilatory support (PIMPPVS) was defined as a continuation of postoperative ventilation beyond 48 hours.

### Statistical Analysis

Ten variables that might affect the PRCs following PSDS in children with EOS were analyzed using SPSS software version 19.0 (Chicago, IL, USA). In the univariate testing, categorical variables were analyzed usingPearson chi-square tests and Fisher exact tests where appropriate to examine potential risk factors. Factors with a $p$ value < 0.05 were considered statistically significant and included as potential risk factors in binary logistic regression analysis to identify

---

**TABLE 2 Frequency and percentages of different PRCs among the 16 patients who developed PRCs**

| PRCs                  | Frequency | Percentage (%) |
|-----------------------|-----------|----------------|
| Pleural effusion      | 14        | 25.9           |
| Postoperative pneumonia | 11       | 20.4           |
| Hypoxemia             | 10        | 18.5           |
| Atelectasis           | 8         | 14.8           |
| PIMPPVS               | 4         | 7.4            |
| Bronchospasm          | 2         | 3.7            |
| Reintubation          | 2         | 3.7            |
| Delayed extubation    | 2         | 3.7            |
| Pneumothorax          | 1         | 1.9            |
| Total                 | 54        | 100            |

Abbreviations: PRCs, postoperative respiratory complications; PIMPPVS, prolonged intubation (>48 h) with mechanical positive pressure ventilatory support.

**TABLE 3 Catalogue of cases with or without PRCs on variables**

| Group N = 73 | No. of patients | No. of patients with PRCs | No. of patients without PRCs | $\chi^2$ | $p$ values |
|--------------|-----------------|---------------------------|-----------------------------|--------|------------|
| Gender       |                 |                           |                             |        |            |
| Male (N = 30)| 6               | 24                        | 0.060                       | 0.807  |
| Female (N = 43)| 10          | 33                        |                             |        |            |
| Etiology     |                 |                           |                             |        |            |
| Non-idiopathic (N = 31) | 12  | 19                        | 8.877                       | 0.003* |
| Idiopathic (N = 42) | 4           | 38                        |                             |        |            |
| Combined with pulmonary comorbidities |       |                           |                             |        |            |
| Yes (N = 21) | 10              | 11                        | 9.121                       | 0.003* |
| No (N = 52)  | 6               | 46                        |                             |        |            |
| Major curve angle (>50°) |   |                           |                             |        |            |
| Yes (N = 44) | 9               | 35                        | 0.139                       | 0.710  |
| No (N = 29)  | 7               | 22                        |                             |        |            |
| Kyphosis (N) |                 |                           |                             |        |            |
| Yes (N = 20) | 4               | 16                        | 0.059                       | 0.808  |
| No (N = 53)  | 12              | 41                        |                             |        |            |
| Pretransferrin (<200 mg/dL) |       |                           |                             |        |            |
| Yes (N = 34) | 13              | 21                        | 9.901                       | 0.002* |
| No (N = 39)  | 3               | 36                        |                             |        |            |
| X7: Prealbumin (<3.5 g/dL) |   |                           |                             |        |            |
| Yes (N = 23) | 9               | 14                        | 5.813                       | 0.016* |
| No (N = 50)  | 7               | 43                        |                             |        |            |
| X8: Anesthesia time (≥300 min) |   |                           |                             |        |            |
| Yes (N = 25) | 11              | 14                        | 7.264                       | 0.007* |
| No (N = 48)  | 5               | 43                        |                             |        |            |
| X9: Types of PSDS |           |                           |                             |        |            |
| Distraction-based (N = 28) | 8   | 20                        | 1.175                       | 0.278  |
| Other (N = 45) | 8            | 37                        |                             |        |            |
| X10: BL/TBV (≥15%) |       |                           |                             |        |            |
| Yes (N = 31) | 13              | 18                        | 12.616                      | 0.000* |
| No (N = 42)  | 3               | 39                        |                             |        |            |

Abbreviations: BL/TBV, blood loss to total blood volum ratio.; * $p < 0.05$, statistically significant difference between the two groups.
significant independent risk factors for PRCs following PSDS in children with EOS. Statistical significance was accepted when the P values were less than 0.05 in binary logistic regression analysis. We generated a receiver operating characteristic (ROC) curve using predicted probability values from the logistic regression model. When the area under the curve (AUC) is greater than 50%, the predicted probability value is considered to be more accurate than chance.

Results

Demographics
A retrospective consecutive series of 73 children with EOS who were treated by PSDS were included in this study. Of the 73 children, 30 (30/73, 41.1%) were boys and 43 (43/73, 58.9%) were girls with a mean age of 7 ± 6.2 years (range, 6 years and 2 months–11 years and 4 months) at initial PSDS. Mean follow-up was 22.5 months (range, 12–49 months). The mean BMI was 24.05 ± 2.52 kg/m². There were 42 idiopathic scoliosis (42/73, 57.5%), 12 congenital scoliosis (12/73, 16.4%), 10 syndromic scoliosis (10/73, 13.7%), and nine neuromuscular scoliosis (9/73, 12.3%). Of the 73 children, 58 (58/73, 79.5%) underwent initial PSDS and 15 (15/73, 20.5%) underwent rod-lengthening procedures. Twenty-eight (28/73, 38.4%) and 45 (45/73, 61.6%) children underwent distraction-based and other techniques, respectively, according to the type of PSDS. The initial and last follow-up coronal and sagittal main curve magnitudes were 72.16° ± 20.21° and 30.28° ± 18.67°; 54.26° ± 13.33° and 44.58° ± 16.53°, respectively (Table 1).

Incidence of Postoperative Respiratory Complications
PRCs were detected in 16 children (16/73, 21.9%; 6 boys and 10 girls) with nine different PRCs. Some children developed more than one complication. The total frequency of detected PRCs was 54 in this study. The most frequent PRC was pleural effusion (14/54, 25.9%). Other pathologies were postoperative pneumonia (11/54, 20.4%), hypoxemia (10/54, 18.5%), atelectasis (8/54, 14.8%), PIMPPVS (4/54, 7.4%), bronchospasm (2/54, 3.7%), reintubation (2/54, 3.7%), delayed extubation (2/54, 3.7%) and pneumothorax (1/54, 1.9%) (Table 2).

Univariate Testing between the Groups of Children with and without Postoperative Respiratory Complications
In general factors, compared with children without PRCs, children with PRCs were strongly positively associated with nonidiopathic scoliosis (P = 0.003). These patients were also more likely to have pulmonary comorbidities (P = 0.003). Regarding laboratory factors, the blood biochemical indicators, pretransferrin (P = 0.002) and prealbumin (P = 0.016), which reflects nutritional status and oxygen carrying status, were lower in children with PRCs. Regarding the surgical factors, more anesthesia time (P = 0.007) was consumed, and more BL/TBV (P = 0.000) was detected in children with PRCs than in those without PRCs. No significant difference in gender, major curve angle, kyphosis, or types of PSDS was observed (Table 3).

Binary Logistic Regression between the Variables with Significant Differences in Univariate Testing
The six variables that were significantly different were further analyzed using binary logistic regression analysis. The results of binary logistic regression indicated that children with EOS following PSDS were positively linear correlated with the following factors with regard to the PRCs: BL/TBV ≥15% (B = 3.374, odds ratio OR = 29.188, P = 0.010), combined with pulmonary comorbidities (B = 2.956, OR = 19.216, P = 0.012), pretransferrin < 200 mg/dL(X6)(B = 2.443, OR = 11.503, P = 0.024), and non-idiopathic scoliosis (B = 2.032, OR = 7.632, P = 0.046). Compared with standard partial regression coefficients (OR), BL/TBV ≥15% was the most significant factor

| TABLE 4 | Weight assignment of variables |
|----------|-----------------------------|
| Factors                          | Value assignment |
| Etiology                          | 1 = “Non-idiopathic”; 2 = “idiopathic” |
| Combined with pulmonary comorbidities | 1 = “Yes”; 2 = “No” |
| Pretransferrin (<200 mg/dL)       | 1 = “Yes”; 2 = “No” |
| Prealbumin (<3.5 g/dL)            | 1 = “Yes”; 2 = “No” |
| Anesthesia time (≥300 min)        | 1 = “Yes”; 2 = “No” |
| BL/TBV (≥15%)                     | 1 = “Yes”; 2 = “No” |

| TABLE 5 | Results using binary logistic regression analysis method |
|----------|----------------|
| Variables | B   | S.E. | Wald | OR  | Sig. | 95% CI for EXP (B) |
| Etiology                          | 2.032 | 1.020 | 3.970 | 7.632 | 0.046* | 1.034 | 56.342 |
| Combined with pulmonary comorbidities | 2.956 | 1.178 | 6.291 | 19.216 | 0.012* | 1.908 | 193.524 |
| Pretransferrin (<200 mg/dL)       | 2.443 | 1.083 | 5.085 | 11.503 | 0.024* | 1.377 | 961.121 |
| BL/TBV (≥15%)                     | 3.374 | 1.310 | 6.636 | 29.188 | 0.010* | 2.241 | 380.183 |

Abbreviations: OR odds ratio; SE standard error.; * P < 0.05, statistically significant.
The incidence of postoperative respiratory complications

The previous literature indicated different incidences of PRCs and used different definitions of PRCs, which makes the results lack clinical guidance significance. To obtain more reliable results, we used standardized definitions of PRCs in this study. We examined 73 children with EOS following PSDS, and we found a higher incidence of PRCs (21.9%) than other investigators, who demonstrated an average incidence of approximately 11%–15% for PRCs associated with congenital or nondegenerative scoliosis.

The high incidence of PRCs in children with EOS is likely to be caused by anatomical changes. In contrast to other types of scoliosis, EOS is a progressive spinal deformity that occurs during the critical period of lung development (within the first 10 years) and is generally associated with the development of restrictive thoracic cages, ribs, and sternums, limiting the number of alveoli and the lung volume. This eventually leads to lung defects, as demonstrated by a decrease in lung volume, vital capacity, and chest wall compliance based on pulmonary function testing. In addition, this progressive spinal deformity is likely to affect the position of various organs and the maximal strength of the respiratory muscle groups residing in the chest cavity, causing mechanical airway obstruction. In most children with EOS, restrictive lung disease occurs due to a reduced intrathoracic volume and increased chest wall stiffness over time. The obstructive mechanism is the compression of a main stem bronchus from the “intrathoracic spinal hump” and mediastinal contents.

Children with EOS may also develop symptoms of lower airway obstruction, which may be the result of chronic airway inflammation and reduced bronchial cilia function secondary to the poor clearance of secretions. The changes in anatomy due to spinal deformity ultimately led to changes in exercise capacity and breathing patterns. Furthermore, patients usually experience severe pain after surgery. These patients are likely to have shallower breathing, thus increasing the possibility of progressive atelectasis. In addition, narcotic agents and analgesics have a similar effect. All of these pathological changes mentioned above contribute to a higher incidence of PRCs in children with EOS following PSDS.

Nine different PRCs were detected, and the total frequency of detected PRCs was 54 in this study. The most frequent PRC was pleural effusion (25.9%). In terms of pathological changes, these complications are mutually causal during their occurrence and development. Massive amounts of fluid input in a relatively short period of time during surgery, surgical manipulation around the pleura and pleural injury during surgery often lead to the development of pleural effusions, pulmonary edema and pneumothorax. Due to surgical trauma, being placed in the prone position may impair the chest wall mechanics and lung pathological changes secondary to spinal deformity, so children with EOS are at increased risk of progressive atelectasis, pneumonia, and hypoxemia. All of these progressive blood oxygen exchange disorders lead to PIMPPVS, delayed extubation and reintubation. The tendency to become hypoxic...
The results of our Segreto According to the characteristics of EOS, this
In this group of children, respi-
A cluster
vascular endothelium, which leads to impaired microvascular
decrease cellular deformability and increase adhesion to the
PRCs. Moreover, the storage of blood products can
injury or immune suppression and increasing susceptibility
the immune system, resulting in transfusion-related lung
ble bioactive substances. These bioactive substances activate
related immunomodulation because of the infusion of solu-
osaline pressures. Second, transfusion results in transfusion-
period of time, causing tremendous shifts in hydrostatic and
EOS receive massive amounts of
patients undergoing surgery. First, low-weight children with
between intraoperative blood transfusion and PRCs in
research has proposed some hypotheses about the association
PRCs following PSDS in children with EOS. It is
well established that a high rate of pulmonary comorbidities,
which can exacerbate the effect of spinal deformity on pul-
function, is expected in EOS cohorts.

Combined with Pulmonary Comorbidities
According to our study, combined with pulmonary comor-
oids was an independent risk factor for the develop-
ent of PRCs following PSDS in children with EOS. Compared with adults, children with EOS have different
hemodynamic characteristics during surgery. The absolute
blood volume is much smaller in low-weight children with
EOS, indicating that even minor absolute blood loss will
result in hemodynamic instability. Therefore, this study
thinks it is more appropriate to use BL/TBV instead of blood
loss volume to evaluate the intraoperative blood loss in this
type of research. Intraoperative blood loss is a well-
documented risk factor for mortality and morbidity in EOS
surgery. Previous studies have shown that massive blood loss
during surgery can cause end-organ damage and increased
postoperative complications, including multiple respiratory
complications, in addition to hemodynamic instability. \(^{14,15}\)

Blood Loss to Total Blood Volume Ratio (BL/TBV)
In the current study, the regression analysis demonstrated
that BL/TBV \(\geq 15\%\) was an independent risk factor for the
development of PRCs following PSDS in children with EOS.
Compared with adults, children with EOS have different
hemodynamic characteristics during surgery. The absolute
blood volume is much smaller in low-weight children with
EOS, indicating that even minor absolute blood loss will
result in hemodynamic instability. Therefore, this study
thinks it is more appropriate to use BL/TBV instead of blood
loss volume to evaluate the intraoperative blood loss in this
type of research. Intraoperative blood loss is a well-
documented risk factor for mortality and morbidity in EOS
surgery. Previous research has proposed some hypotheses about the association
between intraoperative blood transfusion and PRCs in
patients undergoing surgery. First, low-weight children with
EOS receive massive amounts of fluid in a relatively short
period of time, causing tremendous shifts in hydrostatic and
osmotic pressures. Second, transfusion results in transfusion-
related immunomodulation because of the infusion of solu-
able bioactive substances. These bioactive substances activate
the immune system, resulting in transfusion-related lung
injury or immune suppression and increasing susceptibility
to PRCs. Moreover, the storage of blood products can
decrease cellular deformability and increase adhesion to the
vascular endothelium, which leads to impaired microvascular
flow and reduced oxygen delivery. \(^{14,15}\) The results of our
study suggested that reducing blood loss during surgery and
perioperative blood transfusion help decrease PRCs.

Transferrin
Our data demonstrated that a lower level of preoperative
serum transferrin was an independent risk factor for the
development of PRCs following PSDS in children with EOS.
The optimization of preoperative nutrition can help reduce
perioperative complications, including PRCs, in pediatric
scoliosis populations. The serum albumin level and total
lymphocyte count have been commonly used as sensitive
indicators of nutritional status (malnutrition is commonly
defined as a total lymphocyte count \(<1500\) cells/mm\(^3\),
serum albumin level \(<3.0\) g/dL, or serum transferrin
level \(<200\) mg/dL). \(^{16}\) Serum transferrin, prealbumin, and
retinol-binding protein are recognized as rapid turnover pro-
teins because their serum half-life values are shorter than
that of albumin. This characteristic makes them better nutri-
tional biomarkers for the early detection of nutritional defi-
cits. Therefore, transferrin has been identified as a
perioperative marker of serum protein and iron status that is
useful in the prediction of perioperative morbidity and mor-
tality. Our analysis indicated that it is important to perform
a thorough evaluation of nutritional status to decrease PRCs
due to perioperative malnutrition.

Etiologic Factor
EOS is a group of heterogeneous diseases with highly vari-
able manifestations and is medically complex. To describe
and guide optimal care and predict outcomes within the
EOS population, Williams et al. proposed an EOS classifica-
tion system. \(^{6}\) According to the characteristics of EOS, this
classification system contains several key factors, including
age, etiology, the severity of the deformity in the coronal and sagittal planes and curve progression. Therefore, the author thinks that it is appropriate to use this classification system to evaluate EOS patients in this research.

Based on the current study, the regression data demonstrated that etiology (nonidiopathic scoliosis) was an independent risk factor for the development of PRCs following PSDS in children with EOS. Neuromuscular scoliosis is the second most prevalent spinal deformity after idiopathic scoliosis. Previous studies have illustrated that PRCs are the most frequent postoperative complications in patients with neuromuscular scoliosis, with a particular risk of aspiration pneumonia. Various potential risk factors for these patients’ vulnerability to PRCs have been suggested. Many individuals with neuromuscular scoliosis have impaired motor function, muscle strength and coordination, especially regarding the respiratory muscles. In addition, concurrent comorbidities in individuals with neuromuscular scoliosis may also increase the risk of PRCs, including seizures, swallowing disorders and gastroesophageal reflux. Similarly, congenital/syndromic scoliosis is related to genetic defects or metabolic disorders and is usually associated with nonskeletal abnormalities, including respiratory system abnormalities. A significant proportion of individuals with congenital/syndromic scoliosis have aspiration and restrictive lung defects. Consequently, some studies have revealed that pulmonary/respiratory complications are major complications that occur following the surgical correction of nonidiopathic scoliosis. Our result is consistent with those of previous studies and confirms that comprehensive preoperative assessments and therapy of EOS require a multidisciplinary involvement.

Limitations

The findings of this study should be viewed after considering the following limitations. It is difficult to launch a prospective protocol to reduce the incidence of PRCs, given that only a fraction of EOS children have been treated with PSDS in the low incident EOS population. Also, the findings in this study are also limited by its retrospective nature to draw any strong conclusions. Furthermore, relatively smaller sample size in a single institute may lead to sample bias. Multiple-center, large-sample, randomized clinical trials are required to confirm our conclusion in the future. However, the results of this research still offer valuable risk information for surgeons considering intervention with PSDS in children with EOS.

Conclusion

PRCs are the major postoperative nonneurological complications following PSDS in children with EOS. The incidence of PRCs was 21.9% and the most frequent PRC was pleural effusion. This study showed that BL/TBV $\geq$15%, combined with pulmonary comorbidities, pre-transferrin < 200 mg/dL, and nonidiopathic scoliosis were independent risk factors for the development of PRCs following PSDS in EOS population.

Although this research demonstrated some independent risk factors for the development of PRCs, there are still significant unresolved clinical questions need to be found to decrease PRCs. A validated respiratory risk questionnaire would be useful for enabling clinicians to provide evidence-based care for children with EOS at risk of PRSs following PSDS.

Acknowledgments

We would like to acknowledge the significant contribution of the patients, families, researchers, clinical staff, and sponsors included in this study. The authors thank Ms. Mi Yang for the assistance of grammatical modification. The manuscript submitted does not contain information about medical device(s)/drug(s).

Author Contributions

Yang Zhang, Yingsong Wang and Jingming Xie contributed to the conception and design of this manuscript, the acquisition of the data, the analysis and the interpretation of the data and the drafting of the manuscript. Ni Bi, Zhi Zhao, Tao Li, and Zhiyue Shi, followed up and collected the data. Wuyao Li, Kaiwen Gu, Bing Gao and Tianyi Huang were responsible for the data collection and radiographic measurements. Tianyi Huang conceived the study and participated in its design and coordination, revised the manuscript critically for important intellectual.

Funding

Fund from the National Natural Science Foundation of China (NSFC). (Grant No. 82060414; 81860403) and the “Special and Joint Program” of Yunnan Provincial Science and Technology Department & Kunming Medical University (Grant No. 202101AY070001-150) was received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

References

1. El-Hawary R, Akbarnia BA. Early onset scoliosis—time for consensus. Spine Deform. 2015;3:105–6.
2. Baulesh DM, Huh J, Judkins T, Garl S, Miller NH, Erickson MA. The role of serial casting in early-onset scoliosis (EOS). J Pediatr Orthop. 2012;32: 658–63.
3. Hod-Feins R, Abu-Kishk I, Eshel G, Barr Y, Ankestein Y, Mirovsky Y. Risk factors affecting the immediate postoperative course in pediatric scoliosis surgery. Spine. 2007;32:2355–80.
4. Reamers DL, Smith JS, Fu KMG, Polly DW Jr, Ames CP, Berven SH, et al. Complications in the surgical treatment of 19,360 cases of pediatric scoliosis: a review of the Scoliosis Research Society morbidity and mortality database. Spine. 2011;36:1484–91.
5. Sharma S, Wu C, Andersen T, Wang Y, Hansen ES, Banger CE. Prevalence of complications in neuromuscular scoliosis surgery: a literature meta-analysis from the past 15 years. Eur Spine J. 2013;22:1230–49.
6. Williams BA, Matsumoto H, McCalla DJ, et al. Development and initial validation of the classification of early-onset scoliosis (C-EOS). J Bone Joint Surg Am. 2014;96:1359–67.
7. JI, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine:
European perioperative clinical outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. Eur J Anaesthesiol. 2015;32:88–105.

8. Yin S, Tao HR, Du H, et al. Postoperative pulmonary complications following posterior spinal instrumentation and fusion for congenital scoliosis. PLoS One. 2018;13:e0207657.

9. Wang YS, Hai Y, Liu YZ, Guan L, Liu L. Risk factors for postoperative pulmonary complications in the treatment of non-degenerative scoliosis by posterior instrumentation and fusion. Eur Spine J. 2019;28:1356–62.

10. Koumbourlis AC. Scoliosis and the respiratory system. Paediatr Respir Rev. 2006;7:152–60.

11. Mayer OH, Redding G. Early changes in pulmonary function after vertical expandable prosthetic titanium rib insertion in children with thoracic insufficiency syndrome. J Pediatr Orthop. 2009;29:35–8.

12. Motoyama EK, Yang CI, Deeney VF. Thoracic malformation with early-onset scoliosis: effect of serial VEPTR expansion thoracoplasty on lung growth and function in children. Paediatr Respir Rev. 2009;10:12–7.

13. Redding GJ, Hurn H, White KK, White KK, Bompadre V, Emerson J, et al. Persistence and progression of airway obstruction in children with early onset scoliosis. J Pediatr Orthop. 2020;40:190–5.

14. Glance LG, Dick AW, Mukamel DB, Fleming FJ, Zullo RA, Wissler R, et al. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. Anesthesiology. 2011;114:283–92.

15. Meyer HM, Torborg A, Cronje L, Thomas J, Bhettay A, Diedericks J, et al. The association between preoperative anemia and postoperative morbidity in pediatric surgical patients: a secondary analysis of a prospective observational cohort study. Paediatr Anaesth. 2020;30:759–65.

16. Segreto FA, Vasquez-Montes D, Bortz CA, Horn SR, Diebo BG, Vira S, et al. Impact of presenting patient characteristics on surgical complications and morbidity in early onset scoliosis. Clin Neurosci. 2019;26:105–11.

17. Tan HL, Urquhart DS. Respiratory complications in children with Prader Willi syndrome. Paediatr Respir Rev. 2017;22:52–9.

18. Kudo D, Miyakoshi N, Hongo M, Kasukawa Y, Ishikawa Y, Mizutani T, et al. Relationship between preoperative serum rapid turnover proteins and early-stage surgical wound infection after spine surgery. Eur Spine J. 2017;26:3156–61.

19. Duckworth AD, Mitchell MJ, Tsirikos AI. Incidence and risk factors for postoperative complications after scoliosis surgery in patients with Duchenne muscular dystrophy: a comparison with other neuromuscular conditions. Bone Joint J. 2014;96:943–9.

20. Giampietro PF, Dunwoody SL, Kusumi K, Pourquié O, Tassy O, Offiah AC, et al. Progress in the understanding of the genetic etiology of vertebral segmentation disorders in humans. Ann N Y Acad Sci. 2009;1151:38–67.