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ORIGINAL ARTICLE

Acute normovolemic hemodilution reduced the frequency and amount of perioperative allogeneic blood transfusion in pediatric and adolescent scoliosis surgery: a retrospective observational study

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Abstract

Purpose The aim of the present study is to investigate whether acute normovolemic hemodilution (ANH) can reduce the frequency and amount of perioperative allogeneic blood transfusion (ABT) (intraoperative ABT and postoperative ABT until discharge from the hospital) in pediatric and adolescent scoliosis surgery.

Methods This single-center, retrospective, observational study included the perioperative data of 147 patients who were 18 years old or younger and underwent scoliosis surgery. Patients were divided into groups according to whether they received ANH: i.e., an ANH group and control group. Propensity-score-adjusted multivariable logistic regression analysis was performed to determine whether ANH can reduce the frequency of perioperative ABT.

Results A total of 125 patients were analyzed, 95 and 30 in the ANH and control group, respectively. The intraoperative/postoperative ABT frequency was significantly lower in the ANH group than in the control group (17.9% vs. 36.7%, $p=0.044$). The amount of ABT [median (IQR): 0 (0, 0) mL/kg vs. 0 (0, 16.3) mL/kg, $p=0.033$] was also significantly lower in the ANH group than in the control group. Propensity-score-adjusted multivariable logistic regression analysis indicated that ANH use [odds ratio: 0.15; 95% confidence interval: 0.03, 0.77; $p=0.023$)] was associated with a lower risk of ABT after adjusting for intraoperative blood loss and duration of surgery.

Conclusion ANH use can reduce the frequency and amount of perioperative ABT in pediatric and adolescent scoliosis surgery.

Keywords Acute normovolemic hemodilution · Scoliosis · Allogeneic blood transfusion

Introduction

Scoliosis surgery, which entails extensive soft-tissue dissection and osteotomy, is one of the most invasive and complex of the orthopedic surgeries. Since the amount of intraoperative and postoperative blood loss tends to be high, intraoperative and postoperative allogeneic blood transfusion (ABT) is often given to patients undergoing this surgery [1].

Accumulating evidence indicates that ABT is involved in increased risks for some complications including allergic reaction, transfusion-transmitted infectious disease, transfusion-related acute lung injury, and transfusion-associated circulatory overload [2]. Transfusion-related immunomodulation is also a negative aspect of ABT [3]. Indeed, perioperative ABT has been found to be an independent risk factor for SSI after spine surgery [4]. Thus, it is important to prevent perioperative ABT or to keep ABT to a minimum to improve patient's postoperative outcomes.

Acute normovolemic hemodilution (ANH) is a type of autologous blood transfusion, which removes whole blood from a patient before surgery under general anesthesia and replaces withdrawn blood volume with an equal volume of colloid infusion. Previous studies have shown that ANH can reduce the frequency and amount of perioperative ABT without increasing postoperative complications in cardiac and non-cardiac surgery [5–7]. Our PubMed search revealed three studies evaluating the efficacy of ANH in scoliosis surgery [8–10]. One of these studies showed that ANH reduced the frequency and amount of perioperative ANH [8], but two of these studies did not [9, 10]. Thus, whether ANH

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reduce the frequency and amount of perioperative ABT is still controversial.

The aim of the present study was to gather more data on the question of whether ANH can reduce the frequency and amount of perioperative ABT in pediatric and adolescent scoliosis surgery.

Methods

Study procedure and patients

This single-center, retrospective, observational study was approved by the ethical review board of the Hirosaki University Graduate School of Medicine, Hirosaki, Japan and was publicized on our department and hospital homepage using an opt-out approach (2022–142). Written informed consent from each patient was waived because of the study's retrospective manner. This study enrolled 147 patients who were 18 years old or younger and underwent scoliosis surgery at Hirosaki University Hospital between April 1, 2013 and December 12, 2021. Patients who underwent rod adjustment surgery and/or implant removal were excluded because the amount of blood loss during these surgeries is low. Patients were divided into groups according to ANH use: i.e., an ANH group and a control group.

Data collection

The following data were obtained from medical and anesthesia records: gender, age, body weight, height, body mass index, American Society of Anesthesiologists Physical Status (ASA-PS), diagnosis, preoperative autologous blood donation (PAD) use, amount of PAD, ANH use, amount of ANH, duration of anesthesia and surgery, amount of intraoperative vasopressors use, control mean arterial pressure (MAP) (MAP before anesthetic induction), intraoperative minimum MAP (we excluded hypotension within 15 min after anesthetic induction.), amount of intraoperative blood loss, amount of intraoperative urine output, amount of intraoperative fluid infusion, amount of intraoperative cell salvage (ICS), amount of intraoperative and postoperative ABT (perioperative ABT is defined as intraoperative ABT and postoperative ABT until discharge from the hospital in the present study), preoperative and postoperative Cobb angle of major curve, correction rate of major curve, number of fusion segments, surgical procedure, postoperative complications, length of intensive care unit (ICU) stay, length of hospital stay, and preoperative and postoperative laboratory data.

The following perioperative laboratory data were collected: hemoglobin (Hb) level, hematocrit, platelet count, activated partial thromboplastin time, prothrombin time, and lactate level. The preoperative laboratory data of patients who underwent PAD were collected after PAD. The postoperative laboratory data were collected at ICU admission.

Indication for PAD

The indication for PAD in our institution is an estimated blood loss of more than 10 mL/kg and an Hb level of more than 11 g/dL. Exclusion criteria for PAD at our institution were infectious disease, heart failure (New York Heart Association functional class ≥ 3), renal failure, active ischemic heart disease, and/or refusal by the patient.

Anesthesia and ANH procedure

In our institution, ANH was performed in pediatric and adolescent scoliosis surgery in the case with an estimated blood loss of more than 10 mL/kg, or when the surgeon asks for ANH and the patient's Hb level is more than 10 g/dL. Exclusion criteria for ANH at our institution were same as that for PAD.

All scoliosis surgeries were performed under general anesthesia. ICS was performed in all patients during the surgery. For induction anesthesia, we used a combination of propofol, remifentanil, ketamine and rocuronium, or a combination of sevoflurane, nitrous oxide and rocuronium. For maintenance anesthesia, we used a combination of propofol, remifentanil and/or fentanyl, ketamine and rocuronium or a combination of sevoflurane, remifentanil/fentanyl and rocuronium. After anesthetic induction, blood was withdrawn from the central venous line for ANH. Even though our institution does not have specific criteria of the withdrawn blood volume for ANH, we usually select the volume using the following formula to avoid an Hb level of less than 8.0 g/dL after hemodilution.

$$\text{Withdrawn blood volume} \leq \left(1 - \frac{8}{\text{Hbi}}\right) \times \frac{\text{BW} \times 1000}{13}$$

Hbi is the initial hemoglobin, BW is the body weight.

We manage hypotension during blood removal by administration of phenylephrine or bolus administration of colloid. If the patient does not respond to these therapies, we stop blood removal. The withdrawn blood volume was replaced with the same volume of colloid. The collected blood was stored in a standard blood collection pack (JMS Blood Bag CPD400; JMS, Tokyo, Japan) at room temperature (22–26 °C) on a shaker (60–80 rpm). When rod implantation and screw fixation into the vertebrae was completed, the collected blood was reinfused to the patients.

In our institution, the FloTrac/Vigileo system (Edwards Lifescience, Tokyo, Japan) was used for fluid management in scoliosis surgery. Even though our institution does not have specific criteria for fluid management, we carefully control fluid volume by referring to stroke volume variation (SVV) and cardiac index (CI). In the most case, we maintain SVV between 10 and 14% after hemodilution considering reinfusion of collected blood and adjust SVV < 10% after reinfusion of collected blood. We maintain CI > 2.2 L/min/m^2 during the surgery.

Criteria for ABT

At our institution, the transfusion threshold is generally set at an Hb of less than 7.0 g/dL. When the Hb is below 7.0 g/dL, we transfuse autologous blood (ICS and ANH), if it is available. If Hb is still below 7.0 g/dL after this transfusion, we perform ABT.

Statistical analysis

Patient characteristics, perioperative data, and postoperative outcomes are presented as medians (25th to 75th percentile) and numbers (percentage of each group). Statistical differences between the ANH and control groups were assessed using Fisher's exact test for categorical variables and Mann–Whitney's *U* test for continuous variables.

We performed propensity-score-adjusted multivariable logistic regression analysis to evaluate whether ANH use can reduce the frequency of ABT. We calculated the propensity score, the predicted probability to be included in the ANH group, considering patients' characteristics as covariates in multivariable logistic regression analysis. Age, sex, ASA-PS, and preoperative Hb level were included in this logistic regression analysis. Additionally, diagnosis, the number of fusion segments and surgical procedure were forced into the model based on the existing knowledge that these variables can be significant predictors for ABT in scoliosis surgery [11]. Height and body weight were also included because these variables were significantly different between the ANH group and control group in univariable analyses. PAD use was also included, because PAD is reported to reduce the frequency and amount of ABT [12]. We used the above-calculated propensity score as a covariate in our model to adjust for preoperative confounding factors. The presence of ANH was forced into the model. In addition, as intraoperative blood loss and duration of surgery were related with perioperative ABT, these variables, intraoperative confounding factors, were also forced into the model. It has been suggested that the number of events per predictor variable in a multivariable logistic regression analysis should be at least 10 to provide an adequate predictive model [13]. However, a recent simulation study suggested that 5–9 events per predictor variable is sufficient [14]. In the present study, considering the number of events (28 patients received ABT), we included the 4 variables in each model (one variable was included in the model for 7 events). Multicollinearity among the variables was checked using variance inflation factor (VIF). Discrimination was measured using the area under the curve (AUC). The results are presented as adjusted odds ratios (aORs) with corresponding 95% confidence intervals (CIs).

Additionally, we compared the efficacy of ANH and PAD at reducing the frequency of ABT using multivariable logistic regression analysis. The use of ABT and PAD were forced into this model. As in the above analysis, since intraoperative blood loss and duration of surgery were related with perioperative ABT, these variables were also forced into the model.

We performed Kaplan–Meier curve analysis with log-rank test to investigate the effect of ANH on length of hospital stay, and we compared the probability of hospital stay among the ANH and control group. We also performed cox proportional hazard analysis to investigate the effect of ANH on length of hospital stay. ANH was forced into the model. Age, height, body weight, ASA-PS, diagnosis, and surgical procedure were included to the model. The results are presented as adjusted hazard ratios (aHRs) with 95% CIs. In this model, HR < 1 means that the probability of discharge is reduced, and the risk of prolonged length of hospital stay is increased.

We performed all analyses using R software version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). Standardized differences between the two group for each patient's characteristic were calculated. A two-tailed *P* value < 0.05 was considered statistically significant in all analyses.

Results

Of the 147 included patients, 19 patients who underwent rod adjustment surgery and 2 patients who underwent implant removal were excluded. Thus, 125 patients were finally analyzed, with 95 and 30 patients in the ANH and control groups, respectively (Fig. 1).

Table 1 shows the patients' characteristics. There were no significant differences in gender, BMI, ASA-PS, PAD use, or the amount of PAD between two groups. However, age, height, body weight, and diagnosis were significantly different between the two groups.

Table 2 shows perioperative data of the patients. Twenty-eight patients (22.4%) received intraoperative and/or postoperative ABT in the study. The intraoperative/postoperative ABT frequency was significantly lower in the ANH group than in the control group (17.9% vs. 36.7%, $p = 0.044$). The amount of ABT was also significantly lower in the ANH group than in the control group. The frequency of RBC transfusion (i.e., what percentage of patients required RBC

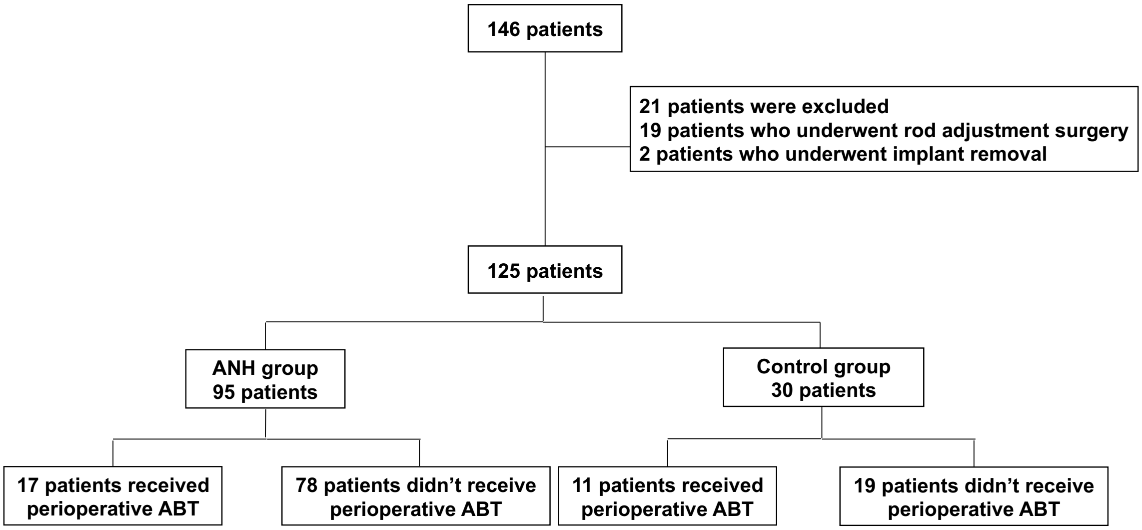

Fig. 1 Flow chart of this study cohort. *ANH* acute normovolemic hemodilution

Table 1 Characteristics of patients

	ANH group	Control group	*P* value	|Standardized difference|
N	95	30		
Male (*n*)	21 (22.1%)	9 (30.0%)	0.462	0.181
Age (year)	14 (13, 16)	13 (11, 15)	0.005*	0.563
Height (cm)	152 (147, 158)	142 (130, 154)	0.004*	0.630
Body weight (kg)	45.0 (36.3, 50.0)	35.9 (24.6, 46.3)	0.028*	0.469
BMI (kg/m^2)	18.8 (16.5, 20.5)	17.9 (13.8, 22.0)	0.395	0.224
ASA-PS			0.069	0.502
1 (*n*)	11 (11.6%)	1 (3.3%)		
2 (*n*)	67 (70.5%)	18 (60.0%)		
3 (*n*)	17 (17.9%)	11 (36.7%)		
Diagnosis			0.021*	0.668
Idiopathic (*n*)	69 (72.6%)	14 (46.7%)		
Congenital (*n*)	4 (4.2%)	1 (3.3%)		
Neuromuscular (*n*)	11 (11.6%)	11 (36.7%)		
Neurofibromatosis (*n*)	5 (5.3%)	1 (3.3%)		
Syndromic (*n*)	6 (6.3%)	3 (10.0%)		
PAD (*n*)	40 (42.1%)	14 (46.7%)	0.528	0.159
PAD (mL/kg)	7.76 (6.32, 11.5)	9.01 (5.72, 10.19)	0.794	0.151

Differences between the ANH and control groups were estimated using Fisher's exact test for categorical variables and Mann–Whitney test for continuous variables. Data are shown as number (a percentage of each group) or median (25 to 75th percentile)

BMI body mass index, *ASA-PS* American Society of Anesthesiologists Physical Status, *PAD* preoperative autologous blood donation

*Statistical significance

transfusion) and amount of RBC transfusion were significantly lower in in the ANH group than in the control group, but the fresh-frozen plasma (FFP) and platelet concentrate (PC) transfusion frequency and the amounts of FFP and PC transfusion were not significantly different between the two groups. There were no significant differences in surgical procedure, number of fusion segments, preoperative and postoperative Cobb angle of major curve and correction

Table 2 Perioperative data of the patients

	Group ANH	Group non-ANH	*P* value
Surgical procedure			0.347
PLIF (*n*)	85 (89.5%)	24 (80%)	
Glowing rod procedure (*n*)	4 (4.2%)	2 (6.7%)	
Others (*n*)	6 (6.3%)	4 (13.3%)	
Fusion segments	10 (8, 12)	11 (8.5, 13)	0.501
Pre. Cobb angle (°)	61.0 (51.0, 78.3)	73.0 (52.0, 96.0)	0.198
Post. Cobb angle (°)	22.0 (14.8, 38.5)	23.0 (17.0, 47.0)	0.280
Correction rate (%)	63.0 (51.0, 72.0)	59.0 (51.0, 69.0)	0.601
Perioperative labo data			
Hb (g/dL)			
Pre	13.6 (12.9, 14.2)	13.4 (12.6, 14.1)	0.221
Post	9.00 (8.40, 9.90)	9.20 (8.03, 10.4)	0.569
Hematocrit (%)			
Pre	40.5 (38.7, 42.0)	39.3 (36.8, 41.7)	0.245
Post	27.4 (25.8, 29.9)	28.4 (24.5, 32.3)	0.527
Plt ($\times 10^4$/μL)			
Pre	24.4 (20.8, 27.9)	25.3 (22.9, 28.0)	0.303
Post	15.5 (12.6, 17.2)	15.4 (10.1, 18.0)	0.849
PT (s)			
Pre	12.6 (11.7, 13.9)	12.8 (11.7, 14.1)	0.850
Post	14.8 (13.1, 16.2)	14.3 (13.4, 15.3)	0.537
APTT (s)			
Pre	31.9 (29.7, 33.6)	32.7 (30.3, 34.6)	0.314
Post	33.6 (30.9, 37.1)	34.6 (32.3, 37.2)	0.567
Lac (mmol/L)			
Pre	0.90 (0.70, 1.20)	0.85 (0.70, 1.30)	0.567
Post	1.00 (0.80, 1.40)	1.00 (0.72, 1,45)	0.479
Max	1.20 (0.85, 1.55)	1.10 (0.80, 1.37)	0.232
Vasopressors use Ephedrine (mg)	4.00 (0.00, 8.00)	2.00 (0.00, 7.50)	0.772
Phenylephrine (mg)	0.00 (0.00, 0.30)	0.00 (0.00, 0.00)	0.017*
MAP (mmHg)			
Baseline	84.3 (77.5, 92.7)	81.0 (71.6, 88.9)	0.106
Min	51.3 (46.3, 55.5)	52.2 (46.3, 55.2)	0.917
Duration of anesthesia (h)	7.25 (6.32, 8.71)	7.93 (6.40, 9.50)	0.510
Duration of surgery (h)	5.17 (4.47, 6.62)	5.64 (4.40, 6.80)	0.654
Intra			
Blood loss (mL/kg)	16.0 (9.29, 27.2)	14.3 (5.92, 25.8)	0.290
UO (mL/kg/h)	2.59 (1.90, 3.85)	2.85 (1.65, 3.64)	0.826
Cell salvage (mL/kg)	4.49 (2.45, 8.72)	4.80 (0.00, 8.57) 0.676	
Fluid infusion			
Total (ml/kg/h)	9.98 (8.28, 12.2)	9.12 (7.81, 11.2)	0.197
Crystalloid (mL/kg/h)	6.70 (5.21, 8.76)	7.22 (5.76, 9.26)	0.130
Colloid (mL/kg/h)	3.23 (2.66, 3.89)	1.41 (0.00, 2.45)	<0.001*
Albumin (mL)	0 (0, 0)	0 (0, 0)	0.200
Intra. and post. ABT			
Total (*n*)	17 (17.9%)	11 (36.7%)	0.044*
Total (mL/kg)	0 (0, 0)	0 (0, 16.3)	0.033*
RBC (*n*)	12 (12.6%)	9 (30.0%)	0.046*
RBC (mL/kg)	0 (0, 0)	0 (0, 9.38)	0.028*
FFP (*n*)	15 (15.8%)	10 (33.3)	0.094
FFP (mL/kg)	0 (0, 0)	0 (0, 10.3)	0.055

Table 2 (continued)

	Group ANH	Group non-ANH	*P* value
PC (*n*)	4 (4.2%)	1 (3.3%)	1.000
PC (mL/kg)	0 (0.0)	0 (0, 0)	0.845
Postoperative complications			
SSI	2 (2.1%)	0 (0%)	1.000
Other infections	3 (3.2%)	5 (16.7%)	0.019*
Respiratory failure	0 (0%)	3 (10.0%)	0.013*
Length of			
ICU stay (day)	1 (1, 1)	1 (1, 2)	0.060
Hospital stay	20 (17, 24)	23.5 (20, 28.5)	0.010*

Differences between the ANH and control groups were estimated using Fisher's exact test for categorical variables and Mann–Whitney *U* test for continuous variables. Other infections included pneumonia, urinary tract infection, and etc. Data are presented as number (percentage of each group) or median (25th to 75th percentile). ANH: acute normovolemic hemodilution

PLIF posterior lumbar interbody fusion, *Pre* preoperative, *Intra* intraoperative, *Post* postoperative, *Hb* hemoglobin, *Plt* platelet count, *PT* prothrombin time, *APTT* activated partial thromboplastin time, *Lac* lactate, *Max* maximum, *MAP* mean arterial pressure, *Min* minimum, *UO* urine output, *ABT* allogeneic blood transfusion, *RBC* red blood cell, *FFP* fresh-frozen plasma, *PC* platelet concentrate, *SSI* surgical site infection, *ICU* intensive care unit

*Statistical significance

rate of major curve between the two groups. Preoperative and postoperative laboratory data were not significantly different between the two groups. There were no significant differences in the amount of intraoperative ephedrine use, baseline MAP, and minimum MAP between the two groups. On the other hand, the amount of intraoperative phenylephrine use was significantly higher in the ANH group than in the control group. The duration of anesthesia and surgery, amount of intraoperative blood loss, urine output, and amount of cell salvage were not significantly different between the two groups. Regarding fluid infusion, the only difference was the amount of colloid infusion, which was significantly greater in the ANH group than in the control group. Although the incidence of SSI was not significantly different between the groups, the incidence of other infectious complications including pneumonia and urinary tract infection, and the incidence of respiratory failure were lower in the ANH group than in the control group. Additionally, the length of hospital stay was shorter in the ANH group than in the control group.

Table 3 shows the result of the propensity-score-adjusted multivariable logistic regression analysis. ANH use was independently and negatively associated with perioperative ABT (aOR: 0.15, 95% CI 0.03, 0.77; $p = 0.023$), which suggests that ANH use can reduce frequency of perioperative ABT. Additionally, intraoperative blood loss and duration of surgery were also independently associated with perioperative ABT.

Table 4 shows the result of the multivariable logistic regression model comparing the efficacy of ANH and PAD for reducing the frequency of ABT. ANH use was independently associated with perioperative ABT (aOR: 0.14, 95% CI 0.03, 0.64; $p = 0.011$), but PAD use was not, after adjusting for intraoperative blood loss and duration of surgery.

Table 3 Propensity score-adjusted multivariable logistic regression model to identify the predictive factors of perioperative ABT

	aOR	95% CI	*P* value
ANH	0.15	0.03, 0.77	0.023*
Intra. Blood loss (per 1 mL/kg increase)	1.09	1.04, 1.13	< 0.001*
Duration of surgery (per 1 h increase)	1.78	1.18, 2.68	0.006*
Propensity score	0.38	0.01, 10.3	0.567

The propensity score was estimated using multivariable logistic regression analysis with the following variables: age, sex, height, body weight, American Society of Anesthesiologists Physical Status, preoperative hemoglobin level, the number of fusion segments, surgical procedure, diagnosis, and preoperative autologous blood donation use. The propensity score was 0.78 (25th to 75th percentile: 0.72, 0.91). ANH use, intraoperative bleeding, duration of surgery and the propensity score were included in this model. No variance inflation factor value was up to 10, indicating that there was no collinearity in the model. The area under the curve was 0.948 (95% CI 0.912, 0.985)

ABT allogeneic blood transfusion, *ANH* acute normovolemic hemodilution, *aOR* adjusted odds ratio, *CI* confidence interval, *Intra*. Intraoperative

*Statistical significance

Figure 2 shows the result of Kaplan–Meier curve analysis with log-rank test to compare the length of hospital stays among the ANH and control group. The length of hospital stay of the ANH group was significantly shorter than that of the control group. Table 5 shows the result of the

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Table 4 Multivariable logistic regression model to compare the odds ratio of the risk of ABT between ANH use and PAD use

	aOR	95% CI	*P* value
ANH	0.14	0.03, 0.64	0.011*
PAD	0.33	0.08, 1.40	0.133
Intra. Blood loss (per 1 mL/kg increase)	1.09	1.04, 1.14	< 0.001*
Duration of surgery (per 1 h increase)	1.91	1.25, 2.91	0.003*

ANH use, PAD use, intraoperative blood loss, and duration of surgery were included in this model. No variance inflation factor value was up to 10, indicating that there was no collinearity in the model. The area under the curve was 0.956 (95% CI 0.923, 0.989)

ABT allogeneic blood transfusion, *ANH* acute normovolemic hemodilution, *aOR* adjusted odds ratio, *CI* confidence interval, *Intra.* intraoperative, *PAD* preoperative autologous blood donation

*Statistical significance

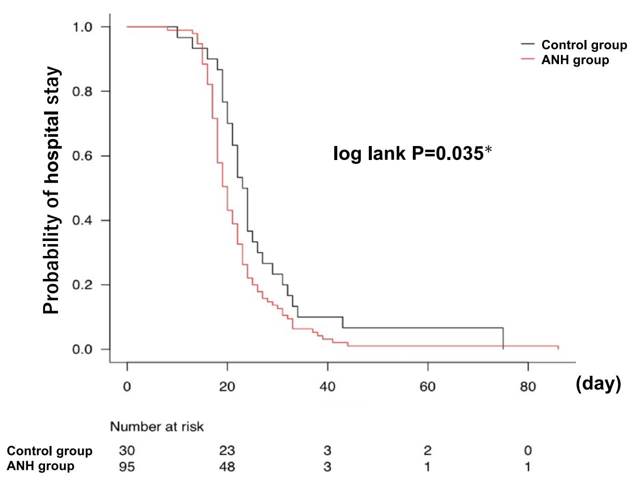

Fig. 2 Kaplan–Meier curve analysis with log-rank test to compare the probability of hospital stay among the patients with and without ABT. *ABT* allogeneic blood transfusion. *Statistical significance

cox proportional hazard analysis to investigate the effect of ANH on length of hospital stay. ANH is not associated with length of hospital stay after adjusting for confounding factors. Lower height and congenital scoliosis are significantly associated with increased risk of prolonged length of hospital stay.

Discussion

The present study showed that the frequency and amount of the perioperative ABT were significantly lower in the ANH group than in the control group in pediatric and adolescent scoliosis surgery. Propensity-score-adjusted multivariable logistic regression analysis showed that ANH can reduce frequency of perioperative ABT. The incidence of infectious

Table 5 Cox proportional hazards analysis to identify the effect of ANH to the length of hospital stay

	aHR	95% CI	*P* value
ANH	1.13	0.71, 1.79	0.614
Age, per 1 y.o. increase	0.90	0.81, 1.00	0.055
Height, per 1 cm increase	1.03	1.00, 1.06	0.027*
Body weight (per 1 kg increase)	1.00	0.97, 1.02	0.774
ASA-PS			
1	Reference		
2	0.68	0.36, 1.29	0.239
3	0.54	0.23, 1.26	0.154
Diagnosis			
Idiopathic	Reference		
Congenital	0.20	0.07, 0.58	0.003*
Neuromuscular	0.56	0.30, 1.05	0.071
Neurofibromatosis	0.39	0.14, 1.09	0.072
Syndromic	0.48	0.20, 1.12	0.088
Surgical procedure			
PLIF	Reference		
Glowing rod procedure	0.77	0.30, 1.98	0.583
Others	0.68	0.29, 1.57	0.363

ANH use, Age, Height, Body weight, ASA-PS, diagnosis, and surgical procedure were included in this model

ANH acute normovolemic hemodilution, *ASA-PS* American Society of Anesthesiologists Physical Status, *PLIF* posterior lumbar interbody fusion, *aHR* adjusted hazard ratio, *CI* confidence interval, *Intra.* Intraoperative

*Statistical significance

complications other than SSI, and the incidence of respiratory failure were lower in the ANH group than in the control group, and the length of hospital stay was shorter in the ANH group than in the control group. However, cox proportional hazard analysis showed that ANH is not associated with length of hospital stay after adjusting for confounding factors.

The main purpose of autologous blood transfusion is to reduce the frequency and amount of ABT and the complications that come with it. There are three types of autologous blood transfusion: ICS, PAD, and ANH. As the only contraindication of ICS is the patient's refusal, ICS is recommended in all cases for which significant blood loss is expected [15]. A meta-analysis reported that ICS can significantly reduce the amount of perioperative ABT in scoliosis surgery [16]. Indeed, ICS is conducted in all scoliosis surgeries at our institution.

The safety of PAD and its efficacy have been reported for pediatric and adolescent scoliosis surgery [17, 18]. In the present study, 43.2% of patients underwent PAD. We compared the efficacy of ANH and PAD at reducing the frequency of perioperative ABT, and this analysis showed that ANH independently reduced the frequency of perioperative

ABT, but PAD did not. Thus, ANH may be more beneficial than PAD for reducing the frequency of perioperative ABT in pediatric and adolescent scoliosis surgery, perhaps because a secondary effect of hemodilution is to reduce the mass of red cells lost per unit volume blood loss. Indeed, although there was no significant difference in the intraoperative blood loss between the two groups, the frequency and amount of perioperative ABT were lower in the ANH group than in the control group.

The present study showed that the incidences of respiratory failure and infectious complications other than SSI were lower in the ANH group than in the control group, and that the length of hospital stay was shorter in the ANH group than in the control group in univariable analyses. As patients in the ANH group had lower ABT frequency, this result may be due the fact ANH reduced the complications that often accompany ABT. Perioperative ABT is reported to increase length of hospital stay and postoperative complications in non-cardiac surgery [19]. However, in the present study, there were significant differences in patient characteristics such as age, height, body weight and diagnosis between the groups, which may have affected the result. Indeed, cox proportional hazard analysis showed that ANH is not associated with length of hospital stay and lower height and congenital scoliosis are significantly associated with increased risk of prolonged length of hospital stay. This result may have reflected that ABT affects length of hospital stay more than ANH. As patients with a small body surface area have a small amount of circulating blood volume, ABT may be required even if the amount of bleeding is small. There were more patients with neuromuscular disease in the control group than in the ANH group. As patients with neuromuscular disease and congenital scoliosis may have poor respiratory condition, they may have been transfused without restriction. A previous study showed that ANH can cause intraoperative fluid infusion increase, which causes postoperative complications [20]. In the present study, there were no significant differences in the total amount of fluid infusion. We carefully controlled the fluid infusion by referring to SVV and CI, which may have enabled ANH without increasing complications.

The present study has several limitations. First, because of the study design, single-center, retrospective study, there may have been selection bias and undetected confounders which can affect the results. Second, the diagnosis was significantly different between the ANH and control groups: the ANH group contained many more idiopathic scoliosis patients who had no medical history and whose general condition was good. Pediatric patients with neuromuscular disease tend to develop postoperative respiratory failure due to upper airway obstruction, chest wall restriction, ineffective airway clearance [21], which may have affected the result of postoperative outcomes. Additionally, we did not assess preoperative respiratory condition. Differences in preoperative respiratory condition due to the differences in diagnosis may have also affected the result of postoperative respiratory failure. Third, as we did not follow the patients' courses after hospital discharge, postoperative complications after hospital discharge and long-term outcomes could not be evaluated. Delayed infectious complications were reported to be observed an average of 27 months after initial surgery [22]. Thus, cohort studies are needed to assess postoperative complications more thoroughly.

In conclusion, the present study demonstrated that ANH use can reduce the frequency and amount of intraoperative and postoperative ABT in pediatric and adolescent scoliosis surgery without increasing postoperative complications. However, as this was a retrospective observational study, larger prospective studies are needed to strengthen this result.

Author contributions SU, HK, and DT collected the data. DT analyzed the data and drafted the manuscript. JS and KH made the critical revision. All authors read and approved the final manuscript for submission.

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Declarations

Conflict of interest None.

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