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*Int J Spine Surg* 2017, 11 (4)

doi: <https://doi.org/10.14444/4027>

<https://www.ijssurgery.com/content/11/4/27>

This information is current as of May 17, 2025.

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# Tranexamic Acid Reduced the Percent of Total Blood Volume Lost During Adolescent Idiopathic Scoliosis Surgery

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## Abstract

### Background

Multilevel posterior spine fusion is associated with significant intraoperative blood loss. Tranexamic acid is an antifibrinolytic agent that reduces intraoperative blood loss. The goal of this study was to compare the percent of total blood volume lost during posterior spinal fusion (PSF) with or without tranexamic acid in patients with adolescent idiopathic scoliosis (AIS).

### Methods

Thirty-six AIS patients underwent PSF in 2011-2014; the last half (n=18) received intraoperative tranexamic acid. We retrieved relevant demographic, hematologic, intraoperative and outcomes information from medical records. The primary outcome was the percent of total blood volume lost, calculated from estimates of intraoperative blood loss (numerator) and estimated total blood volume per patient (denominator, via Nadler's equations). Unadjusted outcomes were compared using standard statistical tests.

### Results

Tranexamic acid and no-tranexamic acid groups were similar (all  $p > 0.05$ ) in mean age (16.1 vs. 15.2 years), sex (89% vs. 83% female), body mass index (22.2 vs. 20.2 kg/m<sup>2</sup>), preoperative hemoglobin (13.9 vs. 13.9 g/dl), mean spinal levels fused (10.5 vs. 9.6), osteotomies (1.6 vs. 0.9) and operative duration (6.1 hours, both). The percent of total blood volume lost (TBVL) was significantly lower in the tranexamic acid-treated vs. no-tranexamic acid group (median 8.23% vs. 14.30%,  $p = 0.032$ ); percent TBVL per level fused was significantly lower with tranexamic acid than without it (1.1% vs. 1.8%,  $p = 0.048$ ). Estimated blood loss (milliliters) was similar across groups.

### Conclusions

Tranexamic acid significantly reduced the percentage of total blood volume lost versus no tranexamic acid in AIS patients who underwent PSF using a standardized blood loss measure.

Level of Evidence: 3. Institutional Review Board status: This medical record chart review (minimal risk) study was approved by the University of Minnesota Institutional Review Board.

OTHER AND SPECIAL CATEGORY

KEYWORDS: TRANEXAMIC ACID, ADOLESCENT IDIOPATHIC SCOLIOSIS, BLOOD LOSS, POSTERIOR SPINAL FUSION

VOLUME 11 ISSUE 4 DOI: 10.14444/4027

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## Introduction

Spinal fusion surgery for adolescent idiopathic scoliosis (AIS) is associated with significant blood loss, and up to 30% of patients receive perioperative blood transfusions.<sup>1,2</sup> Modern techniques aim to reduce intraoperative blood loss and the subsequent need for transfusion due to the inherent risks associated with

allogenic blood transfusions,<sup>3,4</sup> including transfusion reactions and blood-borne pathogen transmission.

Risk factors for perioperative blood transfusion in AIS deformity-correcting surgeries include procedure and patient-related factors, such as long fusions (>9 levels), posterior or combined posterior-anterior approaches, and thoracic hyperkyphosis, all of which

increase operative duration.<sup>5,6</sup> Although surgeon factors are infrequently reported, surgical technique and experience also impact operative duration and blood loss.

Strategies to reduce allogeneic blood transfusion include autologous donation, hemodilution, hypotension, cell salvage/autotransfusion systems, bipolar sealant devices, intraoperative coagulopathy monitoring with thromboelastometry, and antifibrinolytic pharmacotherapy.<sup>3-7</sup>

The most commonly used newer antifibrinolytic is tranexamic acid, which inhibits the conversion of plasminogen to plasmin, thereby preventing fibrin degradation (clot breakdown) by plasmin.<sup>8</sup> Evidence indicates that tranexamic acid reduces intraoperative blood loss compared to placebo during pediatric spinal fusion surgeries<sup>2,9,10</sup> with minimal adverse effects in this population.

Direct comparison of intraoperative blood loss estimates in tranexamic acid versus no- tranexamic acid spine fusion patients is problematic because total blood volume varies by body size and sex.<sup>2</sup> Although body weight or body mass index (BMI) are commonly used as a control for body size in intraoperative blood loss studies,<sup>2,11,12</sup> the proportion of total blood volume lost considers blood loss as it relates to estimated total blood volume per patient.<sup>13</sup>

The goal of this retrospective cohort study was to compare the impact of tranexamic acid versus no tranexamic acid on estimated intraoperative blood loss in AIS patients who underwent posterior spinal fusion using the percent of total blood volume lost to account for variable body mass indices.

## Materials and Methods

This is a retrospective cohort study of all patients who underwent multilevel posterior spinal fusion (PSF) for AIS at one academic center by one orthopaedic spine surgeon between October 2011 and August 2014. The first 18 surgeries were performed without tranexamic acid; the following 18 used intravenous tranexamic acid when that became the standard of care at our institution.

All study information was obtained from medical record review. We included patients who were age 10 to 24 years with a primary diagnosis of adolescent idiopathic scoliosis. Patients with osteogenesis imperfecta, neuromuscular scoliosis or infantile/juvenile scoliosis and those who underwent revision surgery were excluded. We retrieved age, sex, preoperative hemoglobin, height, weight and BMI from medical records. Intraoperative data included the number of spinal levels fused, the number of Smith-Petersen osteotomies, the duration of surgery (hours), estimated blood loss (EBL), and units of allogenic blood products delivered.

The primary outcome was the percent of total blood volume lost (TBVL) per patient, with or without tranexamic acid, calculated from estimates of intraoperative blood loss (numerator) and the estimated total blood volume per patient (denominator). For context, we also report the percent of estimated blood loss per level fused. Estimated blood loss in milliliters was determined from automated red blood cell salvage estimates (*AutoLog® Cell Saver* Medtronic, Minneapolis, MN), plus the weight of the surgical sponges minus the total volume of irrigation used. Estimated preoperative total blood volume was calculated using Nadler's equations, which estimate total blood volume in adults based on sex, height and weight<sup>14</sup>(Table 1).

Tranexamic acid was administered using a bolus dose of 10mg/kg with the induction of anesthesia, followed by a maintenance intraoperative infusion of 1mg/kg/hour, which was discontinued at the conclusion of surgery. No postoperative tranexamic acid was used. All other intraoperative hemostatic measures were identical between the two groups.

Anesthetic and surgical techniques were similar for all patients. Patients were positioned prone on a Jackson four-poster table. Intravenous anesthesia and vasoactive medications were used to maintain a mean

**Table 1. Nadler's<sup>14</sup> Equations to Estimate Total Blood Volume in Adults.**

Sex	Estimated total blood volume (L)
Female	$= (0.3561 * Ht[m]^3) + (0.03308 * Wt[kg]) + 0.1833$
Male	$= (0.3669 * Ht[m]^3) + (0.03219 * Wt[kg]) + 0.6041$

Ht: height in meters. Ht[m]<sup>3</sup>: (height in meters)<sup>3</sup>. Wt: weight in kilograms

arterial pressure of 70 mm mercury (Hg) during exposure and screw placement, and 80 mm Hg during deformity correction.

Intraoperative transfusion was performed once estimated blood loss reached 10% of estimated total blood volume for any patient. Transfusions from cell salvage were preferentially given. Any allogenic blood transfusions were recorded as the number of units delivered.

This medical record chart review (minimal risk) study was approved by the University of Minnesota Institutional Review Board.

### Statistical Methods

Continuous variables were compared using two-tailed t tests if normally-distributed, or the Wilcoxon Mann-Whitney test if not. Post-hoc calculation of the minimum sample size needed to detect a difference in estimated blood loss as the proportion of total blood volume between tranexamic acid and no-tranexamic acid groups with 80% power and a Type 1 error probability of 0.05 was 46 per group. Since this study had 18 patients per group, the study power was 40%.

## Results

From October 2011 to August 2014, 36 consecutive patients underwent PSF for AIS by a single spine surgeon at our academic institution. The first half (n=18) of patients did not receive tranexamic acid, while the following 18 received intraoperative tranexamic acid.

Overall, the mean age was 15.6 ( $\pm$ 3.2) years and 86.1% (31/36) were female (Table 2). The groups were similar on age, sex, BMI, preoperative hemoglobin and estimated total blood volume (TBV) at baseline (Table 2). The groups were similar on the operative factors of number of levels fused, number of Smith-Petersen osteotomies, and the duration of surgery (Table 3).

The percent of total blood volume (TBV) lost in the tranexamic acid-treated patients (median 8.23%, Table 3) was significantly lower than the percent of

TBV lost in the no-tranexamic acid group (median 14.30%,  $p = 0.032$ ). Similarly, the percent of total blood volume lost per level fused was significantly lower in the tranexamic acid group than no-tranexamic acid patients (Table 3,  $p=0.048$ ). However, estimated blood loss in tranexamic acid (mean 474 ml, median 285 ml) versus the no-tranexamic acid group (mean 583 ml, median 500ml) was not signifi-

**Table 2. Characteristics and Baseline Hematologic Status of Patients who Underwent Posterior Spine Fusion for Adolescent Idiopathic Scoliosis.**

Patients	Tranexamic acid N=18 Mean (sd)	No tranexamic acid N=18 Mean (sd)	P value
Females n (%)	16 (88.9)	15 (83.3)	0.63
Age (yrs.)	16.1 (3.1)	15.2 (3.4)	0.44
Body mass index (kg/m <sup>2</sup> )	22.2 (5.2)	20.2 (3.3)	0.19
Preoperative hemoglobin (g/dL)	13.9 (1.3)	13.9 (1.1)	1.00
Estimated total blood volume (L) <sup>14</sup>	3.80 (0.89)	3.38 (0.48)	0.15

N: number, Yrs: years, kg/m<sup>2</sup>: kilograms per meter squared, g/dL: grams per deciliter, L: Liter.

**Table 3. Operative Factors and Blood-related Outcomes of Patients who Underwent Posterior Spine Fusion for Adolescent Idiopathic Scoliosis.**

Variable	Tranexamic acid n=18		No tranexamic acid n=18		P value
	Mean(sd)	Median [range]	Mean(sd)	Median [range]	
Number of levels fused	10.5 (2.2)	11.0	9.6(2.0)	10.0	0.21
Number of osteotomies	1.6 (2.5)	[0-8]	0.9 (1.6)	[0-5]	0.34
Duration of operation (hours)	6.1(1.1)	6.0	6.1(1.2)	6.3	1.00
Estimated blood loss (ml)	474 (382)	285	583 (316)	500	0.12
Est. blood loss/level fused (ml)	44 (31)	33	61(33)	46	0.06
Percent total blood volume lost	12.1(8.8)	8.23	17.3 (8.8)	14.30	<b>0.03</b>
Percent TBV lost/level fused	1.1(0.7)	1.0	1.8 (1.0)	1.0	<b>*0.05</b>

TBV: total blood volume, \* $p=0.048$ , Bold =  $p<0.05$ , Est.: estimated, ml: milliliters.

cantly different between the treatment groups ( $p=0.12$ ).

The percentage of TBV lost per level fused ranged from 1% to 4% across all patients, and was lower in the tranexamic acid group (mean 1.1% per level, Table 3). Eight patients (22.2%) received allogenic blood products, 4 in each group.

There were no adverse effects related to tranexamic acid use.

## Discussion

Patients who received intraoperative tranexamic acid lost approximately 6% less of estimated total blood volume during PSF surgery for AIS than patients who did not receive tranexamic acid. Despite our relatively small sample size, the percent of total blood volume lost and the percent of total blood volume lost per level fused were significantly lower among patients with AIS who received intraoperative tranexamic acid than among those who did not.

Perioperative transfusion rates are dependent upon the transfusion trigger selection, such as direct measures of blood volume lost, the proportion of estimated total blood volume lost, or hematocrit level. In this study, the treating surgeon used an intraoperative transfusion trigger of 10% of estimated blood volume lost. While this threshold (trigger) varies by surgeon, institution, and patient condition, the 10% trigger for transfusion of any blood product(s) was a consistent threshold used in all patients in this study.

Patients with adolescent idiopathic scoliosis who were treated with tranexamic acid lost an average of 1.1% of estimated total blood volume per level fused. Given the inherent limitations of measuring surgical blood loss, we suggest discretion to avoid overinterpreting our results based on this small patient sample. We did not initiate transfusions until patients lost at least 10% of their estimated total blood volume; only 1 in 5 patients received intraoperative blood product transfusions, and there was no difference in transfusion rate between the two groups. Future research is needed to determine the utility of tranexamic acid in AIS patients who undergo PSF of

9 spinal levels or fewer (typically less than 10% of total blood volume lost) to resolve remaining research questions regarding when, and in whom, tranexamic acid should be used in AIS surgeries. Although lacking in the observational literature to date,<sup>13</sup> surgeon variability in operative duration and blood loss should also be accounted for in multi-surgeon AIS studies.

We did not observe any adverse events from the use of tranexamic acid in otherwise-healthy patients with adolescent idiopathic scoliosis. However, uncommon adverse effects from the use of antifibrinolytic agents in broader samples of spine fusion patients include deep venous thrombosis, pulmonary embolism, myocardial infarction, hypersensitivity reaction, renal insufficiency, and rarely, seizures.<sup>10,15,16</sup>

The main strengths of this study are the use of a uniform reporting method to estimate intraoperative blood loss that accounts for varied body mass indices, and our exclusive focus on AIS patients, which differs from tranexamic acid-spine fusion studies that included mixed samples of primary and secondary scoliosis patients.<sup>11,17</sup> Children with secondary scoliosis may have greater perioperative blood loss<sup>11,18</sup> and lower BMI<sup>13</sup> than children with AIS,<sup>17</sup> so it is clinically important to report these patient groups separately.

We acknowledge several limitations of this retrospective cohort study. Since our study was not randomized, there may be differences in unmeasured variables between groups that were not accounted for. Although we found significant differences in the percent of total blood volume lost and the percent per level fused, the limitation of a small sample size<sup>10</sup> may have diminished our ability to detect differences in other outcomes, even if they existed. A larger sample would be necessary to conduct multivariate analyses.<sup>13</sup> Resolving the ongoing (dichotomous) question of whether tranexamic acid also reduces the need for blood product transfusion requires substantially more patients<sup>2</sup> and is beyond the scope of this single-site study. Also, Nadler's equations were developed to estimate blood volume in normal adults, not pediatric patients. Nonetheless, 63.9% of the patients were age 15 or over, so the use of an adult

equation to estimate total blood volume is plausible. Finally, the difference in measurement error between this method, due to estimating intraoperative blood loss and total blood volume, versus other methods, is unknown.

Administration of intraoperative tranexamic acid reduced the percentage of total blood volume lost versus no tranexamic acid in patients who underwent PSF for AIS using a standardized blood loss measure. Larger samples are necessary to determine if tranexamic acid can significantly reduce the use of perioperative blood transfusions for AIS patients who undergo PSF, and to compare the utility of this estimating approach to other methods.

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## Conflicts of Interest

Dr. Ledonio is a consultant to Greatbatch, Inc.; he has received research grants through the Orthopaedic Research and Education Foundation, Department of Defense, Scoliosis Research Society, AOSpine, Medtronic and the University of Minnesota. Dr. Cohn has received research funding and honoraria from Fenwal (a Fresenius-Kabi Company), research funding from Octapharma, and research fund-

ing and consulting fees from Ortho Diagnostics. No conflicts of interest were declared by the remaining authors.

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Published 4 August 2017.

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