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Cost-Benefit Analysis of Using A Single Dose of Tranexamic Acid in Degenerative Lumbar Scoliosis Patients Undergoing Long-Segment Spinal Fusion Surgery: A Retrospective Study

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Statistical Analysis C
Data Interpretation D
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Background: Degenerative lumbar scoliosis (DLS) patients undergoing posterior long-segment spinal fusion surgery often require perioperative blood transfusions, and previous studies have reported that increased complications and additional costs accompany these transfusions. One method for decreasing transfusions is the administration of tranexamic acid (TXA). We sought to evaluate the costs and benefits of preoperative administration of 1 g of intravenous TXA, without maintenance, in DLS patients undergoing long-segment spinal fusion surgery.





Material/Methods: Patients who received TXA (TXA group) were compared with patients who did not receive TXA (NTXA group) with regard to blood loss, units of packed red blood cells (PRBC) transfused, hemostasis costs, and perioperative complications. The benefits and costs were estimated through analysis of the spending on NTXA and TXA patients, and were compared. The difference between the cost per patient in the 2 groups was designated as the net cost-benefit. Then, both groups were substratified into non-osteotomy and osteotomy subgroups for further analysis.

Results: Of the 173 patients who met the inclusion criteria, 54 TXA patients had significantly reduced perioperative blood loss and total hemostasis costs compared with NTXA patients (n=119). In the group without osteotomy (n=72), TXA (n=13) reduced perioperative blood loss but did not significantly decrease PRBC units and hemostasis costs. However, in patients undergoing osteotomy (n=101), a remarkable net cost savings of ¥648.77 per patient was shown in the TXA group (n=41) ($P<0.001$). This was because patients undergoing osteotomy in the TXA group received fewer PRBC units (3.7 vs 5.7, $P=0.001$).

Conclusions: A single dose of TXA significantly decreased perioperative blood loss and total hemostasis costs for DLS patients undergoing osteotomy. Furthermore, TXA led to no additional net costs in patients without osteotomy.

Keywords: **Blood Loss, Surgical • Cost-Benefit Analysis • Scoliosis • Tranexamic Acid**

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Background

Degenerative lumbar scoliosis (DLS) is a degenerative spinal disease in which lumbar scoliosis develops in an adult with no previous scoliosis. The prevalence of DLS varies enormously among studies and ranges from 1.4 to 68% [1,2], which is about 13.3% of the Chinese Han population aged more than 40 years [3]. With the increased number of aged people and technical advances, more and more patients are requesting surgical treatment. Decompression for neurological compromise, long-segment fusion, and deformity correction are options for patients with severe sagittal and/or coronal imbalance [4]. Due to the complicated and extensive nature of the deformity, DLS patients undergoing posterior spinal fusion can experience massive intraoperative blood loss and often require perioperative allogeneic or autogenous blood transfusions, especially for patients undergoing osteotomy [5]. Excessive perioperative blood loss may lead to anemia, organ damage, coagulopathy, and the need for blood transfusion. Blood transfusion, in turn, increases the risk of transfusion-transmissible infections, immunological transfusion reactions, and mis-transfusion, as well as long-term mortality rates [6,7]. In addition, the use of allogeneic blood products results in significant cost increases.

Many preoperative and intraoperative strategies have been applied to minimize perioperative blood loss, including intraoperative blood salvage, coagulation factor substitution, antifibrinolytic drugs, hypotensive anesthesia, and measures to avoid hypothermia [8,9]. Aprotinin, tranexamic acid (TXA), and epsilon-aminocaproic acid are antifibrinolytics currently offered as prophylactic agents to reduce surgery-associated blood loss. A previous network meta-analysis found that high-dose TXA administration could be used as an optimal treatment to reduce blood loss and the need for transfusion in spinal surgeries [10]. TXA competitively blocks lysine-binding sites of plasminogen and reduces perioperative blood loss and the need for transfusion in major surgeries. Multiple studies have reported that TXA is widely used due to its proven benefits in reducing blood loss and blood transfusion requirements [11-14]. Furthermore, TXA has helped to decrease costs for total joint arthroplasty [15-17]. Evangelista et al [15] reported that perioperative TXA administration significantly reduced blood transfusion requirements and costs in total hip arthroplasty and total knee arthroplasty participants. McGoldrick et al [16] showed that intravenous TXA led to lower transfusion rates, shorter hospital stay, and an estimated financial savings of €114 586 per patient. Cost-benefit analysis can help decision-makers compare the costs and benefits of various options to manage population health, formulate reasonable, cost-effective prescriptions for treatment, and provide a decision-making basis for the clinical formulation of scientific treatment plans [18]. However, the optimal dose of TXA used in spinal surgery remains unclear, and, until

now, there has been no study evaluating the benefit of TXA administration in DLS surgery.

In the present study, we performed a cost-benefit analysis of the use of a single dose of TXA, with no maintenance dose, for DLS patients undergoing correction surgery. We hypothesized that using a single dose of TXA would be cost-effective for DLS patients undergoing correction surgery, especially for those who are undergoing osteotomy.

Material and Methods

Study Design and Patient Population

After obtaining approval from the Ethics Committee (IRB00006761-M2018076) in our institution and registering the study in the Chinese Clinical Trial Registry (registration ID: ChiCTR2000030948. <http://www.chictr.org.cn/index.aspx>), we retrospectively analyzed all DLS patients who underwent posterior long-segment spinal fusion (≥ 5 vertebrae) in our hospital from April 2014 to June 2018. Inclusion criteria were the following: 1) age 40 years or older at the time of surgery; 2) preoperative coronal Cobb angle $\geq 20^\circ$; 3) de novo lumbar scoliosis; 4) fusion of at least 5 vertebrae. Patients with chronic renal failure, cirrhosis of the liver, chronic heart failure, allergy to TXA, history of thromboembolic disease, bleeding disorders, hypercoagulation status, disseminated intravascular coagulation, those undergoing revision surgery, those receiving antiplatelet and anticoagulant drugs, and those with dural tear during the operation were excluded. From April 2014 to June 2018, 461 DLS patients were treated in our hospital. Among them, 215 patients underwent long-segment (≥ 5 vertebrae) surgery. After meeting the inclusion and exclusion criteria, 173 patients were enrolled. Among these, 54 received a single dose of TXA (1g mixed in 100 mL saline) intravenously over 15 min before incising the skin; these were categorized as the TXA group. Patients who did not use TXA during the same period were placed in the NTXA group (not receiving TXA).

Anesthesia and Intraoperative Monitoring

Intravenous drugs, including midazolam, sufentanil, propofol, and atracurium, were used for general anesthesia induction. Remifentanil, propofol, and atracurium were used for anesthesia maintenance. Consecutive standard monitoring and arterial blood pressure monitoring were performed during the surgery. The mean arterial pressure (MAP) was maintained at 70 mmHg from the dissection phase until the spine was exposed. The MAP was then controlled at about 20% below the preoperative baseline pressure during the decompression, osteotomy, fusion, and instrumentation procedures, following which the MAP was returned to the baseline. MAP was

raised higher if there were any changes in spinal cord evoked potentials. Indications for blood transfusion during the operation included a significant drop in systolic blood pressure (<50 mmHg), any perceived rapid loss of blood, decreased urine output, and alterations in the spinal cord monitoring responses decided by the surgeon and anesthesiologist. Packed red blood cells (PRBC) were administered when the postoperative hemoglobin (Hb) was less than 80 g/L, or 80 to 100 g/L, combined with symptoms such as tachycardia, fatigue, lethargy, pallor, and poor appetite.

Data Collection

Demographic data collected included age, sex, body mass index (BMI), comorbidities, and coagulation status. Preoperative radiographic evaluation included the Cobb angle, the sagittal vertical axis (SVA), the coronal vertical axis from the central sacrum vertical line (CSVL), and overall lumbar lordosis. Operative details assessed included the adult spinal deformity surgery (ASD-S) score [19], the number of fused and fixation levels, the number of interbody fusion levels, and osteotomy grades as classified by Schwab et al [20], estimated intraoperative blood loss (EBL), postoperative drainage volume, intra-/postoperative packed red blood cells (PRBC) units, intraoperative autogenous transfusion volume by intraoperative cell salvage (ICS) system, and surgical duration. No preoperative blood donation was obtained from any of the patients. Cell salvage autologous blood recovery system was used in all cases. Intraoperative EBL was calculated by adding the blood volume collected by both suction and cell-saver systems and weighing the surgical sponges. The postoperative drainages were recorded daily at 6:00 AM from the drainage bag until the drain tube was removed when the volume was less than 50 mL/day or the drainages were clear and colorless. The estimated blood volume (EBV) was calculated by multiplying 70 mL/kg by the patient's weight, as previously reported [21]. The sum of the EBL and postoperative drainage was calculated as the total blood loss. The transfusion cost, perioperative hemoglobin, and hematocrit levels were assessed, as were possible thromboembolic complications related to TXA usage that required treatment, including stroke, symptomatic deep vein thrombosis (DVT), symptomatic pulmonary embolism, and myocardial infarction.

The present study's primary outcome was the total cost of TXA and blood transfusions. The secondary outcomes were mean intraoperative blood loss, postoperative drainage, total blood loss, numbers per patient of intra-/post-operative PRBC units given, in-hospital thrombotic events, and length of hospital stay. To examine the influence of osteotomy in terms of cost-benefit, both groups were substratified into non-osteotomy and osteotomy groups for subanalysis. In calculating costs, we included the costs of drugs, the saline in which the

drugs were dissolved, the consumables, and staff- and transfusion-related costs. Each vial of TXA (500 mg/vial) costs ¥4.8 (TXA cost per patient in the TXA group was ¥9.6), and the direct acquisition cost of PRBC transfusion is reported as ¥220 per unit (PRBC unit acquisition-only cost). The total transfusion cost per time includes PRBC cost and materials and staff costs, which is ¥25 per time. PRBC unit total cost refers to the total transfusion cost per patient. The difference between the cost for each patient given TXA vs each patient not using TXA was calculated as the net cost-benefit.

Statistical Methods

The data were analyzed by SPSS software version 22 (SPSS, Inc., Chicago, IL). The descriptive results are expressed as mean and standard deviation (SD) for continuous variables with an approximately normal distribution or median and interquartile range. Categorical values are presented as the frequency and the percentage. A simple comparison of data between groups was performed by *t* test or Mann-Whitney U-test. Categorical variables were compared using the χ^2 test or Fisher's exact test. Additionally, to calculate the net cost-benefit of TXA administration, we subtracted the costs incurred by each group receiving TXA from the costs of transfusions in the group not receiving TXA. A *P* value <0.05 was considered statistically significant.

Results

There were 173 patients (148 women and 25 men), with a mean age of 62.87 ± 6.52 years, enrolled in either the TXA ($N=54$) or NTXA ($n=119$) group. **Table 1** shows the preoperative, intraoperative, and postoperative variables for the TXA and NTXA groups. No significant difference was seen in demographic data, preoperative radiographic parameters, or preoperative or postoperative laboratory parameters. Similarly, the mean surgical invasiveness score was approximately 23 (22.92 ± 4.88 vs 23.80 ± 5.34 , $P=0.287$) in both groups and there was no significant difference between them. There was, however, a significant difference in how many patients underwent osteotomy: 75.93% of patients in the TXA group and 50.42% of patients in the NTXA group underwent osteotomy ($P=0.002$). The patients in the TXA group had significantly lower intraoperative blood loss ($P<0.001$), lower postoperative drainage ($P=0.003$), and a lower volume of total blood loss ($P<0.001$) than the patients in the NTXA group. No statistically significant difference was seen in the mean number of PRBC units transfused intraoperatively between the 2 groups (2.19 ± 1.88 units vs 2.80 ± 2.29 units, $P=0.087$). However, patients treated with TXA required fewer postoperative PRBC units (1.32 ± 1.62 vs 2.11 ± 2.47 , $P=0.032$). Both groups had similar rates of postoperative thromboembolic events and similar hospitalization duration.

Table 1. Data for patients with or without intraoperative TXA.

	NTXA (n=119)	TXA (n=54)	P value
Demographic factors			
Sex, F/M (n)	98/21	50/4	0.076
Age (years)	63.50±6.51	63.32±5.48	0.850
BMI (Kg/m ²)	25.81±4.02	25.61±3.60	0.758
Hypertension (n,%)	52 (43.70%)	22 (40.74%)	0.716
Diabetes mellitus (n,%)	15 (12.61%)	8 (14.81%)	0.692
EBV (mL)	4557.35±767.24	4498.98±643.28	0.627
ASA physical status, I: II: III (n)	13:100:6	9:42:3	0.572
Pre-operative radiographic values			
Cobb angle (°)	29.08±10.49	31.30±10.88	0.239
CSVL (mm)	20.29±11.84	22.59±13.83	0.293
SVA (mm)	57.85±42.08	54.75±35.42	0.638
LL (°)	25.45±19.26	22.88±21.38	0.434
Laboratory parameters			
Preoperative Hb (g/L)	134.01±12.93	133.00±13.45	0.640
Preoperative hematocrit (%)	40.56±4.2	40.35±3.8	0.752
Preoperative PLT (×10 ⁹ /L)	223.26±61.08	232.30±53.54	0.352
Preoperative APTT (S)	32.25±3.04	31.76±2.92	0.320
Preoperative INR	0.99±0.06	0.98±0.06	0.641
Postoperative D1 Hb (g/L)	103.62±16.92	102.09±14.49	0.569
Postoperative D1 hematocrit (%)	30.97±4.99	30.72±4.24	0.758
Hb change (g/L)	31.58±15.60	31.28±12.46	0.740
Hematocrit change (%)	10.00±5.1	10±3.6	0.583
Operative factors			
ASD-S score	22.92±4.88	23.80±5.34	0.287
Duration of surgery (min)	261.80±63.16	271.33±69.47	0.374
Fixation and fused levels (n)	5.77±1.51	5.96±1.48	0.421
Decompression levels (n)	3.05±1.21	3.13±1.12	0.684
Osteotomy (n,%)	60 (50.42%)	41 (75.93%)	0.002**
Osteotomy grades, 0: 2: 3 (n,%)	59:47:13	13:34:7	0.006**
No. of intervertebral fusion (n)	1.27±0.98	1.41±0.90	0.383
Blood loss and transfusion			
IBL (mL)	1381.54±854.75	963.43±548.63	<0.001**
Postoperative drainage (mL)	1399.30±501.59	1164.65±380.09	0.003**
Total blood loss (mL)	2780.84±1119.68	2128.07±816.29	<0.001**

Table 1 continued. Data for patients with or without intraoperative TXA.

	NTXA (n=119)	TXA (n=54)	P value
Cell saver (mL)	460.51±284.92	321.14±182.86	<0.001**
Intraoperative PRBC	2.80±2.29	2.19±1.88	0.087
Intraoperative transfusion rate (n,%)	88 (73.95%)	36 (66.67%)	0.325
Postoperative PRBC	2.11±2.47	1.32±1.62	0.032*
Postoperative transfusion rate (n,%)	69 (57.98%)	25 (46.30%)	0.153
Length of hospital stay (days)	11.63±5.63	10.46±3.66	0.165
DVT/PE	1 (0.84%)	0 (0%)	>0.999

Values are presented as the mean ± SD or number (%). TXA – the group that received tranexamic acid; NTXA – the historically recruited no-TXA group; BMI – body mass index; EBV – estimated blood volume; ASA – American Society of Anesthesiologists; CSVL – coronal vertical axis from the central sacrum vertical line; SVA – sagittal vertical axis; LL – lumbar lordosis; Hb – hemoglobin; PLT – platelets; APTT – activated partial thromboplastin time; INR – international normalized ratio; ASD-S – adult spinal deformity surgery; IBL – intraoperative blood loss; PRBC – packed red blood cells; DVT – deep vein thrombosis; PE – pulmonary embolism.

* $P<0.05$, ** $P<0.01$.

Table 2. Pricing of TXA and transfused PRBC units in patients with or without intraoperative TXA.

	NTXA (n=119)	TXA (n=54)	P value
Transfusion-treated patients	111 (93.28%)	47 (87.04%)	0.289
PRBC units given during hospital stay	4.91±3.39	3.50±2.34	0.002**
TXA cost per patient	¥0	¥9.60	–
PRBC unit acquisition-only cost	¥1079.66±746.88	¥770.00±514.17	0.002**
PRBC unit net acquisition-only cost+TXA cost	¥1079.66±746.88	¥779.60±514.17	0.003**
PRBC unit total cost	¥1211.81±937.87	¥786.20±525.22	<0.001**
PRBC unit net total cost+TXA cost	¥1211.81±937.87	¥795.80±525.22	<0.001**

Values are presented as the mean±SD, total cost (including acquisition cost+overhead costs) of 1 unit of PRBCs, including materials and labor. TXA – the group that received tranexamic acid; NTXA – the historically recruited no-TXA group; PRBC – packed red blood cells. * $P<0.05$; ** $P<0.01$.

Throughout the hospital stay, 93.3% of patients in the NTXA group and 87.04% in the TXA group needed at least 1 transfusion. Regarding total PRBC units used during the patients' hospital stay, the NTXA group received an average of 4.91±3.39 units, and the TXA group received 3.50±2.34 units ($P=0.002$). Significantly lower PRBC acquisition costs, PRBC acquisition+TXA cost, PRBC total cost, and PRBC total cost+TXA cost were seen in the TXA group ($P<0.001$) (Table 2).

In the subanalysis, the without-osteotomy cohort consisted of 59 patients who had not received TXA and 13 patients who had received TXA. No significant differences were seen in demographic factors, preoperative radiographic values, preoperative and postoperative laboratory values, or operative factors between the 2 groups (Table 3). The patients who received TXA

had significantly lower intraoperative blood loss ($P=0.034$), postoperative drainage ($P=0.014$), and total blood loss ($P=0.005$). The total number of PRBC units used during the hospital stay, postoperative thromboembolic events, and hospitalization duration showed no statistically significant difference between the TXA and NTXA groups. There were also no significant differences in postoperative thromboembolic events and hospitalization duration. Of the patients who did not receive TXA, 89.9% required at least 1 blood transfusion during their hospital stay, compared with 76.9% of the TXA patients ($P=0.418$). Considering the "acquisition-only cost," this equated to an average PRBC cost of ¥ 898.64 for the NTXA group and ¥ 609.23 for the TXA group. However, when adding the cost of TXA to the acquisition-only PRBC cost, there was no significant difference in the 2 groups' net costs ($P=0.186$) (Table 4).

Table 3. Data from subanalyses of patients without osteotomy.

	NTXA (n= 59)	TXA (n=13)	P value
Demographic factors			
Sex, F/M (n)	44/15	11/2	0.681
Age (years)	63.88±6.31	65.08±6.41	0.539
BMI (Kg/m ²)	25.87±4.29	26.02±3.63	0.905
Hypertension (n, %)	23 (39.0%)	5 (38.5%)	0.972
Diabetes mellitus (n, %)	11 (18.6%)	4 (30.8%)	0.550
EBV (mL)	4687.03±876.04	4666.15±593.39	0.935
ASA physical status, I: II: III (n)	10:46:3	2:10:1	0.934
Pre-operative radiographic values			
Cobb angle (°)	25.13±8.03	24.45±4.52	0.679
CSVL (mm)	20.71±10.21	25.43±13.54	0.160
SVA (mm)	56.62±42.37	48.17±37.51	0.509
LL angle (°)	31.67±15.46	31.78±19.70	0.983
Laboratory parameters			
Pre-operative Hb (g/L)	136.83±13.80	133.85±11.58	0.473
Pre-operative hematocrit (%)	41.09±3.8	41.00±3.1	0.939
Pre-operative PLT (×10 ⁹ /L)	223.89±63.59	236.15±53.11	0.246
Pre-operative APTT (S)	32.34±2.50	31.78±2.68	0.478
Pre-operative INR	1.00±0.06	0.99±0.07	0.675
Post-operative D1 Hb (g/L)	104.50±15.60	105.08±15.71	0.905
Post-operative D1 hematocrit (%)	31.18±4.5	31.92±4.5	0.590
Hb change (g/L)	31.98±15.03	28.77±12.56	0.479
Hematocrit change (%)	10.00±4.4	9±3.5	0.546
Operative factors			
ASD-S score	20.75±3.81	20.31±3.09	0.700
Duration of surgery (min)	239.32±49.44	220.00±39.30	0.192
Fixation and fused levels (n)	4.93±0.98	4.77±0.83	0.580
Decompression levels (n)	3.27±1.08	3.08±0.86	0.546
No. of intervertebral fusion (n)	1.35±0.78	1.46±0.66	0.620
Blood loss and transfusion			
IBL (mL)	1125.15±641.40	719.15±444.45	0.034*
Postoperative drainage (mL)	1385.54±465.34	1035.23±404.14	0.014*
Total blood loss (mL)	2510.69±867.31	1754.38±727.72	0.005**
Cell saver (mL)	375.05±213.80	239.72±148.15	0.034*
Intraoperative PRBC	1.97±1.95	1.69±1.60	0.638

Table 3 continued. Data from subanalyses of patients without osteotomy.

	NTXA (n= 59)	TXA (n=13)	P value
Intraoperative transfusion rate (n, %)	36 (61.0%)	8 (61.5%)	0.972
Postoperative PRBC	2.12±2.59	1.08±1.55	0.168
Postoperative transfusion rate (n, %)	34 (57.6%)	5 (38.5%)	0.209
Length of hospital stay (d)	11.00±4.71	9.31±2.93	0.219
DVT/PE	0	0	–

Values are presented as the mean±SD or number (%). TXA – the group that received tranexamic acid; NTXA – the historically recruited no-TXA group; BMI – body mass index; EBV – estimated blood volume; ASA – American Society of Anesthesiologists; CSVL – coronal vertical axis from the central sacrum vertical line; SVA – sagittal vertical axis; LL – lumbar lordosis; Hb – hemoglobin; PLT – platelets; APTT – activated partial thromboplastin time; INR – international normalized ratio; ASD-S – adult spinal deformity surgery; IBL – intraoperative blood loss; PRBC – packed red blood cells; DVT – deep vein thrombosis; PE – pulmonary embolism. * $P<0.05$, ** $P<0.01$.

Table 4. Data from subanalyses of TXA pricing and units of transfused PRBCs for non-osteotomy and osteotomy constructs with or without intraoperative TXA.

	Non-osteotomy (n=72)			Osteotomy (n=101)		
	NTXA (n=59)	TXA (n=13)	P value	NTXA (n=60)	TXA (n=41)	P value
Transfusion-treated patients	53(89.9%)	10(76.9%)	0.418	58(96.7%)	37(90.2%)	0.362
PRBC units given during hospital stay	4.08± 3.27	2.77± 2.39	0.175	5.72± 3.35	3.73± 2.30	0.001**
TXA cost per patient	¥0	¥9.60	–	¥0	¥9.60	–
PRBC unit acquisition-only cost	¥898.64± 719.63	¥609.23± 524.89	0.175	¥1257.67± 735.92	¥820.98± 506.54	0.001**
PRBC unit net acquisition-only cost+TXA cost	¥898.64± 719.63	¥618.83± 524.89	0.190	¥1257.67± 735.92	¥830.58± 506.54	0.001**
PRBC unit total cost	¥922.37± 738.70	¥622.69± 539.55	0.172	¥1496.42± 1027.92	¥838.05± 516.46	<0.001**
PRBC unit net total cost+TXA cost	¥922.37± 738.70	¥632.29± 539.55	0.186	¥1496.42± 1027.92	¥847.65± 516.46	<0.001**

TXA, the group that received tranexamic acid; NTXA – the historically recruited no-TXA group; PRBC – packed red blood cells; ** $P<0.01$.

The osteotomy cohort consisted of 41 patients without TXA and 60 patients receiving TXA. There were no significant differences between demographic factors, preoperative radiographic values, preoperative and postoperative laboratory values, or operative factors between the 2 groups (Table 5). The group that received TXA had significantly lower intraoperative blood loss ($P=0.001$), postoperative drainage ($P=0.035$), and total blood loss ($P=0.001$). The TXA group had a lower intraoperative transfusion rate (68.3% vs 86.7%, $P=0.025$) and received significantly fewer units of PRBC during the operation than the NTXA group ($P=0.005$). Of the patients who did not receive TXA, 96.7% required at least 1 blood transfusion, compared with 90.2% of the TXA patients ($P=0.362$). The NTXA

group received an average of 5.72 units during their hospital stay, compared with 3.73 units in the TXA group ($P=0.001$), which equated to a PRBC acquisition-only cost of ¥1257.67 for the NTXA group and ¥820.98 for the TXA group ($P<0.001$). When adding the acquisition costs of TXA and PRBC in the TXA group, the net cost savings was ¥648.77 per patient with TXA ($P<0.001$) (Table 4). Overall, we found that the net cost-benefit of a single dose of TXA in the osteotomy group was greater than that in the non-osteotomy group, with a total cost difference of ¥358.68.

Table 5. Data from subanalyses of patients undergoing osteotomy surgery.

	NTXA (n= 60)	TXA (n=41)	P value
Demographic factors			
Sex, F/M (n)	54/6	39/2	0.575
Age (year)	63.12±6.73	62.76±5.11	0.761
BMI (Kg/m ²)	25.74±3.76	25.48±3.63	0.725
Hypertension (n,%)	29 (48.3%)	17 (41.5%)	0.496
Diabetes mellitus (n,%)	4 (6.7%)	4 (9.8%)	0.850
EBV (mL)	4429.83±624.12	4445.98±656.28	0.901
ASA physical status, I: II: III (n)	3:54:3	7:32:2	0.139
Pre-operative radiographic values			
Cobb angle (°)	32.96±11.21	33.48±11.42	0.822
CSVL (mm)	19.87±13.33	21.68±13.99	0.512
SVA (mm)	59.06±42.11	56.83±34.95	0.780
LL (°)	19.32±20.74	20.06±21.34	0.863
Laboratory parameters			
Pre-operative Hb (g/L)	131.33±11.53	132.73±14.11	0.586
Pre-operative hematocrit (%)	40.07±4.5	40.15±4.0	0.927
Pre-operative PLT (×10 ⁹ /L)	222.65±59.13	227.90±53.57	0.650
Pre-operative APTT (S)	32.17±3.50	31.75±3.02	0.538
Pre-operative INR	0.98±0.06	0.99±0.06	0.894
Post-operative D1 Hb (g/L)	102.78±18.18	101.15±14.16	0.631
Post-operative D1 hematocrit (%)	30.76±5.5	30.34±4.1	0.678
Hb change (g/L)	28.42±18.83	31.59±12.75	0.319
Hematocrit change (%)	10±5.8	10±3.6	0.741
Operative factors			
ASD-S score	25.05±4.90	24.90±5.44	0.887
Duration of surgery (min)	283.90±67.62	287.61±69.30	0.789
Fixation and fused levels (n)	6.58±1.49	6.34±1.44	0.419
Decompression levels (n)	2.83±1.30	3.15±1.20	0.224
Osteotomy grades, 2: 3 (n,%)	47:13	34:7	0.569
No. of intervertebral fusion (n)	1.20±1.15	1.40±0.97	0.388
Blood loss and transfusion			
IBL (mL)	1633.65±962.49	1040.88±560.37	0.001**
Postoperative drainage (mL)	1412.83±538.45	1205.68±367.76	0.035*
Total blood loss (mL)	3046.48±1274.02	2246.56±815.01	0.001*
Cell saver (mL)	544.55±320.83	346.96±186.79	<0.001**

Table 5 continued. Data from subanalyses of patients undergoing osteotomy surgery.

	NTXA (n= 60)	TXA (n=41)	P value
Intraoperative PRBC	3.62±2.32	2.34±1.96	0.005**
Intraoperative transfusion rate (n,%)	52 (86.7%)	28 (68.3%)	0.025*
Postoperative PRBC	2.10±2.37	1.39±1.66	0.100
Postoperative transfusion rate (n,%)	35 (58.3%)	20 (48.8%)	0.344
Length of hospital stay (d)	12.25±6.39	10.83±3.82	0.205
DVT/PE	1 (1.7%)	0	>0.999

Values are presented as the mean±SD or number (%). TXA – the group that received tranexamic acid; NTXA – the historically recruited no-TXA group; BMI – body mass index; EBV – estimated blood volume; ASA – American Society of Anesthesiologists; CSVL – coronal vertical axis from the central sacrum vertical line; SVA – sagittal vertical axis; LL – lumbar lordosis; Hb – hemoglobin; PLT – platelets; APTT – activated partial thromboplastin time; INR – international normalized ratio; ASD-S – adult spinal deformity surgery; IBL – intraoperative blood loss; PRBC – packed red blood cells; DVT – deep vein thrombosis; PE – pulmonary embolism. * $P<0.05$, ** $P<0.01$.

Discussion

The present study found that a single dose of 1 g of TXA significantly decreased perioperative blood loss and total hemostasis costs for DLS patients undergoing osteotomy. For patients without osteotomy, TXA decreased perioperative blood loss and led to no additional net costs.

Our findings are consistent with those reported by some other authors investigating the use of TXA. Choi et al [22] reported a statistically significant reduction in intraoperative blood loss and postoperative transfusion relative to patients receiving placebo in 132 patients undergoing multilevel posterior spinal segmental instrumented fusion. A randomized controlled trial [13] of adult patients who underwent posterior instrumented spine surgery also found that administration of TXA could significantly reduce perioperative blood loss. Wong et al [23] similarly found that TXA significantly reduced intraoperative, postoperative, and total blood loss but did not influence transfusion outcomes. Regarding transfusion, previous studies have yielded varying results. In complex multilevel spine fusion with and without an osteotomy procedure, TXA was reported to reduce the total red blood cells transfused [24]. Raksakietisak and colleagues [13] observed that TXA reduced blood transfusion by 64.6% in a prospective randomized study. However, many other studies have concluded that TXA could not significantly reduce allogeneic transfusion requirements [13,23,25]. In the present study, the TXA group had a lower transfusion rate than the NTXA group but this difference was not statistically significant. Nevertheless, TXA reduced postoperative and total transfusion volume.

In the present study, the allogeneic transfusion rate was 87.04% in patients receiving TXA vs 93.28% in the control

group. This rate seems much higher than in some previous studies [23,26]. The transfusion trigger in related studies may impact the transfusion rate, as may surgery characteristics, such as decompression levels, osteotomy grade, surgery duration, preoperative Hb level, and TXA dose. In our study, the postoperative transfusion trigger was Hb level <80 g/L or 80 to 100 g/L combined with exhibited symptomatic anemia, although some other studies set the transfusion trigger at Hb <7 g/dL [23]. More than 80% of our study patients underwent fusion of more than 5 segments and decompressed more than 3 levels, with 50.42% of the patients in the NTXA group and 75.93% of those in the TXA group undergoing osteotomy. The intraoperative allogeneic transfusion rate (73.95% in the NTXA group vs 66.67% in the TXA group) in our study was less than the rate reported by Choi et al [22] (88.4% in the NTXA group vs 74.2% in the TXA group), who reported results from spinal deformity surgery. Recent studies have concluded that osteotomy and a posterior approach in spine surgery are risk factors for blood transfusion requirement [8,27].

There has been no consensus on the optimal regimen for TXA delivery in spine surgery. A meta-analysis [28] demonstrated that high-dose TXA (>20 mg/kg) had a better effect than low-dose TXA (<20 mg/kg) in controlling blood loss during scoliosis surgery. Hui et al [29] also revealed that high-dose rather than low-dose TXA could reduce both operative duration and perioperative allogeneic transfusion rates. The blood half-life of TXA is 2 h, and the plasma concentration of TXA is maintained during the first 16 h after administration [30]. We used a single dose of 1000 mg TXA without a maintenance dose, which was lower than 20 mg/kg. That may be a contributory cause for the high blood transfusion rate in our study.

The present study's main objective was to determine whether a single dose of 1000 mg TXA is cost-effective for DLS patients. A recent study showed that TXA administration significantly reduced intraoperative bleeding and total hemostasis costs for patients undergoing surgery of more than 4-level fusion [18]. However, this study included patients with degenerative pathology, and neither described osteotomy. In our analysis, we first performed a comparison of the TXA cost among osteotomy and non-osteotomy patients. In this subanalysis, patients who underwent osteotomy and received TXA had a net cost-benefit of ¥ 648.77, while patients without osteotomy who received TXA had a net cost-benefit of ¥ 290.08. The ASD-S score has been demonstrated to be accurate in explaining variation in estimated blood loss and operative time in ASD surgery [19], and a significantly higher mean ASD-S score was seen in the osteotomy group (24.99 ± 5.10 vs 20.67 ± 3.68 , $P < 0.001$) than in the non-osteotomy group. This study suggested that as a surgery's invasiveness increases, the cost savings will be expected to increase.

Reducing blood transfusions and the volume of blood transfused has many health and economic benefits. First of all, it reduces the risk of transfusion-transmissible infections [6] such as hepatitis C virus, hepatitis B virus, and human immunodeficiency virus. Various studies have estimated cost savings in arthroplasty [15,17,31]. Although many factors can lead to discrepancies, most studies offer strong evidence that TXA use is cost-effective [32]. In our study, from the evaluation of costs related to blood transfusions, we can estimate that with the introduction of TXA administration, our hospital saved ¥416.01 per DLS patient undergoing posterior long-segment fixation and fusion surgery. The prevalence of DLS in the Chinese Han population aged older than 40 years was approximately 13.3% [3]. Although we do not know exactly how many people need surgery, it is a large number of surgeries, and this savings would add up to substantial cost savings. As a result of the large volume of surgery, elective surgery is sometimes delayed due to insufficient blood products in the hospital's blood banks, which results in prolonging the length of hospitalization and increasing other costs. Our analysis showed that using a single dose of TXA decreased total allogeneic transfusion, which may alleviate the blood shortage.

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A major concern about TXA management is the potential for increasing the risk of perioperative thromboembolic complications. In our study, only 1 patient in the NTXA group (a patient with DVT) had a thrombotic complication, and there was no statistically significant difference in the complication rate between the 2 groups. Many studies and meta-analyses have demonstrated that using TXA has no association with any increase in incidence of pulmonary embolism, deep venous thrombosis, or myocardial infarction [14,23,33,34].

Our study has some limitations. Firstly, it was a single-center, retrospective study. However, the demographic data and surgical techniques, and the dose of TXA, were comparable. The only difference was a higher osteotomy rate in the NTXA group, and thus a subanalysis was performed next. Additionally, after adjusting for potential bias and confounding variables, TXA still effectively reduced perioperative bleeding. Secondly, the number of patients in the TXA group was lower than that in the NTXA group, which was also due to the study's retrospective nature. Our results suggested that administration of a single dose of 1 g TXA, without a maintenance dose, also shows high efficacy and safety in DLS patients undergoing posterior correction surgery, but further studies are needed to find the optimal TXA dose.

Conclusions

A single dose of TXA significantly decreased perioperative blood loss and total hemostasis costs for DLS patients undergoing osteotomy. Furthermore, TXA decreased perioperative blood loss and led to no additional net costs in patients without osteotomy.

Statement

Tranexamic acid is approved by the National Medical Products Administration for this indication.

Conflict of Interest

None.

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