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Recombinant coagulation factor VIIa—a novel haemostatic agent in scoliosis surgery?

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Abstract Spinal fusion surgery in children and adolescents with idiopathic scoliosis is often associated with severe haemorrhage. Recombinant coagulation factor VIIa (rFVIIa) has previously been shown to be an effective haemostatic treatment for severe bleeding associated with a variety of coagulopathic and non-coagulopathic indications. The aim of this retrospective study was to assess the safety and haemostatic efficacy of rFVIIa in a series of 26 consecutive adolescent patients with scoliosis (22 females; mean age 16.6 years) undergoing correctional surgery. A second series of 26 consecutive patients (20 females; mean age 16.2 years) who received standard therapy during surgery, represented historical controls. Blood loss, transfusion requirements, duration of surgery, and peri-operative measurements of coagulation parameters were compared between the two groups. Intra-operative and combined intra-operative and post-operative blood losses were significantly smaller in the rFVIIa-treatment group than in the

historical controls ($P=0.003$ and 0.032 , respectively); rFVIIa-treated patients also demonstrated significantly reduced blood loss per vertebral segment fused ($P=0.032$) and per hour of surgery ($P<0.001$). Intra-operative requirements for packed red blood cells were also significantly lower in the treatment group ($P=0.042$). Patients in the treatment group demonstrated rapid and maintained reduction of prothrombin time and international normalised ratio; values among rFVIIa-treated patients remained significantly lower than those in the control group at all time points evaluated ($P<0.001$). There were no deaths and no adverse events. These results suggest that rFVIIa is a safe and effective haemostatic agent for use during spinal fusion surgery in adolescent patients with idiopathic scoliosis; however, further research and randomised, placebo-controlled trials are needed to confirm these findings.

Keywords Bleeding · Haemostasis · Scoliosis · Surgery · rFVIIa

Introduction

Spinal fusion surgery for the correction of idiopathic scoliosis in children and adolescents is often associated with severe haemorrhage [2, 18] that may approach or

even exceed the patient's total estimated blood volume (EBV) [12]. This is reflected by reports in the current literature: Kannan et al. [18] reported a median loss of 20% of the total blood volume (range: 2–82%) in patients with idiopathic scoliosis, and this was higher

(78%; range: 25–127%) in patients with an underlying neuromuscular disorder. In another study, Zheng et al. [45] reported mean intra-operative blood losses of 1073 ± 716 ml and blood transfusion requirements of 1.04 ± 1.17 units in 112 adult patients undergoing revision surgery for degenerative lumbar spinal stenosis. Furthermore, post-operative bleeding has been shown to exceed intra-operative haemorrhage in approximately 20% of cases [12].

Although multifactorial in origin, peri-operative haemorrhage associated with spinal fusion techniques results primarily from disruption of internal vertebral veins, decortication of large areas of bone [18], and instrumentation of the vertebrae. Furthermore, haemostatic abnormalities may increase the risk of bleeding in some patients: consumption coagulopathy, dilution coagulopathy caused by normovolaemic haemodilution [29], reduced factor VII (FVII) levels [18], and abnormal platelet aggregation [34, 42, 44] have all been cited as possible contributors to an increased haemorrhagic tendency. Finally, inferior vena cava tear is a rare but potentially life-threatening cause of bleeding during surgical intervention [43].

Previous studies claim that the number of vertebrae fused and the duration of surgery are the most important factors influencing peri-operative blood loss and requirements for allogeneic blood [12, 45], although excessive body weight and high pre-operative haemoglobin levels have also been shown to correlate with severe bleeding during surgery [45]. Other factors affecting blood loss include surgical technique, site and size of autologous bone graft harvest [12]; mean arterial pressure [24, 32] and patient position [35].

Several methods are employed to limit blood loss during spinal fusion surgery, including pre-operative autologous blood donation [28, 30], careful patient positioning to avoid abdominal compression [35], controlled hypotensive anaesthesia to lower mean arterial pressure [24, 32], acute normovolaemic haemodilution [6], epinephrine infiltration of paravertebral tissues, application of fibrin sealant to decorticated bone, and the use of intra-operative blood salvage (cell-saver) systems [9]. Procoagulant and antifibrinolytic drugs, such as aprotinin [5], ϵ -aminocaproic acid [9], and desmopressin [19], have also provided some efficacy in reducing both blood loss and exposure to allogeneic blood products during spinal fusion.

Despite these findings, there remains a need for new therapies and techniques that can further reduce blood loss and transfusion requirements, thus reducing the associated risk of infection in this primarily youthful patient population. As transfusion requirements correlate with the length of hospital stay [45], alternative therapies might also provide cost benefits. One approach may entail the application of topical haemostatic agents, such as absorbable porcine gelatine,

regenerated oxidised cellulose, and a more recently developed haemostatic matrix derived from bovine gelatine [FloSeal (formerly known as Proceed), Baxter, Deerfield, IL, USA]. An alternative approach to haemostasis during surgical correction of scoliosis may involve recombinant coagulation factor VIIa (rFVIIa; NovoSeven, Novo Nordisk, Bagsvaerd, Denmark). Recombinant FVIIa is a safe and effective haemostatic agent for patients with haemophilia and inhibitors to factor VIII or IX, and for patients with FVII deficiency or Glanzmann's thrombasthenia. The agent is thought to act locally at the site of vessel damage by binding directly to the surface of activated platelets, thus initiating the activation of factor X and subsequent thrombin generation [15, 26]. This mode of action suggests that rFVIIa may also be useful as a haemostatic agent in patients without pre-existing coagulopathy. Indeed, numerous clinical trials and individual reports over recent years have indicated that this drug may be efficacious in trauma-related haemorrhage [21], in patients undergoing surgical procedures [1, 10], and in those with intracerebral haemorrhage [22, 31]. Further potential advantages of this pro-haemostatic agent include its relatively short half-life (approximately 2–3 h) and the low incidence of adverse events associated with its use [20].

In light of these findings, the aim of this retrospective study was to evaluate the effects of rFVIIa administration on blood loss and transfusion requirements in a consecutive series of adolescent patients undergoing spinal fusion surgery for correction of idiopathic scoliosis.

Patients and methods

The case records of 52 consecutive patients undergoing surgical correction of idiopathic scoliosis were retrospectively reviewed. All procedures took place between 2001 and 2003 at the Children's and Adolescents' Regional Specialist Hospital in Szczecin, Poland. A total of 26 patients, chosen at random from a consecutive series of patients who required surgical correction of idiopathic scoliosis, received rFVIIa (mean dose: $23.0 \mu\text{g/kg}$) 30 min before the start of surgery. A second group ($n = 26$), chosen at random from a consecutive series of patients who did not receive rFVIIa to manage peri-operative haemorrhage, served as historical controls. Patients who had previously undergone correctional surgery using the Harrington method were excluded from the control group. Pre-surgical preparation in all patients involved hypervolaemic haemodilution using 20 ml/kg 5% glucose in 0.9% NaCl (ratio 1:1), along with administration of a compound electrolyte solution. Patients were placed in the prone position with head

traction, support at the shoulders and pelvis to avoid abdominal compression, and flexion of 70° and 90° in the hip and knee, respectively. In both groups, intra-operative haemostasis was maintained using electrocoagulation, application of bone wax, and administration of fresh frozen plasma (FFP) as needed. Packed red blood cells (pRBC) were used to relieve blood loss where necessary.

Efficacy measurements

Intra-operative blood loss was calculated by determining the pre-surgical and post-surgical weight of the swabs and by measuring the blood drained from the operative field in order to derive a value for 'established blood loss'. Using calculations developed by Mercuriali and Inghilleri [25], Brecher et al. [3], and Gross [11], we also measured the change in haematocrit to determine the loss of packed erythrocyte mass and thus ascertain the 'calculated blood loss'. Post-operative blood loss was determined by measuring the amount of blood collected in wound drains and monitored until cessation of bleeding. Transfusion requirements (FFP, pRBC, whole blood, and crystalloids) were recorded intra-operatively and on a daily basis post-operatively.

Duration of surgery, blood loss, and transfusion requirements were compared between historical controls and rFVIIa-treated patients. Blood losses (intra-operative, post-operative, and combined) were expressed as a total amount and as a percentage of EBV, as well as loss per kg body weight, per vertebral segment fused, and per hour of surgery. The effect of pre-operative platelet levels on surgical bleeding (historical controls) and efficacy of rFVIIa (treatment group) was evaluated, and data from historical controls were used to confirm previously reported predictors of peri-operative blood loss and transfusion requirements. Treatment efficacy in the treatment group was evaluated in the same way as in the control group.

Safety

Blood was drawn pre-operatively, immediately after haemodilution (historical controls) or rFVIIa administration (treatment group), and at 15 min, 2 h, and 4 h after the start of surgery for assessment of coagulation parameters [haematocrit, haemoglobin, platelets, prothrombin time (PT), international normalised ratio (INR), activated partial thromboplastin time (aPTT), and fibrinogen]. Values from historical controls were compared with those from rFVIIa-treated patients. Adverse events were monitored for 10 days post-operatively.

Statistical analysis

All patients were included in statistical analysis of the data. The transfusion requirement data (pRBC and FFP) did not conform to a Gaussian distribution and were therefore described by median values and 90% ranges (calculated from the 5th and 95th percentiles of the distribution). Data for pRBC and FFP were further described by the number of patients who received 0, 1, 2, and 3+ units, and the two groups were compared by means of Pearson chi-square tests. All other data (except those for gender) were summarised by means and standard deviations and compared between the two groups using *t*-test for independent samples. Gender was compared using the Pearson chi-square test. Pair-wise associations were assessed using Spearman rank correlation analysis. Changes in coagulation parameters from pre-operative values were assessed by repeated measures analysis of variance. A $P \leq 0.05$ was considered statistically significant. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (Version 11; SPSS Inc., Chicago, IL, USA).

Results

Fifty-two patients undergoing surgical correction of idiopathic scoliosis were included in the study. The historical control group and the rFVIIa-treatment group each comprised 26 consecutive patients (historical controls: 20 females, mean age 16.2 years; rFVIIa-treatment group: 22 females, mean age 16.6 years). Patient characteristics, diagnoses, and type of surgery were similar in both groups (Table 1). One patient in the control group had comorbid conditions (Noonan syndrome, hypoplasia of the left kidney, and nephropathy of the right kidney), although none of the patients showed evidence of a pre-existing coagulation disorder.

Efficacy measurements

Total intra-operative and combined intra-operative and post-operative blood losses were significantly smaller in rFVIIa-treated patients when compared with historical controls (1081.4 vs. 1513.4 ml, $P=0.003$; and 1881.9 vs. 2317.6 ml, $P=0.032$, respectively). Post-operative blood loss alone, however, was similar in the two groups (Table 2). Mean loss of EBV and blood loss per kg body weight differed significantly between the two groups only for the intra-operative phase [loss of EBV: 30.7% in rFVIIa-treated patients versus 40.7% in controls ($P=0.013$); loss per kg body weight: 20.9 and 27.4 ml in rFVIIa-treated patients and controls, respectively

Table 1 Patient characteristics and surgical interventions

	Historical controls	rFVIIa treatment group	P value
Number of patients	26	26	–
Sex (number of female)	20	22	0.482
Age (years) [mean (range)]	16.2 (12–19)	16.6 (10–22)	0.446
Weight (kg) [mean (SD)]	56.9 (9.1)	52.3 (8.5)	0.065
Type of scoliosis			
Type I, grade II	1	1	–
Type I, grade III	0	1	–
Type II, grade II	9	7	–
Type II, grade III	2	2	–
Type III, grade I	0	1	–
Type III, grade II	8	5	–
Type III, grade III	4	4	–
Type III, grade IV	0	1	–
Type IV, grade II	2	0	–
Type IV, grade IV	0	1	–
Type V, grade III	0	2	–
Type VI, grade IV	0	1	–
Number of vertebrae fused [mean (SD)]	11.7 (1.2)	11.8 (1.7)	0.854
Duration of surgery (h) [mean (SD)]	3.1 (0.6)	3.2 (0.8)	0.675

SD standard deviation

($P=0.016$]. When compared with controls, the rFVIIa-treated patients also demonstrated significantly reduced blood loss per segment fused (161.1 vs. 200.9 ml; $P=0.032$) and per hour of surgery (345.9 vs. 487.4 ml; $P<0.001$) (Table 2). In support of these findings, increased visibility of the surgical field was also noted in rFVIIa-treated patients throughout the procedure (Fig. 1). There was no difference between the two groups in duration of surgery.

Intra-operative requirements for pRBC were significantly lower in the rFVIIa-treatment group when compared with historical controls ($P=0.042$) (Table 2). No significant differences in requirements for post-operative pRBC, or for FFP and crystalloids during the entire peri-operative period were observed between the two groups (Table 2).

Analysis of historical control data showed that there was no significant correlation between pre-surgical platelet level and intra-operative blood loss (measured as a total amount, loss of EBV or loss per kg body weight) ($r_s=0.2$ – 0.3 ; $P=NS$). Furthermore, the efficacy of rFVIIa treatment was not influenced by pre-surgical platelet levels: $246.8 \pm 70.5 \times 10^9 \text{ l}^{-1}$ in patients with 'markedly reduced' blood loss, versus $266.7 \pm 116.8 \times 10^9 \text{ l}^{-1}$ in patients who showed 'reduced' bleeding ($P=0.598$).

Predictors of blood loss in historical controls

Spearman rank correlation analysis showed that there was a positive correlation between duration of surgery and the following: total intra-operative blood loss ($r=0.542$, $P=0.004$); intra-operative loss of EBV

($r=0.499$, $P=0.009$); and intra-operative blood loss per kg body weight ($r=0.478$, $P=0.013$).

A positive correlation was also observed between pre-surgical haematocrit levels and total intra-operative blood loss ($r=0.449$, $P=0.021$), intra-operative loss of EBV ($r=0.388$, $P=0.05$), and intra-operative blood loss per kg body weight ($r=0.392$, $P=0.048$).

There were no significant correlations between intra-operative bleeding and number of vertebrae fused or pre-surgical haemoglobin levels, although a weak trend for the latter ($r=0.321$, $P=0.110$) was found for total intra-operative blood loss. Although patient weight did not significantly influence total intra-operative loss of blood or EBV, there was a trend towards a negative correlation between weight and intra-operative blood loss per kg body weight ($r=-0.393$, $P=0.052$).

Coagulation parameters

Mean PT in the historical control group was 14.5 s immediately after haemodilution, compared with 13.2 s immediately after rFVIIa administration in the treatment group ($P=0.001$). Values for PT among rFVIIa-treated patients remained significantly lower than those in the control group at all other time points evaluated (15 min, 2 h and 4 h after the start of surgery; all $P<0.001$) (Fig. 2a). Mean INR also remained significantly lower in the treatment group at these time points when compared with controls ($P<0.01$).

Following haemodilution (historical controls) or rFVIIa administration (treatment group), the mean values for aPTT were 40.7 and 33.0 s, respectively ($P=0.022$). When compared with historical controls, significant reductions in aPTT were also observed in the

Table 2 Blood loss and transfusion requirements

	Historical controls	rFVIIa treatment group	P value
Total blood loss (ml) [mean (SD)]			
Intra-operative	1513.4 (610.3)	1081.4 (372.2)	0.003
Post-operative	804.2 (512.1)	800.5 (458.5)	0.978
Combined	2317.6 (791.2)	1881.9 (619.0)	0.032
Loss of EBV (%) [mean (SD)]			
Intra-operative	40.7 (16.4)	30.7 (11.2)	0.013
Post-operative	21.1 (12.7)	22.2 (12.1)	0.739
Combined	61.7 (21.2)	52.9 (17.2)	
Blood loss (ml/kg) body weight [mean (SD)]			
Intra-operative	27.4 (10.8)	20.9 (7.7)	0.016
Post-operative	13.8 (8.6)	14.9 (8.4)	0.639
Combined	41.2 (13.5)	35.9 (11.8)	0.140
Blood loss per segment fused (ml) [mean (SD)]	200.9 (72.7)	161.1 (57.0)	0.032
Blood loss per hour of surgery (ml) [mean (SD)]	487.4 (154.7)	345.9 (103.1)	<0.001
pRBC transfusion requirements (units)			
Intra-operative			
Median (90% range)	0 (0–2)	0 (0–1)	–
Number with 0/1/2/3+ units	14/10/2/0	22/4/0/0	0.042
Post-operative			
Median (90% range)	0 (0–2.7)	0 (0–1.7)	–
Number with 0/1/2/3+ units	16/7/2/1	14/11/1/0	0.502
Combined			
Median (90% range)	1 (0–4.3)	0.5 (0–2)	–
Number with 0/1/2/3+ units	8/12/4/2	13/9/4/0	0.460
FFP transfusion requirements (units)			
Intra-operative			
Median (90% range)	0 (0–1)	0 (0–1)	–
Number with 0/1 units	18/8	23/3	0.090
Post-operative			
Median (90% range)	0 (0–0.7)	0 (0–1)	–
Number with 0/1 units	25/1	21/5	0.083
Combined			
Median (90% range)	0 (0–1)	0 (0–1)	–
Number with 0/1 units	17/9	18/8	0.768
Crystalloids administered (ml) [mean (SD)]			
Pre-operative	1412 (153)	1521 (630)	0.393
Intra-operative	4260 (664)	4192 (838)	0.750
Post-operative	2644 (875)	2308 (749)	0.143
Combined	6904 (972)	6500 (1233)	0.196

EBV estimated blood volume, FFP fresh frozen plasma, pRBC packed red blood cells

treatment group at 2 h after the start of surgery ($P=0.038$) (Fig. 2b).

Mean fibrinogen levels at 4 h were significantly lower in the treatment group than in control patients ($P=0.04$). However, haemoglobin levels at 15 min were significantly lower in controls when compared with rFVIIa-treated patients ($P=0.03$). No significant differences in haematocrit or platelet levels were observed between the two groups at any of the time points evaluated.

Safety

There were no deaths among the patients whose cases were reviewed. No adverse events such as surgical wound infection or haematoma were recorded in the study population, and no thromboembolic events, such as deep vein thrombosis, pulmonary embolism, or myocardial infarction, were observed during the 10-day follow-up period.

Fig. 1 Operative field in a control patient (*left panel*) and a patient treated with rFVIIa (*right panel*) at various stages of the procedure. Exposure of spinal processes (**a**); removal of spinal processes (**b**); implantation and distraction of scoliosis (**c**); final view of instrumentation (**d**)

Discussion

Several methods have traditionally been employed to reduce the severe bleeding associated with surgical correction of idiopathic scoliosis in children and adolescents. Aprotinin and ϵ -aminocaproic acid have both shown efficacy in decreasing blood loss during spinal reconstruction in adolescents and adults [5, 9], whereas administration of conjugated oestrogens has reduced haemorrhage following spinal surgery in paediatric patients [23]. In another study, Letts et al. [19] compared the efficacy of desmopressin with that of placebo in patients undergoing spinal fusion surgery for neuromuscular scoliosis. Desmopressin administration reduced mean total blood loss by 19% and mean blood loss per vertebra fused by 15% when compared with placebo, although these results were not statistically significant. Topical haemostatic agents, such as absorbable porcine gelatine, regenerated oxidised cellulose, and bovine gelatine matrices, have also been used to control haemorrhage and diffuse capillary or venous oozing during various kinds of spinal surgery [38, 40]. A further alternative to address the urgent need for effective haemostatic support in patients undergoing surgery for the correction of idiopathic scoliosis may involve the use of rFVIIa.

This retrospective study evaluated the effect of rFVIIa on bleeding and transfusion requirements in adolescent patients undergoing spinal fusion surgery for the correction of idiopathic scoliosis. Our results indicate that rFVIIa administration plus standard therapy (haemodilution, FFP, and pRBC) significantly reduces intra-operative and combined intra-operative and post-operative blood loss when compared with standard therapy alone ($P=0.003$ and 0.032 , respectively). Treatment with rFVIIa also reduced peri-operative blood loss per segment fused ($P=0.032$) and per hour of surgery ($P<0.001$). Accordingly, intra-operative requirements for pRBC were significantly lower in the rFVIIa-treatment group ($P=0.042$; Table 2). Although the duration of surgery did not differ between the two groups of patients, the use of rFVIIa may help to maintain a clear surgical field, thus facilitating safer surgery and minimising the risk of nerve damage that is often associated with poor visibility caused by haemorrhage from the operative site (Fig. 1).

Coagulation parameters (PT and aPTT) showed significant improvements following rFVIIa administration,

Fig. 2 Mean prothrombin time (PT) (a) and mean activated partial thromboplastin time (aPTT) (b) before and after haemodilution (control group) or rFVIIa administration (treatment group). * $P=0.022$; ** $P=0.038$; † $P=0.001$; ‡ $P<0.001$; §Immediately after haemodilution (control group) or rFVIIa administration (treatment group)

when compared with placebo (Fig. 2a, b). However, caution is advised when interpreting these results, as normalisation of laboratory parameters—particularly PT—does not necessarily reflect clinical correction of the haemostatic defect [8, 20]. For instance, the PT is very sensitive to increased concentrations of FVIIa; thus, the observed improvements in PT may be an ex vivo effect rather than a reflection of improved haemostasis in vivo [8, 20].

The mode of action of rFVIIa may help to explain its observed clinical efficacy. One mechanism may involve the formation of complexes between tissue factor and rFVIIa at sites of vessel damage, thus helping to 'drive' the coagulation process [14]. An alternative theory suggests that rFVIIa is able to act independently of tissue factor by binding directly to the surface of activated platelets at the injury site, leading to activation of factor

X and subsequent thrombin generation [15, 26]. These actions may also help to explain the agent's efficacy in coagulopathies such as FVII deficiency [16, 17, 27, 41] and Glanzmann's thrombasthenia [4, 36, 37]—indeed, rFVIIa has recently been licensed in Europe for the treatment of bleeding episodes associated with both these conditions. Furthermore, the current study suggests that rFVIIa is able to exert its haemostatic effects even when platelet levels are low: Spearman rank correlation analysis revealed a non-significant trend towards greater efficacy in those patients with lower platelet levels prior to surgery.

All patients survived, and no adverse events were reported. The observed lack of adverse effects in the rFVIIa-treatment group reflects the highly favourable safety profile of the agent; by November 2002, over 400,000 standard doses (90 µg/kg) had been administered in a wide variety of indications, but the incidence of serious adverse events remains less than 1% [39]. The demonstrated safety of rFVIIa may be facilitated by its localised mode of action, which ensures that haemostatic mechanisms are induced at the bleeding site whilst avoiding systemic activation of coagulation and thus reducing the risk of thrombosis. Although isolated thrombotic events have been reported following rFVIIa use [7, 13, 33], they occur primarily in elderly patients with underlying pathological conditions that predispose to the development of thrombosis when thrombin generation is enhanced. Therefore, the thrombotic events reported may be attributable to improvement of the coagulation system rather than to rFVIIa treatment per se [39]. Furthermore, in a recent systematic review of rFVIIa use in patients with and without coagulation disorders, Levi et al. [20] suggest that a causal relationship between rFVIIa administration and development of thrombosis is difficult to establish. The half-life of rFVIIa is short (approximately 2–3 h), and the majority of reported thrombotic events in the literature did not develop until several days after drug administration. Therefore, it is unlikely that rFVIIa was responsible for these adverse effects [20]. The current study utilised a 10-day follow-up period for monitoring adverse events; in accordance with Levi et al. [20], we believe that this is sufficient to capture any treatment-related complications. As no adverse events were observed in any patient, we conclude that rFVIIa administration was safe in this population of adolescent patients undergoing spinal fusion surgery to correct idiopathic scoliosis.

A further aim of this study was to use data from the historical control patients to validate previously reported predictors of blood loss in spinal fusion surgery. The ability to predict which patients are most likely to bleed, and how severe the bleeding is likely to be, is of great importance in allowing accurate prediction of the quantity of blood products that will be required to control the haemorrhage. We found that intra-operative

bleeding (total blood loss, loss of EBV, and loss per kg body weight) correlated with the duration of surgery, thus supporting previous claims [12]; however, we found no evidence of a correlation between duration of surgery and number of vertebral levels fused. This is an unexpected finding, as the number of fusion levels has previously been reported as a major predictor of blood loss in scoliosis surgery [12, 45]. In line with previous findings [45], we observed a weak trend between pre-operative haemoglobin levels and intra-operative blood loss; a positive correlation between pre-operative haematocrit and intra-operative bleeding was also found. A previous study by Zheng et al. [45] also considered weight to be a major determinant of peri-operative haemorrhage [45], with higher patient weight predicting higher blood loss. Our findings, however, showed the opposite relationship: we found a non-significant trend towards a negative correlation between weight and intra-operative blood loss per kg body weight. Although interesting, however, this observation must be interpreted with caution; the study by Zheng et al. [45] investigated adult patients rather than adolescents, and so the results from the two studies cannot be directly compared. At present,

we are unable to explain why other findings from the current study failed to confirm those of previous reports. Further investigation is beyond the scope of this article and will require additional studies designed specifically to evaluate the factors that influence peri-operative blood loss.

In conclusion, rFVIIa appears to be effective in reducing blood loss in adolescent patients undergoing spinal fusion surgery for the correction of idiopathic scoliosis, and may reduce the need for transfusion of blood products. Treatment with rFVIIa also appears to be safe, as no adverse events were reported in any patient. Our results also suggest that rFVIIa therapy in the small subset of scoliosis patients with an underlying neuromuscular disorder may be worthy of investigation; such patients are particularly susceptible to haemorrhage during surgery and may therefore benefit from the procoagulant activity provided by rFVIIa. Although our findings are limited by a retrospective study design and the use of a historical control group rather than a double-blind, placebo-controlled design, they nonetheless suggest that further research and clinical trials of rFVIIa use during correctional surgery for scoliosis are warranted.

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