

Recombinant activated factor VII (rFVIIa/NovoSeven®) in intractable haemorrhage: use of a clinical scoring system to predict outcome

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Vox Sanguinis

Background and Objectives Recombinant activated factor VII (rFVIIa/NovoSeven®) has been advocated in the treatment of life-threatening haemorrhage, but appropriate clinical indications remain uncertain. The aim of this study was to detect factors predictive of outcome and to incorporate them into a prognostically significant scoring system.

Materials and Methods Thirty-six patients received rFVIIa for uncontrolled surgical, traumatic or obstetric bleeding in the Northern Region of the UK over a 45-month period. Clinical, laboratory and outcome data were examined. Characteristics of survivor and non-survivor groups were compared. A prognostic scoring system was evaluated retrospectively according to the presence of coagulopathy, renal impairment, hypothermia, greater than 10 units of red cell transfusion, advanced age and obstetric indication, with patients allocated to low, intermediate and high-risk groups.

Results Clinical response occurred in 26 patients (72%) with a reduction in prothrombin time and blood product requirements. Death occurred in 19 (53%). Four patients (11%) suffered thrombotic events. Survivors were younger than non-survivors and less likely to have coagulopathy, renal impairment or hypothermia at the time of administration. Survivors were more likely to have had an initial clinical response in terms of an immediate reduction in haemorrhage. Non-survivors were transfused a greater number of red cell units prior to administration. Survival varied according to prognostic score; low-risk patients had a survival rate of 85%, intermediate-risk patients had a survival rate of 50% and high-risk patients had a survival rate of 18%.

Conclusions FVIIa has a role in the cessation of haemorrhage, but may not improve survival. Use of a clinical scoring system may help to predict outcome.

Key words: coagulopathy, major haemorrhage, massive transfusion, prognostic scoring system, recombinant activated factor VII.

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Introduction

Recombinant activated factor VII (rFVIIa/NovoSeven®) was specifically developed for use in haemophilia A and B patients

with inhibitors [1]. Authorized uses now extend to patients with acquired haemophilia [2], rare congenital coagulation factor deficiencies [3,4] and inherited platelet disorders [5,6].

More recently there has been increasing interest in the use of rFVIIa in the setting of acute, life-threatening bleeding in non-haemophiliacs. First reported in traumatic bleeding [7,8], it is now used in the management of surgical and obstetric haemorrhage when surgical measures and optimal blood product replacement have failed to achieve haemostasis. Under these circumstances, further options are limited [9] and it has been suggested that rFVIIa may be an appropriate salvage agent [10].

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Although several small series report its efficacy in achieving haemostasis, few show a convincing impact on overall survival, with death resulting from multiorgan failure in the majority of non-survivors [11–16]. These series are limited by the lack of control data and by variations in patient selection and in the dosing regime. Furthermore, the reporting of adverse events is lacking.

Differences in patient characteristics are likely to have a major impact on survival. However, apart from one small series that assessed outcome according to severity of coagulopathy [17], a second that assessed the impact of cardiac comorbidities on outcome specifically after cardiac surgery [13], and a third that examined the effect of acidosis and hypothermia on response in trauma patients [15], the importance of factors predictive of poor outcome has yet to be examined.

This report details the use of rFVIIa, within the Northern Region of the UK, for the management of major surgical, traumatic or obstetric haemorrhage in a series of 36 consecutive patients over a period of 45 months. Patient characteristics, response and outcome are examined. Survivor and non-survivor groups are compared, and a prognostic scoring system retrospectively evaluated as a means of predicting survival.

Materials and methods

Protocol for the administration of rFVIIa

A regional protocol was developed for the use of rFVIIa in the management of acute, life-threatening bleeding. rFVIIa was administered, with the approval of a Consultant Haematologist, if significant bleeding (> 200 ml/h) continued despite optimal surgical measures and blood product replacement. Use of rFVIIa was not approved for use in patients whose overall outlook was unlikely to be altered by arresting haemorrhage (i.e. patients with established multiorgan failure). A dose of 90 µg/kg was recommended, with a second dose 3 h later if an initial response was not obtained, to a maximum of two doses. Further doses were not administered apart from in exceptional circumstances. Platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT) and Clauss fibrinogen were measured immediately before, and 15 min after, administration of the first dose. Bilateral lower limb Doppler ultrasound was performed after 3–5 days to assess for the presence of thrombus in patients surviving for more than 24 h.

Collection of data

Thirty-six consecutive patients were evaluated over a period of 45 months between August 2001 and May 2005. Details were obtained from patients' case notes and laboratory records. Demographic data included patient age and gender. Circumstances under which bleeding occurred, time from the start of bleeding until rFVIIa administration, dose of rFVIIa and

Table 1 Prognostic scoring system

Characteristic	Score
Coagulopathy, defined as any of platelet count $\leq 50 \times 10^9/l$ fibrinogen ≤ 1.0 g/l PT/APTT $\geq 1.5 \times$ ULN	1
Renal impairment, defined as creatinine ≥ 120 µmol/l	1
Hypothermia, defined as core temperature ≤ 35 °C	1
≥ 10 units of red cell transfusion	1
Age ≥ 60 years	1
Obstetric indication	-1

APTT, activated partial thromboplastin time; ULN, upper limit of reference range; PT, prothrombin time.

number of doses, were recorded. Co-morbidity at the time of administration, and additional measures taken to achieve haemostasis, were also noted. Clinical response was assessed subjectively by the attending anaesthetist or surgeon, who recorded one of the following responses 1 h after the first dose: bleeding unchanged; bleeding reduced; or bleeding stopped. Laboratory results were collated, and blood products required in the 24 h before and after rFVIIa administration were noted. Details of thrombotic events occurring within 7 days were obtained, as was outcome and, if death occurred, cause of death.

Development of prognostic scoring system

A prognostic scoring system was devised and is shown in Table 1. One point was assigned for the presence of each of the following: coagulopathy (defined as a platelet count of $\leq 50 \times 10^9/l$, fibrinogen ≤ 1.0 g/l or PT/APTT ≥ 1.5 times the upper limit of the reference range); renal impairment (creatinine ≥ 120 µmol/l); hypothermia (core temperature ≤ 35 °C); transfusion of more than 10 units of red cells; and advanced age (≥ 60 years). A negative point was assigned for an obstetric indication. Points were allocated for the presence or absence of features at the time of administration of the first dose of rFVIIa. Patients were stratified into risk groups according to score: low risk (score ≤ 1), intermediate risk (> 1 but < 3) and high risk (≥ 3).

Statistical analysis

Transfusion data and coagulation results, before and after the administration of rFVIIa, were compared using the Wilcoxon signed rank sum test for paired non-parametric data. Patient characteristics were compared between survivor and non-survivor groups using the Mann-Whitney test for unpaired

non-parametric data and the Fisher's exact test for the analysis of binomial variables. The statistical validity of the prognostic scoring system was assessed using a χ^2 -test. *P*-values of < 0.05 were considered significant.

Results

Thirty-six patients [19 men and 17 women; median age 38 years (range 0.2–77 years)] received rFVIIa for major haemorrhage. Indications for treatment included surgical, traumatic or obstetric bleeding, as detailed in Table 2. No patient was known to have a pre-existing inherited disorder of haemostasis. Twenty-nine patients (81%) received the recommended dose of 90 $\mu\text{g}/\text{kg}$ rFVIIa. Doses ranged from 9 to 120 $\mu\text{g}/\text{kg}$, and two patients received an unknown dose. Twenty-five patients (69%) received a single dose, and seven patients (19%) received two doses. The maximum number of doses was five. Median time to administration of rFVIIa was 7 h (range 2–27 h). At the time of administration, 24 patients (67%) had coagulopathy (platelet count $\leq 50 \times 10^9/\text{l}$, fibrinogen $\leq 1.0 \text{ g/l}$ or PT/APTT ≥ 1.5 times the upper limit of the reference range), 13 patients (36%) had renal impairment (creatinine $\geq 120 \mu\text{mol/l}$), five patients (14%) had hypothermia (core temperature $\leq 35 \text{ }^\circ\text{C}$), six patients (17%) had sepsis (core temperature $\geq 38 \text{ }^\circ\text{C}$ requiring antibiotic treatment) and five patients (14%) had a pH of ≤ 7.25 on arterial blood gas sampling. Three had no comorbidity at the time of administration.

A clinical response to rFVIIa (reduction or cessation of bleeding) occurred in 26 patients (72%). Ten patients failed to respond (bleeding was unchanged), including three of the four patients who had received a rFVIIa dose of less than 90 $\mu\text{g}/\text{kg}$. Coagulation screen before and after treatment was available for 35 of the 36 patients. Median pre- and post-treatment PTs were 16 s (range 11–120 s) and 11 s (range 8–29 s) respectively ($P < 0.001$). Thirty-two of the 36 patients showed a shortening of PT, including eight of the 10 non-responders (data not shown). The median APTT also fell significantly ($P = 0.001$), but remained above the normal range following treatment. There was a significant rise in median fibrinogen level following treatment ($P = 0.003$) but no significant change in platelet count (Table 3). Two of the patients were Jehovah's witnesses and received no blood products. The data for all other patients were complete and showed (using the paired Wilcoxon rank sum test) a significant reduction in the requirement for red cells ($P < 0.001$) and fresh-frozen plasma ($P < 0.001$), and a reduction in the requirement for cryoprecipitate ($P = 0.169$) and platelets ($P = 0.166$) following administration of rFVIIa (Fig. 1).

Additional measures to obtain haemostatic control, simultaneous to the administration of rFVIIa, included infusion of antifibrinolytic agents (aprotinin in 39% and tranexamic acid in 31%), surgical ligation of bleeding vessels (22%), surgical wound packing (25%), diathermy (8%), and radiographic

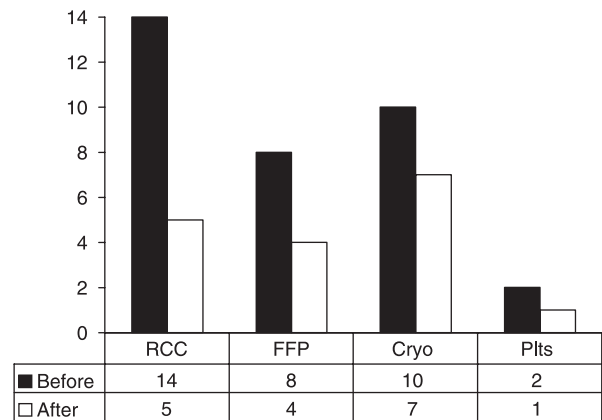


Fig. 1 Blood products transfused 24 h before and after the administration of recombinant activated factor VII (rFVIIa), presented as median number of units transfused. RCC, red cell concentrate; FFP, fresh-frozen plasma; Cryo, cryoprecipitate; Plts, adult platelet pool.

vascular embolization (6%). Three of the five patients receiving rFVIIa for obstetric bleeding required hysterectomy.

Nineteen patients (53%) died, seven within the first 24 h following administration of rFVIIa. Seventeen patients (47%) survived to discharge from hospital. Multiorgan failure was a cause of death in 13 of the 19 non-survivors (68%) and ongoing haemorrhage in eight (42%). Other causes of death were bowel ischaemia (16%) and sepsis (16%). No patient died as a direct result of a thrombotic event.

Four thrombotic events were reported. The case histories for these patients are detailed below, numbered as they appear in Table 2.

Case 22

A 14-year-old male patient was treated for postoperative bleeding following a repeat aortic valve replacement, replacement of pulmonary artery conduit, and repair of the right pulmonary artery and aortic arch. He developed an ischaemic left arm owing to subclavian artery thrombosis occurring 5 h after the administration of rFVIIa. The left subclavian artery had been surgically divided in order to access the operative site, the role of rFVIIa in thrombus formation remaining uncertain. No pre-existing vascular risk factors were present. Bleeding was reduced following the administration of rFVIIa, but he died from cardiac failure 6.5 h later. A postmortem, limited to examination of the thoracic contents only, revealed no evidence of haemorrhage or pulmonary embolism.

Case 26

A 70-year-old female patient with pre-existing coronary artery disease and ascending aortic aneurysm underwent elective

Table 2 Details of patients receiving recombinant activated factor VII (rFVIIa) for intractable haemorrhage

Patient no.	Age (years)	Gender	Diagnosis	Dose of rFVIIa ($\mu\text{g}/\text{kg}$)	Number of doses of rFVIIa	Prognostic score	Initial response	Outcome
1	6	M	Cardiac transplant	60	1	2	Yes	Survived
2	7	M	Cardiac transplant	90	1	3	Yes	Survived ^c
3	72	M	Aortic valve replacement	90	1	1	Yes	Survived ^c
4	15	M	Aortic valve replacement	120	1	1	No	Survived ^c
5	47	M	Lung transplant	90	1	1	Yes	Survived ^c
6	22	M	Lung transplant	90	2	1	Yes	Survived
7	76	M	Emergency AAA repair	90	1	3	Yes	Survived ^c
8	0.2	M	Ischaemic bowel resection	90	1	1	Yes	Survived
9	21	F	Emergency LSCS	90	1	0	No	Survived ^c
10	34	F	Emergency LSCS	90	1	0	Yes	Survived ^c
11	38	F	Elective LSCS	90	1	1	Yes	Survived
12	33	F	Post-partum haemorrhage	90	1	-1	Yes	Survived
13	30	F	Post-partum haemorrhage	90	1	0	Yes	Survived
14	23	F	Burns grafting	?	1	2	Yes	Survived
15	28	M	Multi-trauma	90	1	3	Yes	Survived
16	49	M	Elective spinal surgery	90	1	2	Yes	Survived
17	55	F	Ovarian cystectomy/Jehovah's witness	90	1	0	Yes	Survived ^c
18	77	M	Multi-trauma	90	1	4	Yes	Died (< 24 h) – MOF/haemorrhage ^c
19	25	F	Multi-trauma	40	2	4	No	Died (< 24 h) – Haemorrhage
20	75	M	Elective AAA repair	30	3	4	No	Died (< 24 h) – MOF ^c
21	68	M	Emergency AAA repair	90	3	3	Yes	Died (< 24 h) – haemorrhage/MOF
22	14	M	Aortic valve replacement and aortic root repair	?	1	3	Yes	Died (< 24 h) – cardiac failure ^b
23	43	M	Necrotizing pancreatitis	90	2	2	No	Died (< 24 h) – MOF
24	0.7	F	Brain tumour resection	90	4	1	No	Died (< 24 h) – haemorrhage
25	44	M	Multi-trauma	90	2	3	Yes	Died (4 days) – MOF ^c
26	70	F	Aortic valve replacement	90	1	4	Yes	Died (2 days) – MOF ^{bc}
27	48	M	Thoracic aortic dissection	9	2	3	No	Died (4 days) – haemorrhage ^c
28	69	M	Emergency AAA repair	90	1	4	No	Died (66 days) – MOF ^b
29	68	F	Elective splenectomy for ITP-Jehovah's witness	90	2	2	Yes	Died (28 days) – MOF/haemorrhage ^{ac}
30	30	F	Abdominal wall haematoma/liver disease	90	1	3	Yes	Died (18 days) – haemorrhage/sepsis
31	63	F	Necrotizing pancreatitis	90	1	4	Yes	Died (38 days) – MOF/sepsis ^c
32	75	F	Pelvic clearance/ovarian carcinoma	90	1	3	No	Died (2 days) – MOF ^c
33	4	M	Bleeding mouth tumour	90	1	0	Yes	Died (52 days) – malignancy ^c
34	38	F	Burns grafting	90	1	3	Yes	Died (27 days) – MOF ^b
35	55	F	Liver haematoma postcholecystectomy	90	2	2	Yes	Died (11 days) – MOF/sepsis ^c
36	66	F	Elective splenectomy for myelofibrosis	90	5	3	No	Died (22 days) – MOF/haemorrhage/sepsis ^c

AAA, abdominal aortic aneurysm; ITP, immune thrombocytopenia; LSCS, lower segment Caesarean section; MOF, multiorgan failure.

^aCase previously published [18].

^bPatient with thrombotic event.

^cPatient receiving antifibrinolytic agent.

Table 3 Laboratory investigations immediately before and 15 min after administration of recombinant activated factor VII (rFVIIa), presented as median and range of prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen and platelet count

	Before rFVIIa	15 min after rFVIIa	P-value ^a
Median PT s (range)	16 (11–120)	11 (8–29)	< 0.001
Median APTT s (range)	67 (27–250)	52 (29–200)	0.001
Median fibrinogen g/l (range)	1.4 (0.4–4.9)	2.1 (0.2–5.0)	0.003
Median platelet count $\times 10^9/l$ (range)	79 (2–449)	72 (21–196)	0.354

^aPaired Wilcoxon signed rank sum test.

Reference ranges: PT, 9–13 s; APTT, 24–39 s; fibrinogen, 1.5–4.0 g/l; platelet count, 150–450 $\times 10^9/l$.

Table 4 Comparison of demographic, laboratory, dosing and response characteristics for survivor ($n = 17$) and non-survivor ($n = 19$) groups, presented as percentages unless otherwise stated (median prognostic scores are also compared)

	Survivors	Non-survivors	P-value
Median age (range), years	30 (0.2–72)	55 (0.7–77)	0.027 ^d
Coagulopathy ^a	47%	84%	0.022 ^e
Renal impairment ^b	18%	53%	0.032 ^e
Hypothermia ^c	6%	21%	0.206 ^e
Median number of red cell units transfused (range)	12 (0–83)	22 (0–55)	0.069 ^d
Median time from start of bleeding to rFVIIa administration (range), hours	7 (2–21.25)	6 (1.75–27.25)	0.764 ^d
Clinical response	88%	53%	0.024 ^e
Median prognostic score (range)	1 (–1–3)	3 (0–4)	< 0.001 ^d

^aCoagulopathy defined as any of: platelet count $\leq 50 \times 10^9/l$; fibrinogen ≤ 1.0 g/l; or prothrombin time (PT)/activated partial thromboplastin time (APTT) ≥ 1.5 times the upper limit of reference range.

^bRenal impairment: creatinine ≥ 120 $\mu\text{mol/l}$.

^cHypothermia: core temperature ≤ 35 °C.

^dMann–Whitney test.

^eFisher's exact test.

rFVIIa, recombinant activated factor VII.

surgery for aortic valve replacement, aortic root replacement and triple vessel coronary artery bypass grafting. rFVIIa was administered for postoperative bleeding, and an ischaemic left foot developed 8 h later. Bleeding was reduced following the administration of rFVIIa, but she died from multiorgan failure 2 days later.

Case 28

A 69-year-old male patient with pre-existing coronary artery disease received rFVIIa for retroperitoneal bleeding following emergency repair of a ruptured abdominal aortic aneurysm. Although anuric acute renal failure occurred on day 1 post-operatively, aortic graft thrombosis and left renal artery thrombosis were not confirmed until 13 days after administration of rFVIIa, when computerized tomography (CT) was performed. Bleeding was unchanged after the administration of rFVIIa and he died from multiorgan failure 66 days later.

Case 34

A 38-year-old female patient received rFVIIa for postoperative bleeding following extensive skin grafting for burns. Large bowel ischaemia as a result of small vessel thrombosis (histopathological diagnosis on surgically resected bowel) occurred 5 days later. No pre-existing vascular risk factors were present. Although the bleeding stopped following administration of rFVIIa, she died from multiorgan failure 27 days later.

Of the patients who did not suffer arterial thrombotic events, five had a history of hypertension requiring antihypertensive medication. None had established vascular disease. Thirteen of the 29 patients surviving for more than 24 h underwent bilateral lower limb Doppler ultrasound within 5 days of rFVIIa, none of whom had confirmed deep-vein thrombosis.

Survivor ($n = 17$) and non-survivor ($n = 19$) groups were compared (Table 4). Survivors were younger (median age 30 vs. 55 years, $P = 0.027$) and were significantly less likely

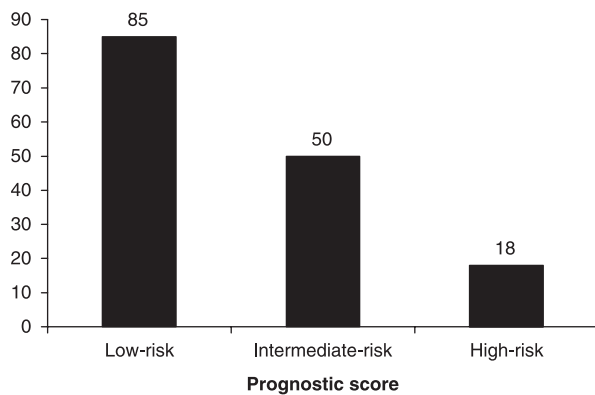


Fig. 2 Survival according to prognostic score. Survival expressed as percentage surviving to discharge from hospital (low risk, $n = 13$; intermediate risk, $n = 6$; high risk, $n = 17$).

to have coagulopathy (47% vs. 84%, $P = 0.022$) and renal impairment (18% vs. 53%, $P = 0.032$) at the time of administration. Survivors were less likely to have hypothermia (6% vs. 21%, not significant) and had fewer units of red cells transfused (median number of units 12 vs. 22, $P = 0.069$) prior to the administration of rFVIIa. Survivors were significantly more likely to have had an initial clinical response (88% vs. 53%, $P = 0.024$). Time from onset of bleeding to administration did not differ significantly between the two groups.

Using the prognostic scoring system (Table 1), patients were assigned to low-risk (score ≤ 1), intermediate-risk (> 1 but < 3) and high-risk (≥ 3) groups. Survival varied significantly ($P \leq 0.01$), with 85%, 50% and 18% survival in low-, intermediate- and high-risk groups, respectively (Fig. 2).

Discussion

This series examines the use of rFVIIa as a haemostatic agent in the management of intractable haemorrhage in a heterogeneous group of patients. By adhering to a local protocol, dose (90 $\mu\text{g}/\text{kg}$) and dosing regime (single dose or 2 doses 3 h apart) were standardized in the majority of cases. Prospective recruitment allowed data collection to be complete, with all patients identified and analysed.

The percentage of clinical responders, mortality rate and death caused by multiorgan failure are comparable to those seen in previous studies [11, 13, 14, 16].

A clinical response was seen in 72% of patients overall, but in only one of the four patients who received a dose of less than 90 $\mu\text{g}/\text{kg}$ rFVIIa. A recently published report showed a more favourable survival rate (61%) using a standard dose of 120 $\mu\text{g}/\text{kg}$ [15]. Both of these findings are contrary to a previous report that suggested the absence of a dose-response effect [11].

A significant reduction in PT within 15 min of administration of rFVIIa is demonstrated. APTT is similarly shortened, but the median APTT after treatment remains above the upper

normal limit, suggesting that the post-treatment PT may not represent *in vivo* correction of coagulopathy. This finding has been reported previously [12, 14, 16] and the potential for monitoring using thromboelastography has been explored in a small subset of patients in a series describing the use of rFVIIa in bleeding trauma patients [16].

Thrombotic events, all of which were arterial, were seen in 11% of the patients treated. In two of these patients, pre-existing vascular risk factors were apparent and, in a third, a surgical cause for arterial thrombosis was identified. The fourth patient developed large bowel ischaemia owing to small vessel thrombosis, a frequent occurrence in critically ill patients. Failure to exclude patients with pre-existing vascular disease from our series may have resulted in a relatively high rate of thrombotic complications. However, the immediate risk of death because of ongoing haemorrhage outweighed the potential for thrombotic complications in these patients.

Comparison of survivor and non-survivor groups highlighted important differences that may influence future criteria for patient eligibility to receive rFVIIa. Patient factors that predict survival are younger age and lack of comorbidity. The five patients receiving rFVIIa for obstetric indications all survived, possibly reflecting their relatively young age and lack of pre-existing comorbidity rather than being a result of the nature of the bleeding episode. This, in addition to previous studies showing good outcome in obstetric practice [19, 20], forms the basis for allocating a negative score for obstetric bleeding when using our prognostic scoring system. Co-morbidity at the time of rFVIIa administration, including significant renal impairment and hypothermia, featured more often in the non-survivor group.

Non-survivors were more likely to have received a greater than 10-unit red cell transfusion. Massive transfusion, accompanied by the development of dilutional coagulopathy, hypothermia and acidosis, frequently predicts mortality in patients with traumatic or surgical bleeding [21]. Conversely, early control of surgical bleeding and aggressive correction of hypothermia and acidosis improves survival [22]. A recently published series has shown a statistically significant reduction in response to rFVIIa in the presence of acidosis with a trend for higher mortality. The same study did not demonstrate hypothermia as an adverse prognostic feature [15].

Our finding, that the median number of red cell units transfused was lower in survivors than in non-survivors, supports the theory that earlier treatment with rFVIIa improves outcome by preventing the complications of massive transfusion and ongoing blood loss. Time from start of bleeding to administration of rFVIIa was not significantly shorter in the survivor group. A poor initial response is predictive of a poor outcome both in this and in a previous study [17].

The presence of severe coagulopathy at the time of rFVIIa administration has been shown in previous series to adversely influence outcome [14, 17] although this effect was not demonstrated in a larger study [13]. Failure to adequately correct

coagulopathy prior to the administration of rFVIIa was a prominent feature in our non-survivor group. The binding of rFVIIa to exposed tissue factor promotes the direct activation of factor X on the surface of activated platelets. Subsequent generation of thrombin from prothrombin forms a fibrin clot, which is then stabilized by factor XIII. In addition, some activation of factor X is thought to occur in the absence of tissue factor, generating a 'thrombin burst' [23]. Although this process can bypass the formation of the Tenase complex, explaining its role in the management of haemorrhage as a result of factor VIII and factor IX inhibitors, it would appear that adequate platelet and fibrinogen levels are still required in order to achieve haemostasis. Failure to correct coagulopathy reduces the efficacy of rFVIIa [17].

This study supports a role for rFVIIa as an adjunctive means of achieving haemostasis in patients with surgical, traumatic or obstetric haemorrhage that has failed to respond to surgical measures and blood product replacement. However, a beneficial effect on overall survival cannot be shown. The efficacy and safety of this agent requires further assessment, and the optimum dose and dosing regime remain to be determined.

There are several important limitations to this study. Without an untreated control group it is not possible to analyse the impact – beneficial or otherwise – of rFVIIa on overall survival. A comparison of 50 recipients of massive transfusion (at least 10 units of red cells) alone and 10 recipients of massive transfusion and rFVIIa showed no survival benefit in those who had received rFVIIa [14]. A further comparison of 81 coagulopathic patients receiving rFVIIa for traumatic bleeding and matched coagulopathic controls also failed to show a survival benefit in the patients treated with rFVIIa [16]. Although blood product requirements in the 24 h after rFVIIa administration are significantly reduced in comparison to the 24 h before, simultaneous surgical procedures, vascular embolization and administration of antifibrinolytics renders it difficult to determine the impact of rFVIIa on achieving haemostasis. Assessment of clinical response is subjective in the majority of patients. In addition, small numbers, and the knowledge that these are unlikely to be independent variables, limit statistical analysis of patient factors differing between the survivor and non-survivor groups.

The difficulty in allocation of this expensive resource still lies in the selection of appropriate patients. Incorporating those features that are shown to influence outcome into a prognostic score has allowed us to predict survival in patients appearing eligible for treatment with rFVIIa. Validation of this prognostic scoring system is required by a prospective study of larger patient cohorts before it can be used to select patients for treatment with rFVIIa.

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