

Antithrombotic and hemostatic stewardship: evaluation of clinical outcomes and adverse events of recombinant factor VIIa (Novoseven®) utilization at a large academic medical center

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Abstract

Background: Recombinant factor VIIa (rFVIIa) [Novoseven®] is utilized for the reversal of anticoagulation-associated bleeding and refractory bleeding in cardiac surgery. In August 2015, rFVIIa was transferred from the blood bank to the pharmacy at New York University (NYU) Langone Health. Concordantly, an off-label dosing guideline was developed. The objective of this study was to describe utilization and cost of rFVIIa and assess compliance to our dosing guideline.

Methods: We performed a retrospective, observational review of rFVIIa administrations post-implementation of an off-label dosing guideline. All patients who received rFVIIa between September 2015 and June 2017 were evaluated. For each rFVIIa administration, anticoagulation and laboratory values, indications for use, dosing, ordering and administration times, concomitant blood products, and adverse events were collected. Adverse events included venous thromboembolism, stroke, myocardial infarction, and death due to systemic embolism and mortality. The primary endpoint was the utilization of rFVIIa in accordance with the off-label dosing guideline. Secondary endpoints included hemostatic efficacy of rFVIIa, adverse events, blood products administered, and cost-effectiveness of rFVIIa transition to pharmacy.

Results: A total of 63 patients [pediatric ($n = 6$), adult ($n = 57$)] received rFVIIa, with the majority of use for refractory bleeding after cardiac surgery. The utilization of rFVIIa decreased after development of the off-label dosing guideline and transition from blood bank to pharmacy. The total incidence of thromboembolic events within 30 days was 19.6%; 17.6% arterial and 2% venous; 70% of patients with an adverse event were over 70 years of age. Use of rFVIIa reduced the median number of units of blood products administered.

Conclusion: Administration of rFVIIa for cardiac surgery appears to be effective for hemostasis. Transitioning rFVIIa from the blood bank to pharmacy and implementation of a dosing guideline appears to have reduced utilization. Patients receiving rFVIIa should be monitored for thromboembolic events. Elderly patients may be at higher risk for thromboembolic events.

Keywords: cardiac surgery, hemorrhage, hemostasis, rFVIIa, thromboembolism

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Introduction

Novoseven® is a recombinant preparation of human factor VIIa (rFVIIa) that facilitates activation of factors X and IX leading to thrombin production, activation of platelets and fibrin, and formation of a clot.¹ Human factor VIIa is currently approved for

the treatment of bleeding episodes and perioperative management in the setting of hemophilia A or B with inhibitors, congenital factor VII deficiency, and Glanzmann's thrombasthenia refractory to platelet transfusions. Recombinant factor VIIa has also been evaluated for surgery or trauma-related

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bleeding, variceal bleeding, reversal of anticoagulation therapy, and life-threatening bleeding refractory to standard of care.²⁻⁹ The optimal dosing strategy of rFVIIa when used for off label indications remains unknown, due to the lack of randomized controlled trials. Furthermore, there are thromboembolic risks associated with utilization of rFVIIa.

The product label for rFVIIa (Novoseven[®]) indicates a warning for serious arterial and venous thrombotic events.¹ Following administration of rFVIIa in clinical trials, thrombotic adverse reactions were seen in 4% of patients with acquired hemophilia and 0.2% of patients with congenital hemophilia.^{1,10-13} Due to circulation of tissue factor or predisposing coagulopathies, patients with disseminated intravascular coagulation (DIC), advanced atherosclerotic disease, crush injury, sepsis, concomitant treatment with four-factor prothrombin complex concentrates (4F-PCC), or uncontrolled post-partum hemorrhage may have an increased risk of thromboembolic events.¹⁰⁻¹³ Caution is advised when administering rFVIIa to patients with an increased risk of thromboembolic events, including patients with coronary heart disease, liver disease, post-operative immobilization, elderly patients, and neonates.¹⁰⁻¹³ Coagulation parameters such as prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT) have shown to be affected by administration of rFVIIa.¹⁴ However, there is no evidence of direct correlation between these parameters and risk of thromboembolic events or achievement of hemostasis.¹⁰⁻¹³ Monitoring of coagulation parameters may be used in conjunction with clinical signs of a hemostatic response to determine efficacy of rFVIIa, but should not be used alone.

Hemostatic agents are considered high-risk and high-cost medications that require close monitoring and careful dose titrations. Standardization of initial dosing strategies for rFVIIa may help balance the risk of bleeding and thrombosis. Several studies have examined the effects of an off-label dosing guideline in response to concerns of inappropriate use, safety, and cost of rFVIIa, and found that a guideline can serve to decrease the utilization and cost of rFVIIa while not sacrificing patient outcomes.^{15,16} Likewise, as part of a quality assessment, we sought to evaluate our transition of rFVIIa from the blood bank to pharmacy, and the overall hemostatic efficacy and safety

when used according to a developed off-label dosing guideline. These findings were presented as a poster at the International Society on Thrombosis and Haemostasis (ISTH) 64th Annual Scientific and Standardization Committee meeting in Dublin, Ireland in July 2018.

Methods

Institutional guideline

The antithrombotic therapy oversight group at New York University Langone Health (NYULH) developed a guideline in August 2015 to provide dosing recommendations for the use of rFVIIa for off-label indications, based on the available literature and local expert opinion (Table 1). These indications included (1) reversal of oral anticoagulant-associated, life-threatening hemorrhage in patients with documented history of heparin induced thrombocytopenia (HIT) or where 4F-PCC, such as Kcentra[®], is contraindicated, (2) reversal of upper gastrointestinal bleeding in the setting of coagulopathy associated with severe liver dysfunction, (3) to limit hematoma expansion in spontaneous intracerebral hemorrhage, (4) treatment of refractory bleeding after cardiac surgery in non-hemophilic patients, and (5) post-partum hemorrhage refractory to uterotonic. Prescribing of rFVIIa is restricted and requires approval by either the antithrombotic therapy team, an attending physician from critical care, hematology, or obstetrics, or a clinical pharmacotherapy specialist. Recombinant FVIIa dosing (rounded to the nearest milligram if weight-based) is selected according to the guideline indication and is administered with phytonadione in the setting of warfarin-associated intracranial hemorrhage or life-threatening bleeding. The guideline also outlines a strategy for repeat rFVIIa dosing if hemostasis is not achieved after the first administration. Following the implementation of the guideline, rFVIIa was relocated from the blood bank to the pharmacy with a goal to prepare and dispense to the bedside within 30 min of order placed in the electronic medical record. Computerized clinical decision support was enhanced to provide dosing recommendations, dose rounding, and administration considerations, per indication for rFVIIa in the off-label dosing guideline. The dosing protocol also recommends maintaining platelet function above 50,000/mm³ and pH >7.4 for efficacy of rFVIIa. There are no restrictions in place at the time of prescriber ordering for these laboratory

Table 1. NYULH off-label guideline indications and dosing recommendations.

Off-label indication	Dose	Concomitant medications or repeat dosing
Warfarin associated intracranial hemorrhage or life-threatening bleeding	Weight < 80 kg: 1 mg Weight > 80 kg: 2 mg	Give with phytonadione 10 mg/50 ml 5% dextrose in water
Non-warfarin, target specific oral anticoagulant associated intracranial hemorrhage or life-threatening bleeding	1 mg	None
Refractory upper gastrointestinal bleeding in severe liver disease	40 µg/kg	May repeat 40 µg/kg 20 min after first dose
Refractory bleeding after cardiac surgery or cardiopulmonary bypass	20 µg/kg	May repeat every 20 min to maximum dose of 80 µg/kg
Spontaneous intracerebral hemorrhage	40 µg/kg	May repeat 40 µg/kg 20 min after first dose
Post-partum hemorrhage refractory to uterotonics	50 µg/kg	May repeat 50 µg/kg 20 min after first dose
NYULH, New York University Langone Health.		

value cutoffs; however, pharmacists were educated on confirmation of these laboratory values prior to verification of the order.

Study design

All patients who received any dose of rFVIIa at NYULH post-implementation of the guideline between 1 September 2015 and 30 June 2017 were included. Data collection was obtained through a retrospective electronic medical record review of baseline demographics and past medical history, including venous thromboembolism (VTE), myocardial infarction (MI), stroke, transient ischemic attack (TIA), atrial fibrillation (AF), hypertension, congestive heart failure (CHF), chronic kidney disease, cirrhosis, coagulopathies, hemophilia, congenital factor VII deficiency, anticoagulant use, antiplatelet use, and indication for anticoagulation. A CHA₂DS₂-VASc score was calculated for patients with a history of AF.¹⁷ For each rFVIIa administration, anticoagulation and laboratory values, indications for use, dosing, ordering and administration times, concomitant blood products within 24 h, and adverse events were collected. Adverse events included VTE, stroke, TIA, death from systemic embolism, MI, hypersensitivity and DIC. Categorical variables were described as frequencies and proportions, and continuous variables were described as medians with interquartile ranges (IQR). Data was managed utilizing Research Electronic Data Capture (REDCap), a secure informatics system designed

to support data collection across various research disciplines.¹⁸ Due to the retrospective nature of this observational project done for quality assurance purposes, informed consent was not required and this project was exempt from review by our institutional review board (IRB). All patient data was de-identified and collected in compliance with the hospital's IRB exempt protocols.

Outcomes

The primary outcome was the utilization of rFVIIa at NYULH, defined by the indication and dose utilized during the study period. Secondary endpoints included adherence to the off-label dosing guideline, cost, hemostatic efficacy, and safety. Adherence to the off-label dosing guideline was assessed by reviewing time to administration, dose administered, and overall total cumulative dose. A subgroup analysis to evaluate adherence, efficacy, and safety of rFVIIa according to the off-label dosing guideline in patients with refractory bleeding after cardiac surgery was also conducted. Cost of rFVIIa was assessed utilizing pharmacy purchasing cost from 2016, comparing blood bank data from 2014 to pharmacy utilization in 2016. Blood bank costs were calculated based on the number of purchased vials in 2014, and pharmacy costs were calculated based on vials of rFVIIa documented as administered in 2016. Hemostatic efficacy was defined by evaluation of blood product administration and coagulation patterns within 24 h before and after administration of

Table 2. Pediatric baseline characteristics.

	Pediatric n = 6
Age, years	0.5 [0, 9]
Male, n (%)	3 (50)
Weight, kg	7 [3, 15]
Length of stay, days	35 [4, 100]
All values expressed as median (IQR) unless otherwise noted. Two patients had hemophilia and one patient had congenital factor VII deficiency. One patient was receiving anticoagulation for ECMO. ECMO, extracorporeal membrane oxygenation; IQR, interquartile range.	

rFVIIa. Safety of rFVIIa was defined by assessment of VTE, stroke, TIA, death from systemic embolism, MI, hypersensitivity, and DIC within 30 days of rFVIIa administration.

Results

Study population

A total of 63 patients [pediatric ($n = 6$), adult ($n = 57$)] received rFVIIa at NYULH between 1 September 2015 and 30 June 2017. The median age of adult patients was 69 years (IQR 55, 78), and the majority of patients were male (44, 77%). The most common comorbidities included hypertension (36, 63%), atrial fibrillation (17, 30%), and congestive heart failure (14, 25%). A total of 21 (37%) patients had an indication for anticoagulation, which was primarily atrial fibrillation (81%). Further baseline characteristics are described in Tables 2 and 3.

Overall utilization of rFVIIa

The utilization of rFVIIa for labeled indications included four (6%) patients with congenital factor VII deficiency, two (3%) patients with bleeding secondary to congenital hemophilia A or B with inhibitors, and one (2%) patient with bleeding secondary to acquired hemophilia (Figure 1). Of those with congenital factor VII deficiency, rFVIIa was used for one bleeding episode and three episodes of perioperative management. The utilization of rFVIIa for indications included on the NYULH off-label dosing guideline included 51 (81%) patients with refractory bleeding after cardiac surgery. Other indications for the use of rFVIIa that were not

Table 3. Adult baseline characteristics.

	Adult n = 57
Age, years, median (IQR)	69 [55, 78]
Male	44 (77)
Weight, kg, median (IQR)	76 [67, 88]
Length of stay, days, median (IQR)	11 [6, 19]
Past Medical History	
VTE	2 (4)
MI	3 (5)
Stroke/TIA	1 (2)
AF	17 (30)
CHA2DS2VASc, median (IQR)	3 [2, 4]
HTN	36 (63)
CHF	14 (25)
GI Bleed	2 (4)
CKD	7 (12)
Cirrhosis	2 (4)
Coagulopathy	1 (2)
Hemophilia	1 (2)
Congenital Factor VII Deficiency	3 (5)
Indication for Anticoagulation	
VTE	2 (10)
AF	17 (81)
Mechanical Heart Valve	2 (10)
All values expressed as n (%) unless otherwise noted. AF, atrial fibrillation; CHF, congestive heart failure; CKD, chronic kidney disease; ECMO, extracorporeal membrane oxygenation; HTN, hypertension; IQR, interquartile range; MI, myocardial infarction; TIA, transient ischemic attack; VTE, venous thromboembolism.	

included on the off-label guideline included one pulmonary hemorrhage, two refractory hemoperitoneum/hemothorax, one episode of oozing of blood during atrial fibrillation ablation, and one undocumented indication. Median weight-based dosing and total dose for each indication is shown in Table 4. All doses for labeled and

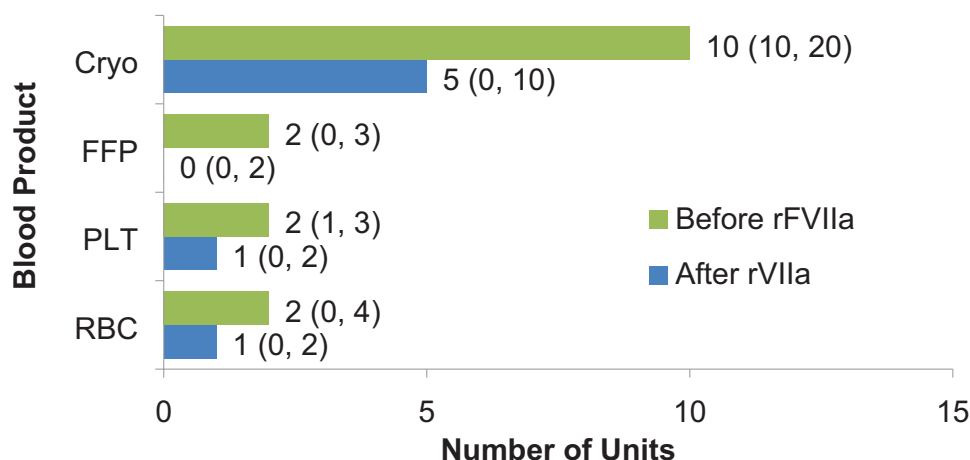


Figure 1. Indications for rFVIIa.

Other indications include pulmonary hemorrhage, refractory hemothorax not responding to blood and platelets, oozing of blood during atrial ablation, and indication not documented.
rFVIIa, recombinant factor VIIa.

Table 4. rFVIIa dose per indication ($n = 63$).

Indication	$\mu\text{g/kg}$	mg
Congenital hemophilia A or B with inhibitors ($n = 2$)	115 (113, 118)	3 (1.8, 4.6)
Congenital Factor VII deficiency ($n = 4$)	17 (14, 21)	0.9 (0.7, 1)
Acquired hemophilia ($n = 1$)	66	5
Refractory bleeding after cardiac surgery or cardiopulmonary bypass ($n = 51$)	21 (16, 27)	2 (1, 2)
Pulmonary hemorrhage ($n = 1$)	97	0.3
Refractory hemoperitoneum/hemothorax not responding to blood and platelets ($n = 2$)	33 (29, 37)	3 (2.5, 3.5)
Oozing of blood into pericardial space during atrial ablation ($n = 1$)	92	8
Indication not documented ($n = 1$)	117	1.2

All values are expressed as median (IQR) unless otherwise noted.
IQR, interquartile range; rFVIIa, recombinant factor VIIa

off-label guideline indications were similar to the recommended dosing strategies per the rFVIIa package insert and NYULH off-label dosing guideline. In all, 35 (56%) patients received one dose, whereas 28 (44%) patients received more than one dose (Table 5). In 2014, the total cost of rFVIIa purchased by the blood bank was \$583,100. After implementation of the off-label dosing guideline and transition to the pharmacy,

the total cost of rFVIIa administered in 2016 from the pharmacy was \$168,600.

Utilization of rFVIIa in cardiac surgery

A subgroup analysis was conducted to evaluate adherence, efficacy, and safety of rFVIIa according to the off-label dosing guideline in patients with refractory bleeding after cardiac surgery (Table 6).

Table 5. Number of doses administered ($n = 63$).

Number of doses	Patients
One	35 (56)
Greater than one	28 (44)
Two	17 (61)
Three	8 (29)
Four	1 (4)
Eight	1 (4)
Other*	1 (4)

All values expressed as n (%) unless otherwise noted.
*Other is a patient with congenital hemophilia A or B with inhibitors who received 111 doses of rFVIIa over the course of our collection period during many separate admissions.

In accordance with the NYULH guideline, the dose was delivered and administered within 30 min of order entry in 33 (65%) patients, and doses were administered greater than 20 min apart in 16 (80%) patients. Although 39 (77%) patients received within 10 $\mu\text{g}/\text{kg}$ of the 20 $\mu\text{g}/\text{kg}$ dose recommended by the NYULH dosing guideline; 9 (18%) patients received a dose greater than 30 $\mu\text{g}/\text{kg}$, and 3 (15%) patients received cumulative doses greater than the recommended maximum dose of 80 $\mu\text{g}/\text{kg}$. In patients who received rFVIIa for refractory bleeding after cardiac surgery, hemostatic efficacy was assessed by blood product administration before and after administration of rFVIIa (Figure 2). The median number of units of cryoprecipitate decreased from 10 (IQR 10, 20) to 5 (IQR 0, 10), of fresh frozen plasma from 2 (IQR 0, 3) to 0 (IQR 0, 2), of platelets from 2 (IQR 1, 3) to 1 (IQR 0, 2), and of red blood cells from 2 (IQR 0, 4) to 1 (IQR 0, 2), after the administration of rFVIIa. A total of 10 (20%) patients experienced a thromboembolic event within 30 days of rFVIIa administration (Figure 3). There was one (2%) occurrence of deep vein thrombosis (DVT) and nine (18%) occurrences of stroke or TIA. The DVT occurred on day 17, in a patient on a heparin bridge to warfarin. Of the nine strokes/TIAs, there were seven ischemic strokes, which occurred on day 0 ($n = 2$), day 1 ($n = 2$), day 2 ($n = 1$), and day 3 ($n = 2$) post rFVIIa administration. Only one out of these seven patients had a prior indication for anticoagulation, which had not been restarted due to thrombocytopenia and risk of bleeding post procedure. Out of the two TIAs that occurred, one occurred on day 2

Table 6. rFVIIa utilization in patients with refractory bleeding after cardiac surgery ($n = 51$).

	Patients
Compliance to Guideline	
One dose [^] ($n = 31$)	18 (58)
More than one dose [#] ($n = 20$)	10 (50)
First Dose* ($n = 50$)	
$20 \pm 10 \mu\text{g}/\text{kg}$	39 (77)
<10 $\mu\text{g}/\text{kg}$	2 (4)
>30 $\mu\text{g}/\text{kg}$	9 (18)
Verification to Administration Time ($n = 51$)	
<30 min	33 (65)
30–60 min	6 (12)
>60 min	9 (18)
Times not documented	2 (4)
Administration before verification	1 (2)
First and Second Doses ($n = 20$)	
>20 min apart	16 (80)
<20 min apart	2 (10)
Not documented	2 (10)
Cumulative Dose ($n = 20$)	
<80 $\mu\text{g}/\text{kg}$	15 (75)
>80 $\mu\text{g}/\text{kg}$	3 (15)
Doses not documented	2 (10)

All values expressed as n (%) unless otherwise noted.
[^]Compliance if met all of the following criteria: dose $20 \pm 10 \text{ mcg}/\text{kg}$, verification to administration time <30 min.
[#]Compliance if met all of the following criteria: dose $20 \pm 10 \text{ mcg}/\text{kg}$, verification to administration time <30 min, first and second doses >20 min apart, cumulative dose < 80 mcg/kg .
^{*}One dose was not documented.

in a patient that had atrial fibrillation, and one occurred day 12 post rFVIIa. Five (50%) adverse events occurred in patients receiving more than one dose, and seven (70%) occurred in patients over 70 years of age. There were no occurrences of

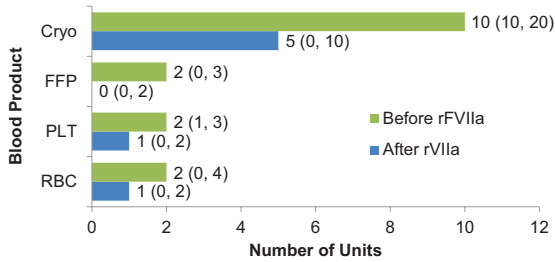


Figure 2. Blood product administration in patients with refractory bleeding after cardiac surgery ($n = 51$).

All values expressed as median (IQR).

Cryo, cryoprecipitate; FFP, fresh frozen plasma; IQR, interquartile range; PLT, platelets; RBC, red blood cell; rFVIIa, recombinant factor VIIa.

pulmonary embolism, MI, hypersensitivity reaction, or DIC.

Discussion

We found that implementation of an off-label dosing guideline and the transition of rFVIIa from the blood bank to the pharmacy appeared to offer a safe and cost-effective strategy for the management of this high-risk, high-cost hemostatic agent. Previously, Owen *et al.* demonstrated that implementation of a guideline for the use of rFVIIa led to an increase in appropriate prescribing, decrease in rFVIIa utilization, and a decrease in costs.¹⁵ They found that the mean total dosage of rFVIIa administered per patient before implementation of the guideline was 81.8 $\mu\text{g}/\text{kg}$ compared with 45.3 $\mu\text{g}/\text{kg}$ after guideline implementation, and there was an overall 49% decrease in rFVIIa administered monthly.¹⁵ This led to a decrease of \$110,014 in the semiannual costs of rFVIIa.¹⁵ Furthermore,

the implementation of a guideline did not show to adversely affect patient outcomes.¹⁵ In addition, Trueg *et al.* conducted an evaluation of rFVIIa and PCC orders before and after implementation of a pharmacist-directed blood factor stewardship program.¹⁹ Mortality at 28 days was similar between groups (53.9% versus 50%, $p = 0.77$); however, there was an annual cost savings of \$375,539, primarily through a significant reduction in rFVIIa utilization.¹⁹ Similar to these studies, we found a decrease in rFVIIa administered with the implementation of an off-label dosing guideline, leading to a \$414,500 decrease in the annual costs of rFVIIa. This may have been attributed to the recommendation for lower initial starting doses, the use of dose rounding, and purchasing multiple vial strengths to limit waste.

The majority of rFVIIa use at NYULH was for refractory bleeding after cardiac surgery or cardiopulmonary bypass. A number of previously published reports have suggested that rFVIIa is appropriate for rescue therapy of massive bleeding in cardiovascular surgery patients.^{9,20–29} The NYULH off-label guideline recommends a dose of 20 $\mu\text{g}/\text{kg}$ for this indication, followed by repeat dosing of 20 $\mu\text{g}/\text{kg}$ to a maximum cumulative dose of 80 $\mu\text{g}/\text{kg}$ if needed. This recommendation was implemented in order to mitigate potential harm associated with the use of rFVIIa, without compromising efficacy. Although previous studies have used higher doses in this patient population, the antithrombotic therapy oversight group along with cardiac surgery at NYULH recommended a lower initial dose, with the ability to repeat dosing if refractory bleeding persisted.^{6,9,20,29} In our evaluation, 77% of doses were according to the NYULH guideline, 4%

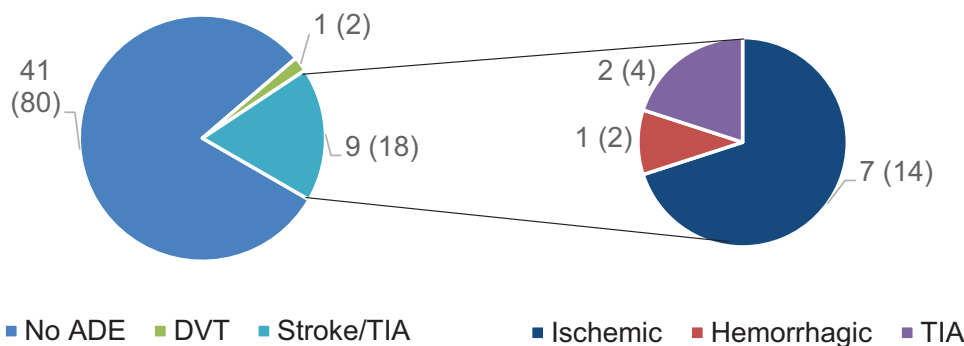


Figure 3. Adverse events in patients with refractory bleeding after cardiac surgery within 30 days ($n = 51$).

All values expressed as n (%). One patient had both an ischemic and hemorrhagic stroke.

ADE, atherosclerotic dyscirculatory encephalopathy; DVT, deep vein thrombosis; TIA, transient ischemic attack.

were lower than recommended, and 18% were higher than recommended.

Transfusion of blood after cardiac surgery has been associated with decreased long-term survival, and there is an 8-fold increase in the risk of death with administration of 5 units of packed red blood cells (pRBC).⁶ Transfusion-related acute lung injury and transfusion-associated circulatory overload contribute significantly to this mortality in post-operative cardiac surgery patients.³⁰ We found that administration of rFVIIa reduced the median number of units of blood products administered, a finding previously reported in the literature.^{6,9,29} In one retrospective, observational review, the units of pRBC and platelets administered decreased by an average of 4.28 ± 6.74 units and 5.15 ± 12.9 units, respectively, after administration of rFVIIa.²⁹ The reduction in units of pRBC administered was significant among dosing quartiles >30 $\mu\text{g}/\text{kg}$, but not in the dosing quartile <30 $\mu\text{g}/\text{kg}$. As the amount of blood products administered prior to rFVIIa was lower in our study, we believe that lower doses of rFVIIa for refractory bleeding in cardiac surgery may be a reasonable approach. Although rFVIIa has been shown to be effective for managing massive blood loss in cardiovascular patients, treatment using rFVIIa carries a significant risk of thromboembolic events.^{6,9,20,29,31} In our study, the total incidence of thromboembolic events within 30 days was 19.6%, with 17.6% being arterial events and 2% being venous events. Seven (70%) patients with an adverse event were over 70 years of age. This finding is higher than previous reported literature, which reports 10.2% total thromboembolic, 5.5% arterial, and 5.3% venous events.³² However, this is consistent with literature supporting higher thromboembolic event rates in patients 65 years of age or older.³² In addition, the utilization of rFVIIa in cardiac surgery patients may have predisposed these patients to a higher risk for arterial thromboembolic events, as the majority of anticoagulation therapy was administered due to underlying atrial fibrillation.

Our study is limited by its retrospective design and moderate sample size. In addition, although blood product administration pre- and post- rFVIIa were collected, the decision to administer these products was up to the cardiac surgery team. In addition, the data available for the indications for rFVIIa from

the blood bank could not be assessed due to lack of documentation of dose or indication in the administration record. Therefore, although we did see a decrease in cost after the transition to the pharmacy, we cannot identify if this decrease is due to the oversight by pharmacy, creation of the dosing guideline, chance, or other reasons. Lastly, patients in our study were not managed according to a standardized blood product administration protocol, and overall use of blood products was lower than reported in similar previous literature.^{24,29}

Conclusion

Implementation of an off-label dosing guideline, enhanced computerized clinical decision support in the electronic medical record, and transition of rFVIIa from the blood bank to the pharmacy appears to have reduced costs associated with the use of rFVIIa. Administration of rFVIIa at the recommended dosage for cardiac surgery appears to be an effective strategy for hemostasis, as determined by reduction in blood product administration. Our analysis supports previously reported literature regarding standardization of an approach to the use of high-risk hemostatic agents.^{15,16} As we found that the majority of thromboembolic events occurred in patients over 70 years of age, we recommend judicious use of rFVIIa, and careful monitoring in this population. Larger, prospective studies are needed to determine the optimal use and dosage of rFVIIa. In addition, strategies, such as the use of other hemostatic agents such as four-factor prothrombin complex concentrates (4F-PCC) may be warranted for the management of refractory bleeding post cardiac-surgery.³³⁻³⁵ Comparing hemostatic agents such as rFVIIa to 4F-PCC, to determine the optimal agent and dose may be necessary, to determine the most safe, cost-effective agent.


Conflict of interest statement

The authors declare that there is no conflict of interest.

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