



## Original Contribution

# Safety and effectiveness of Factor Eight Inhibitor Bypassing Activity for direct oral anticoagulant-related hemorrhage reversal

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## ABSTRACT

**Background:** The incidence of patients who present with life-threatening bleeding complications has been increasing as the use of direct oral anticoagulation (DOAC) has increased. Therefore, effective reversal agents are urgently needed. Current guidelines recommend the use of prothrombin complex concentrates (PCCs) and activated PCCs (aPCC) for reversal of DOAC anticoagulant activity in the setting of traumatic and non-traumatic intracranial hemorrhage (ICH). However, little data is available.

**Objective:** Herein, we investigated the safety and effectiveness of Factor Eight Inhibitor Bypassing Activity [FEIBA (an aPCC)] in a population of patients who required emergent reversal of DOAC for hemorrhage or urgent surgical interventions.

**Methods:** This is a case series study. Medical records from patients who required emergent reversal of DOAC for life threatening hemorrhage or urgent surgical interventions were collected from February 1, 2014, to April 1, 2017 and reviewed. Data, including demographics as well as safety, outcomes, and dosing of FEIBA for reversal of DOAC effects were collected and descriptive statistics were obtained.

**Results:** Forty-two patients who received FEIBA were included in the study. The rates of thrombotic events (10%), hemorrhage progression (10%), and observed mortality (29%) were similar to rates previously published in the limited literature evaluating aPCC use in this population.

**Conclusion:** This case series suggests that FEIBA administration is relatively safe and effective to reverse DOACs in the setting of hemorrhage or need for urgent surgical procedures. Until target-specific reversal agents are available, future studies are warranted to evaluate the effectiveness of aPCC administration for DOAC-associated hemorrhagic complications.

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## 1. Introduction

Anticoagulation-induced bleeding is a serious adverse drug event associated with significant morbidity and mortality. It is also responsible for thousands of emergency department (ED) visits and hospital admissions in the United States (US) annually [1]. Utilization of direct oral anticoagulants (DOACs) is becoming more common due to limitations associated with warfarin therapy, demonstration of lower bleeding risk, and increased guideline support for their use in non-valvular atrial fibrillation and venous thromboembolism [2–6]. With an increasing incidence of DOAC usage in patients who present with life-threatening

bleeding complications, effective reversal agents are desperately needed.

Guidelines recommend the use of prothrombin complex concentrates (PCCs) and activated PCCs (aPCC) for reversal of DOAC anticoagulant activity in the setting of traumatic and non-traumatic intracranial hemorrhage (ICH) [5,6]. Studies show that aPCCs may present a therapeutic advantage over PCCs with a reduced time to thrombin generation. However, these studies were conducted in healthy volunteers [7]. Moreover, the incorporation of activated factor VII may lead to greater risk of thrombosis due to thrombin generation.

Another limitation of aPCC is the paucity of data regarding specific dosing for DOAC reversal. Current dosing schemes have been extrapolated from animal models, healthy human subjects, and case series [8]. Without adequate laboratory testing for DOAC activity, it is difficult to truly validate their effectiveness. Until specific antidotes

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(e.g., andexanet alfa, aripazine) for DOACs are available, guidelines will continue to recommend PCCs and aPCCs as 1st line treatment options for reversal of DOAC for bleeding [5,6].

The primary objective of this study was to assess the safety and effectiveness of Factor Eight Inhibitor Bypassing Activity [FEIBA (an aPCC)] in patients who required emergent reversal of DOAC for bleeding or urgent surgical intervention. Secondary objectives included evaluation of the dosing and effectiveness of aPCCs in patients requiring urgent reversal.

## 2. Methods

### 2.1. Study design

This study was approved by the University of Iowa Institutional Review Board. A single-center, case series was conducted to analyze the use of aPCCs for reversal of DOAC-associated hemorrhage and prevention of hemorrhagic complications in patients needing urgent procedures. The study was conducted at an 811-bed academic referral center. Utilizing our institution's electronic medical record (EMR), patients who received FEIBA in accordance with institutional protocol for acute hemorrhage and pre-operatively for urgent procedures from February 1, 2014, to April 1, 2017 were identified. Our FEIBA dosing protocol for reversal of DOAC-induced life-threatening bleed recommends a dosing range of 25–50 units/kg based on actual body weight and rounded to the nearest vial size. Additional doses or dosages outside the recommended range must be approved by hematology faculty.

Criteria for inclusion were defined as (1) age 18 years and older, (2) received DOAC prior to admission, and (3) received FEIBA for hemorrhage. Patients were excluded if FEIBA was ordered, but not administered, if they did not receive a DOAC prior to admission, if they received FEIBA for reversal prior to surgical procedure not in the setting of hemorrhage, and if they had hemophilia.

### 2.2. Data collection

We abstracted clinical variables from the EMR using both database query and manual data collection by two independent reviewers. Collected data included patient age, gender, weight, height, body mass index, past medical history, creatinine clearance, DOAC indication and use, antiplatelet use, type of hemorrhage, surgical intervention during admission, including craniectomy and external ventricular drain (EVD) placement, administration of other reversal agents such as tranexamic acid, phytonadione (vitamin K), or blood products, dose and time to FEIBA administration, thromboembolic complications, inferior vena cava filter placement, and resumption of anticoagulation. Admission clinical status was evaluated using the Glasgow Coma Scale (GCS), ICH size, and ICH score. Data regarding thromboembolic events for 30 days after FEIBA administration, including the hospital course and post-discharge encounters at our institution, were collected.

For patients with ICH, neuroimaging was reviewed by a neuroradiologist (BP) who reported ICH volumes. ICH scores were calculated at the time of analysis based on available chart data. Hemorrhage progression was assessed by comparing the hemorrhages on initial and follow-up imaging. For patients with extra-cranial hemorrhages, progression of hemorrhage was evaluated based on chart review, including imaging, progress, and procedure notes. Patients without evidence of bleeding on physical exam or follow-up imaging, not requiring additional blood transfusions, and with stable hemoglobin values were considered to have no progression of hemorrhage.

### 2.3. Primary and secondary endpoints

The primary safety endpoint assessed was the prevalence of in-hospital thromboembolic events in this selected patient population. Thromboembolic events were defined as deep vein thrombosis (DVT)

diagnosed by duplex ultrasound, myocardial infarction (MI) diagnosed by clinically defined criteria, including cardiac biomarkers and electrocardiogram patterns, pulmonary embolism (PE) diagnosed by computed tomography angiography, ischemic stroke diagnosed by neuroimaging, and disseminated intravascular coagulation with onset after administration of FEIBA. The primary endpoints related to the effectiveness of FEIBA included hemorrhage progression based on imaging and clinical assessment by patient care providers. Secondary objectives included evaluation of the FEIBA dosing as it relates to the primary endpoints of safety and effectiveness of FEIBA in patients requiring urgent reversal.

### 2.4. Statistical analysis

Descriptive statistics were obtained. Statistical analysis was performed using the GraphPrism software package (GraphPrism, San Diego, CA, USA).

## 3. Results

### 3.1. Patient characteristics

We included 42 patients in the study. Demographic data are presented in Table 1 and indications for FEIBA administration are indicated in Fig. 1. The home DOACs for this population included apixaban in 14 patients (33%), rivaroxaban in 23 patients (55%), and dabigatran in 5

**Table 1**  
Demographics and treatment characteristics of all patients.

	FEIBA recipients n = 42
Demographics	
Gender, males, n (%)	21 (50)
Age at admission, years, median (IQR)	73 (68, 82)
Weight, kg, median (IQR)	84 (69, 98)
CrCl, mL/min, median (IQR)	61 (45, 79)
Transfers to UIHC, n (%)	34 (81)
Anticoagulant, n (%)	
Apixaban (5 mg BID)	14 (33)
Rivaroxaban (20 mg QD)	23 (55)
Dabigatran (150 mg BID–5 patient, QID 1-patient)	5 (12)
Antiplatelet, n (%)	
Aspirin	20 (48)
Clopidogrel	2 (5)
Aspirin, clopidogrel	3 (7)
None	17 (40)
Reason for anticoagulation, n (%)	
Atrial fibrillation	33 (79)
Valve replacement	1 (2)
Pulmonary or venous thromboembolism	7 (17)
Other	1 (2)
Type of hemorrhage, n (%)	
Traumatic intracerebral hemorrhage	18 (43)
Spontaneous intracerebral hemorrhage	12 (29)
Extracranial hemorrhage	12 (29)
Treatment strategy, n (%)	
FEIBA	42 (100)
FEIBA dose, units, median (IQR)	2395 (2122, 3135)
FEIBA dose per weight, <sup>a</sup> units/kg, median (IQR)	30 (25, 37)
Time to reversal agent administration, minutes	
From initial presentation, median (IQR)	292 (195, 419)
From UIHC presentation, median (IQR)	136 (92, 181)
Tranexamic acid	22 (52)
Vitamin K	2 (5)
Fresh frozen plasma	2 (5)
KCentra	4 (10)
Platelet transfusion	5 (12)
Surgical intervention for hemorrhage	17 (40)

CrCl creatinine clearance, FEIBA Factor Eight Inhibitor Bypassing Activity, IQR interquartile range.

<sup>a</sup> Based on actual body weight.

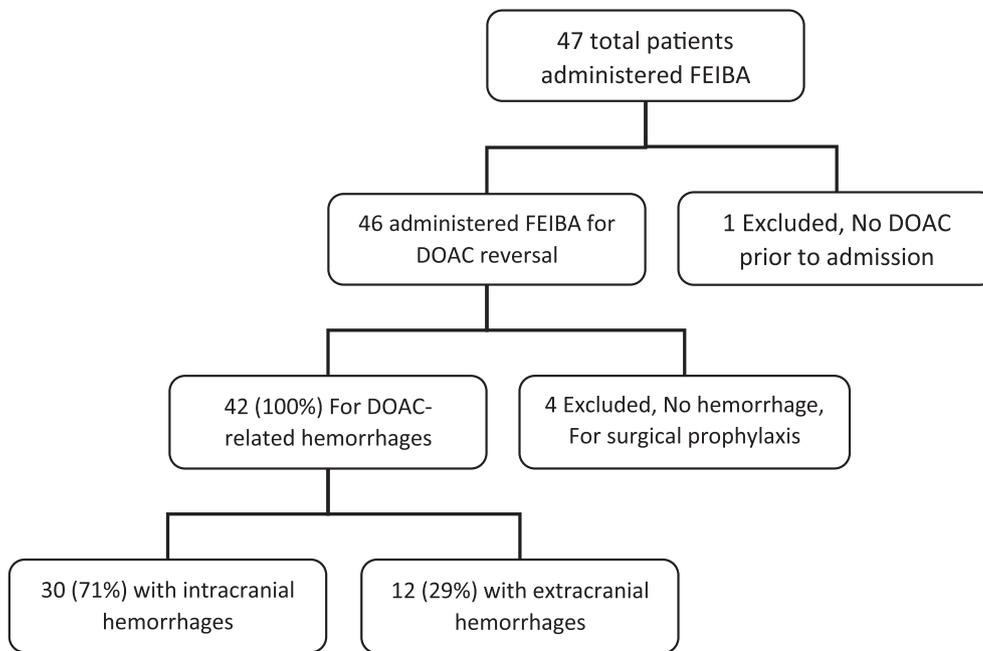


Fig. 1. Patients administered FEIBA at UIHC with reason for administration and injury.

patients (12%). The indication for reversal was ICH in 30 patients (71%). Additional demographic data for ICH patients are presented in Table 2. The indication for reversal in 12 patients (29%) was extracranial hemorrhage, including gastrointestinal bleeding, spinal epidural hematomas, trauma induced arterial bleeding, and tumor induced bleeding.

As shown in Table 1, the median dose of FEIBA was 2395 units (IQR 2122–3135) with a median weight-based dose of 30 units/kg (IQR 25–37). Concomitant anti-platelet use occurred with 25 patients (60%), and five patients (12%) received platelet transfusions. Other administered reversal agents included vitamin K in two patients (5%), fresh frozen plasma in two patients (5%), and 4-factor PCC in four patients (10%) (Table 1). These four patients received 4-factor PCC before transferring to our institution. All other reversal agents were administered at our institution.

### 3.2. FEIBA safety

Thromboembolic events occurred in four patients (10%) after FEIBA administration. Three were diagnosed with DVT and one with MI. The average FEIBA dose for patients with thromboembolic complications was 29 units/kg. The median time to thrombotic event was four days after FEIBA administration. All three patients who experienced DVT were on apixaban prior to admission. Two were only on apixaban and received only FEIBA for reversal with DVT occurring three or less days after FEIBA dose, both eventually discharged from the hospital. The third DVT patient was on apixaban and aspirin, received TXA and FEIBA, and had a DVT five days after FEIBA dose. This patient was compassionately extubated because of no neurologic improvement. The patient who experienced an MI 8 days after FEIBA was on rivaroxaban and aspirin and had received 4-factor PCC at the transferring institution. This patient was unable to be weaned from her ventilator after developing pneumonia and was compassionately extubated.

### 3.3. Effectiveness

Overall, four patients (10%) had progression of their hemorrhages after FEIBA administration and urgent surgical intervention. All of these patients had ICH, two were taking apixaban, two were on

rivaroxaban, two were on aspirin, one was on clopidogrel, and one had no anti-platelet medication. The average dose of FEIBA in patients with hemorrhage progression was 26 units/kg. The average dose of FEIBA in patients without hemorrhage progression was 33 units/kg.

The first patient (ID 28 in Table 3) was on apixaban and aspirin, received FEIBA, desmopressin and TXA, and had a ventriculostomy. Her co-morbidities included atrial fibrillation and hypertension. The second patient (ID 43 in Table 3) was on rivaroxaban and received TXA. Her co-morbidities included atrial fibrillation, hypertension, and chronic obstructive pulmonary disease. The third patient (ID 48 in Table 3) was on rivaroxaban and aspirin and received FEIBA and TXA. Her comorbidities included atrial fibrillation, stage three chronic kidney disease, asthma, diabetes mellitus type two, and heart failure with preserved ejection fraction. She survived her injuries and was discharge to a skilled nursing facility. The fourth patient (ID 50 in Table 3) was on apixaban and clopidogrel. He initially had ventriculostomy, but coagulopathy intraoperatively restricted the patient from having hemicraniectomy and hematoma evacuation. He then received FEIBA, TXA, and platelets. The next morning, he returned for intervention, but intraoperative bleeding was difficult to control from the skin edges, galea, and central line site. The procedure was again aborted. This patient was evaluated by a hematologist who attributed continued hemorrhage to platelet dysfunction secondary to alcohol induced liver cirrhosis. His other comorbidities included history of venous thromboembolism, diabetes mellitus type 2, hypertension, and coronary artery disease with recent NSTEMI.

Thirty six patients (86%) had no progression of hemorrhage after FEIBA administration. Seventeen patients (40%) required surgical interventions for active hemorrhage. One patient presented with acute organ failure with blood around the endotracheal tube, but no obvious source of hemorrhage, and was given FEIBA. Her coagulopathy with an initial INR of 5.4 was thought to be more substantial secondary to liver failure.

Notably, two patients (5%) had unknown hemostasis or progression outcomes due to no prior or follow-up imaging (Fig. 2). These two patients had no imaging either before or after FEIBA administration for various reasons, including poor prognosis and transition to palliative care.

Twelve patients (29%) died during their hospital stay (Table 3). No deaths were attributed to thromboembolic complications. Of the four patients (10%) with hemorrhage progression, three patients were

**Table 2**  
Demographics and treatment characteristics of patients presenting with ICH.

	FEIBA recipients n = 30
<b>Demographics</b>	
Gender, males, n (%)	15 (50)
Age at admission, years, median (IQR)	75 (69, 84)
Weight, kg, median (IQR)	83 (68, 91)
CrCl, mL/min, median (IQR)	58 (45, 74)
Transfers to UIHC, n (%)	25 (83)
<b>Anticoagulant, n (%)</b>	
Apixaban	11 (37)
Rivaroxaban	17 (57)
Dabigatran	2 (7)
<b>Antiplatelet, n (%)</b>	
Aspirin	14 (47)
Clopidogrel	1 (3)
Aspirin, clopidogrel	3 (10)
None	12 (40)
<b>Reason for anticoagulation, n (%)</b>	
Atrial fibrillation	22 (73)
Valve replacement	1 (3)
Pulmonary or venous thromboembolism	6 (20)
Other	1 (3)
<b>Type of hemorrhage, n (%)</b>	
Traumatic intracerebral hemorrhage	18 (60)
Spontaneous intracerebral hemorrhage	12 (40)
<b>Location of hemorrhage, n (%)</b>	
Intraparenchymal hemorrhage	3 (10)
Intraparenchymal hemorrhage with intraventricular hemorrhage	6 (20)
Intraparenchymal hemorrhage with subarachnoid hemorrhage	1 (3)
Intraparenchymal hemorrhage with subdural hemorrhage	2 (7)
Intraventricular hemorrhage	1 (3)
Subdural hemorrhage	9 (30)
Subdural hemorrhage with subarachnoid hemorrhage	3 (10)
Subarachnoid hemorrhage	4 (13)
Intraparenchymal hemorrhage with intraventricular hemorrhage and subdural hemorrhage	1 (3)
<b>Treatment strategy, n (%)</b>	
FEIBA	30 (100)
FEIBA dose, units, median (IQR)	2358 (2098, 2683)
FEIBA dose per weight, <sup>a</sup> units/kg, median (IQR)	30 (25, 37)
Vitamin K	1 (3)
KCentra	3 (10)
Platelet transfusion	3 (10)
Surgical intervention for hemorrhage	9 (30)

CrCl creatinine clearance, FEIBA Factor Eight Inhibitor Bypassing Activity, IQR interquartile range.

<sup>a</sup> Based on actual body weight.

compassionately extubated and one patient was discharged to a skilled nursing facility. Patient outcomes and disposition are presented in Table 4. Of the 30 ICH patients, 10 patients (33%) died prior to discharge.

#### 4. Discussion

The lack of reversal agents has become a challenge for providers and patients with DOAC-associated acute hemorrhage. Currently, no specific antidotes are available for most DOACs with the exception of dabigatran (idarucizumab). Current guidelines recommend the use of PCCs and aPCCs for reversal of DOAC activity in the setting of intracranial hemorrhage. However, there are limitations and risks. Given the lack of data on human subjects with ICH human, current dosing schemes have been extrapolated from animal models, healthy human subjects, and small case series. This combined with the lack of methods for laboratory evaluation of DOAC activity creates difficulty in establishing strong, evidenced based dosing schemes. Additionally, evidence evaluating the dosing,

safety, and effectiveness of aPCCs in the setting of extracranial hemorrhage and for prophylactic DOAC reversal prior to surgery is limited.

This is the largest review of non-hemophilia patients taking DOAC and receiving FEIBA (an aPCC) in the literature to date. Our data indicate that FEIBA is relatively safe to administer in patients with DOAC-associated hemorrhage. Four patients (10%) had thromboembolic complications related to FEIBA administration. None were on pharmacologic venous thromboembolism prophylaxis prior to their complication. All had diagnoses leaving them with limited mobility for extended periods of time. This rate is similar to rates reported ranging from 0% to 18% in the literature evaluating FEIBA use in patients on warfarin or DOACs with ICH [9–12]. All four patients were on apixaban or rivaroxaban for atrial fibrillation or venous thromboembolism, underlying conditions which put these patients at higher risk of developing thrombosis. Our results add to the evidence that aPCCs do pose a thrombotic risk. However, it remains difficult to determine the actual risk in patients with DOAC-associated bleeding.

The current guidelines are based on pre-clinical data and limited data with healthy subjects. There has been no trial in patients with DOAC-associated bleeding performed to date. The administration of FEIBA based on a protocol using weight-based dosing resulted in no patient receiving additional doses of FEIBA. Guidelines and previous reports suggest a dosing range of 25–50 units/kg. Based on our results, a dose closer to 25 units/kg could be used in combination with indicated surgical interventions limited hemorrhage progression in most patients in our study.

Hematoma expansion occurred in 10% of our patients. Yin et al. demonstrated hematoma expansion in 13% of patients [11]. The observed mortality rate was 29% for our patient population with a mortality rate of 33% in ICH patients and 17% in extracranial hemorrhage patients. A systematic review and meta-analysis of randomized control trials compared fatal bleeding outcomes in patients on direct oral anticoagulation compared with vitamin K antagonists showed an overall observed mortality of 7.6% with 39% mortality in the ICH patient population and a 5% mortality rate in the extracranial bleeding population [4]. In studies evaluating the use of FEIBA, mortality rates range from 9% to 27% [9,11,12]. These results highlight the significant morbidity and mortality of anticoagulation-associated hemorrhage especially in the intra-cranial location.

Our study presents several limitations. First, the data were acquired through retrospective chart review which introduces a risk of bias due to poor documentation or missing data. We selected variables that would have been available at the time of the ED visit and likely captured in the EMR. Even with these measures, some relevant data may not have been captured. Secondly, at our institution we do not have the capability to monitor specific studies to assess the anticoagulation effects of DOACs (e.g., dilute thrombin time, Ecarin clotting time, and chromogenic anti-Xa assay). Because of the short half-life of the DOACs and our inability to measure specific anticoagulant effects, patients with sub-therapeutic levels of DOACs could have been included in our study population. Third, we only considered in-hospital thromboembolic complications related to FEIBA administration. This could have led to underreporting of thromboembolic complications that may have occurred after discharge; however, these late complications would unlikely be associated with aPCC administration. Fourth, because of the retrospective nature of our study, we were only able to determine effectiveness based on radiology reports and clinical documentation in the EMR. Fifth, approximately 50% of the patients were also receiving antiplatelet therapy in addition to DOAC therapy. Because of the observational nature of our study, we were unable to determine if the hemorrhagic complication was due to the anticoagulant therapy, antiplatelet therapy, or both. Finally, our patient population includes patients from a single academic center. Although, this could decrease the generalizability of our findings to other centers, our patients with DOAC-associated hemorrhagic complications were very similar to those described in previous reports [9–12].

**Table 3**  
Characteristics of patients who received FEIBA for hemorrhage and had progression or died in-hospital.

ID	Age Sex	GCS initial & 24 h ICH score, INR (pre, post FEIBA)	Anticoagulant Antiplatelet Indication	Hemorrhage type & location	Intervention & hemostasis after FEIBA & surgery	Disposition or cause of death
11	68 M	5T, 8T 3 INR: 1.3 (pre)	Apixaban, Aspirin, A. Fib	IPH, IVH (ICH width 54 mm)	FEIBA 22 units/kg, TXA, bilateral ventriculostomy; no hemorrhage progression after FEIBA; DVT 5 days after FEIBA	Compassionate extubation for poor neurologic prognosis
20	79 M	11T, 3 1 INR: 1.0, 1.0	Rivaroxaban, Aspirin, A. Fib	Traumatic IPH, IVH	FEIBA 38 units/kg, left ventriculostomy; no hemorrhage progression after FEIBA	Compassionate extubation for poor neurologic prognosis
21	82 F	15, 15 1 INR: 1.0 (pre)	Rivaroxaban, Aspirin, A. Fib	R Frontal IPH (ICH width 17 mm), Hemothorax	FEIBA 36 units/kg, bilateral chest tubes; no hemorrhage progression after FEIBA	Compassionate extubation for acute respiratory Failure
28	75 F	9, 3 3 INR: 1.1 (pre)	Apixaban, Aspirin, A. Fib	IPH, IVH (pre/post FEIBA ICH width 41 mm, 48 mm)	FEIBA 16 units/kg, TXA, DDAVP, ventriculostomy; progression after FEIBA	Compassionate extubation for poor neurologic prognosis
30	72 F	6T, 7T 2 INR: 1.0 (pre)	Apixaban, Aspirin, A. Fib	R SDH, R frontal IPH (ICH width 42 mm)	Kcentra @OSH, FEIBA 24 units/kg, platelets, DDAVP, SDH & IPH evacuation, hemicraniectomy, hemorrhaging frontal vessel coagulated; no hemorrhage progression	IPH, status epilepticus, hypotension, bradycardia with propofol (discontinued); pacemaker placed, but developed cardiac arrest
31	71 M	4, 3 4 INR: 1.0 (pre)	Apixaban, Aspirin, A. Fib	R IPH, IVH extension, significant mass effect	FEIBA 2395 units (no weight in EMR prior to death), TXA; unknown - no follow-up imaging before death	Compassionate extubation for poor neurologic prognosis
35	72 F	8, 10T 3 INR: 1.0 (pre)	Rivaroxaban, Clopidogrel, Aspirin, A. Fib	IPH, IVH (ICH width 80 mm)	FEIBA 26 units/kg, TXA, platelets; no hemorrhage progression after FEIBA	Compassionate extubation for inability to wean off ventilator. Tracheostomy and PEG tube not compatible with goals of care
43	77 F	12, 5T 3 INR: 1.2, 1.1	Rivaroxaban, None, A. Fib	IPH (pre/post FEIBA ICH width 36 mm, 85 mm)	FEIBA 27 units/kg, TXA; hemorrhage progression after FEIBA	Compassionate extubation for poor neurologic prognosis
47	89 M	14, 14 1 INR: 1.1 (pre)	Rivaroxaban, Aspirin, A. Fib	SDH, SAH	Kcentra @OSH, FEIBA 26 units/kg, TXA; No hemorrhage progression after FEIBA	Compassionate extubation for poor neurologic prognosis
50	62 M	14, 9T 0 INR: 1.2 (pre)	Apixaban, Clopidogrel, VTE	SAH w/ IPH	FEIBA 29 units/kg, platelets, and TXA. Hemorrhage progression. Hematologic evaluation revealed likely platelet dysfunction secondary to alcoholic cirrhosis	Compassionate extubation for poor neurologic prognosis
22	72 F	15, 10T N/A INR: 1.2, 1.0	Rivaroxaban, Aspirin, A. Fib	Pelvic fracture with hemorrhage, ruptured left diaphragm	Kcentra @OSH, FEIBA 36 units/kg, embolization of the left obturator artery and internal pudendal artery; no hemorrhage progression; MI 8 days after FEIBA	Compassionate extubation after developing acute respiratory failure with chest X-ray suggesting pneumonia
27	62 F	3T, 3 N/A INR: 5.4, 2.8	Apixaban, Aspirin, A. Fib	Blood around endotracheal tube from unknown source	Presented with multi-system organ failure, cardiogenic shock, coagulopathy secondary to liver failure; FEIBA 25 units/kg, FFP, CRYO, Vit K, TXA; no hemorrhage progression	Multi-system organ failure, cardiogenic shock, cardiac arrest
48	68 F	9, 7T 1 INR: 1.1 (pre)	Rivaroxaban, Aspirin, A. Fib	L IPH and L tentorial SDH (pre/post FEIBA ICH width 37 mm to 46 mm)	FEIBA 31 units/kg, TXA; hemorrhage progression after FEIBA	None, discharge (SNF)

A. Fib atrial fibrillation, DDAVP desmopressin, EMR electronic medical record, F female, FEIBA Factor Eight Inhibitor Bypassing Activity, FFP fresh frozen plasma, GCS Glasgow Coma Scale, ICH intracranial hemorrhage, IPH intraparenchymal hemorrhage, INR international normalized ratio, IVH intraventricular hemorrhage, M male, MI myocardial infarction, OSH outside hospital prior to transfer, SAH subarachnoid hemorrhage, SNF skilled nursing facility, TXA tranexamic acid, VTE venous thromboembolism.

**5. Conclusion**

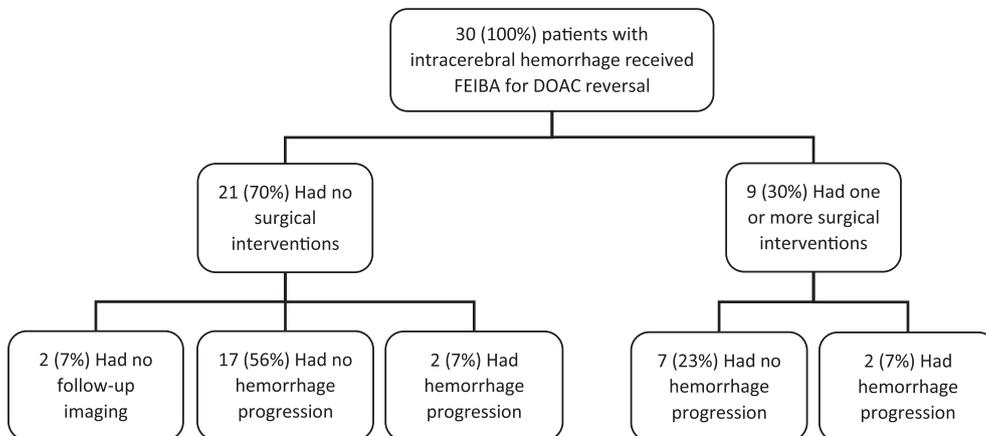
In conclusion, this case series suggests that FEIBA administration is relatively safe and effective to reverse DOACs in the setting of hemorrhage or need for urgent surgical procedures. Until target-specific reversal agents such as andexanet alfa or aripazine are available, future studies evaluating the effectiveness of aPCC administration for DOAC-associated hemorrhagic complications are warranted.

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**Conflict of interest statement**

The authors have no conflict of interest to declare.



**Fig. 2.** Patients who received FEIBA for intracerebral hemorrhage with their interventions and hemostasis outcomes.

**Table 4**  
Clinical outcomes for all patients.

	FEIBA recipients n = 42
Adverse events, n (%)	
Deep vein thrombosis	3 (7)
Myocardial infarction	1 (2)
Hemorrhage progression, n (%)	4 (10)
Disposition, n (%)	
Home	14 (33)
Skilled nursing facility	9 (21)
Acute rehabilitation	5 (12)
Hospice	2 (5)
All-cause mortality, n (%)	12 (29)

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