

Original Research

Andexanet Alfa versus 4-Factor Prothrombin Complex Concentrates for Direct Oral Anticoagulant Reversal Prior to Urgent Surgery or Invasive Procedure

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Background

Andexanet alfa is a modified factor-Xa decoy protein labeled for reversal of direct oral anticoagulants (DOACs) rivaroxaban and apixaban. Fast-track approval stemming from the single-arm ANNEXA-4 trial left questions about efficacy in specific populations, particularly surgical, as patients undergoing surgery or invasive procedures within 12 hours of randomization were excluded. Additionally, the ANNEXA-S trial intended to fill this gap was terminated early for futility. More information is needed to evaluate andexanet alfa alongside alternate reversal strategies, such as 4-factor prothrombin complex concentrates (4F-PCCs), in this population.

Objectives

To determine if there is a significant difference in hemostatic effectiveness between andexanet alfa and 4F-PCCs when used for DOAC reversal in the setting of emergent surgery or procedure.

Methods

This single-center, retrospective study included patients who received andexanet alfa or 4F-PCCs within 24 hours of emergent surgery or procedure. The primary outcome was adequate hemostasis, defined as a composite of stable hemoglobin and lack of additional coagulation factors or transfusions administered at 48 hours post-reversal. Secondary outcomes included repeat reversal administration, type and quantification of transfusions, 30-day incidence of thrombosis, and 30-day mortality.

Results

Twenty-nine patients were included; 14 received andexanet alfa and 15 received 4F-PCCs. The majority of patients underwent general surgery, most commonly exploratory laparotomy. No statistically significant difference was observed for the primary composite outcome; however, a statistically significant difference was observed in the number of patients treated with andexanet alfa who required subsequent administration of 4F-PCCs or fresh frozen plasma (FFP) (50% vs. 26.7%, $p=0.196$).

Conclusion

Periprocedural or perioperative reversal with andexanet alfa may result in an increased need for additional reversal or transfusions compared to 4F-PCCs. Larger prospective comparator trials with diverse procedure types are needed to confirm these findings.

1. INTRODUCTION

Andexanet alfa is a modified factor Xa decoy protein that is FDA-approved for the reversal of the direct oral anticoagulants (DOAC) rivaroxaban and apixaban in patients presenting with life-threatening bleeding.¹ The drug was granted fast track FDA approval in 2018 based on interim results of

the ANNEXA-4 trial.² The ANNEXA-4 trial was a single-arm study of andexanet alfa for anticoagulation reversal in patients taking DOACs presenting with acute major bleeding. While 80% of patients achieved excellent or good hemostatic efficacy, there was a 10.4% incidence of thromboembolic events observed.

A notable concern regarding the real-world applicability of the findings of ANNEXA-4 was the exclusion of patients anticipated to undergo surgical intervention within 12 hours. The coagulopathy and additional thromboembolic risk factors often observed in the perioperative period raise questions regarding safety of andexanet alfa utilization in this population. Additionally, the rapid anti-Xa rebound noted after infusion completion has led to concerns regarding duration and durability of effect. This is especially critical for reversal in surgical settings where prolonged procedural time is expected.² As a follow up to ANNEXA-4, the ANNEXA-S trial was intended to look at the use of andexanet alfa for pre-surgical anticoagulation reversal.³ Study sponsors cited limited utility of a single-armed study as rationale for early termination, contradictory to the study design that led to the drug's initial approval. At the time of termination, 10 participants were enrolled with an observed 50% mortality rate.

Prior to FDA approval of a direct antidote, guidelines recommended fresh frozen plasma (FFP) or 4-factor prothrombin complex concentrates (4F-PCC) for reversal in the setting of DOAC-related major bleeding.^{4,5} To date, no head to head studies have been published evaluating the efficacy of andexanet alfa versus 4F-PCC exclusively in this patient population. Given lack of international guidelines or consensus statements at the time of andexanet alfa's initial approval, at Northwestern Memorial Hospital, an institutional DOAC reversal protocol was developed which allowed for the use of either 4F-PCC or andexanet alfa based on clinician discretion. The purpose of this study is to report institutional experience with utilization of andexanet alfa versus 4F-PCC in patients who required urgent surgical intervention.

2. METHODS

2.1. STUDY DESIGN AND POPULATION

This retrospective, single center study was approved by the local Institutional Review Board (STU00218150). Adult patients (age ≥ 18) admitted to Northwestern Memorial Hospital between May 2018 and September 2022 taking apixaban or rivaroxaban who, during admission to our institution, received either andexanet alfa or 4F-PCCs (either activated or inactivated) within 24 hours of an urgent surgical intervention were included. The institutional DOAC reversal protocol recommended either andexanet alfa dosed using FDA approved regimens or 4F-PCC for pre-surgical reversal; both fixed and weight-based dosing of 4F-PCC were permissible with a maximum 50 units per kilogram or 5000 IU. Final selection of reversal agent was ultimately left to clinician discretion. The policy also outlined guidance in circumstances where additional reversal agent was deemed necessary. Administration of either agent after initial use of andexanet alfa was recognized in the protocol as an unstudied clinical area and off-label use; these clinical scenarios were restricted to pharmacist administrator on-call approval.

Apixaban and rivaroxaban utilization was confirmed by medication administration record (MAR) via Northwestern Memorial Hospital's electronic health record (EHR), MAR from transferring facility, or patient report of last dose. In the event that last dose was unable to be ascertained via these methods, patients were included based on clinical suspicion of recent DOAC ingestion, including patient prescription fill history and coagulopathy identified on anticoagulation labs such as INR, baseline heparin anti-Xa, or DOAC anti-Xa level, though the latter is not standard of care at our institution. Patients whose specific time from last DOAC dose were undetermined were excluded from time from last dose to reversal calculation and statistical analysis.

Patients who received more than one reversal agent were assigned to the arm of the first reversal agent administered. Patients were excluded if they had evidence of an acute intracerebral hemorrhage (ICH) on imaging due to limited ability to evaluate ongoing bleeding or reversal adequacy using standard International Society of Thrombosis and Hemostasis (ISTH) criteria for effective hemostasis. These criteria include stable hemoglobin at 48 hours post reversal defined as less than 10% decrease from baseline, lack of need for additional reversal agents or transfusions at 48 hours, and stable hematoma size or an increase of less than 35% from baseline imaging.⁶

2.2. DATA COLLECTION

Demographic and clinical characteristics were collected from the EHR with the assistance of the Northwestern Medicine Enterprise Data Warehouse for all eligible patients. Patient specific factors collected included age, sex, height, weight, hospital length of stay, and 30-day mortality. Medication parameters collected included DOAC agent with corresponding indication, dose, and time of last administration, concomitant antiplatelet use, and anticoagulant reversal details including agent, dose, and additional reversal administration, if applicable.

In addition, parameters pertaining to procedures were collected, including procedure type, duration, and timing in relation to reversal. For procedures that required intraoperative administration of heparin, heparin resistance was screened for through assessment of heparin rates, activated clotting time (ACT), and antithrombin 3 (ATIII) administration. Hemostatic parameters collected included complete blood count (CBC) at baseline, 24, and 48 hours, and quantification of blood products transfused, including intraoperative blood product and reversal agent administration.

Thromboembolic event data was collected including evidence of deep vein thrombosis (DVT) or pulmonary embolism (PE) on venous duplex or computed tomography, respectively, within 30 days of reversal, as well as timing of anticoagulation resumption, whether the anticoagulation was prophylactic or therapeutic, and timing of thromboembolic event compared to reversal administration. Viscoelastic testing data and intraoperative blood loss were not collected.

2.3. STUDY OUTCOMES AND DEFINITIONS

The primary outcome was a composite endpoint of effective hemostasis. The definition of effective hemostasis was adapted from ISTH and required stable hemoglobin at 48 hours after reversal defined as less than a 10% decrease from baseline, as well as lack of administration of additional reversal agents or blood product transfusions at 48 hours including packed red blood cells (pRBCs), FFP, platelets, or cryoprecipitate. Secondary outcomes of interest included individual components of the primary composite outcome. Safety outcomes included incidence of thromboembolic events and cases of heparin resistance. Other parameters collected included type of procedure, as well as timing and degree (prophylactic or therapeutic) of anticoagulation resumption.

2.4. STATISTICAL ANALYSES

Categorical data was compared between andexanet alfa and 4F-PCC groups with the use of Fisher's exact test or Pearson chi-squared test, as appropriate. Continuous data were compared with Student's t-test for parametric data and Mann-Whitney U test for non-parametric data. These analyses were performed using SPSS 2.0 (Statistical Package for the Social Sciences, Chicago, IL). A p-value of <0.05 was considered statistically significant.

3. RESULTS

3.1. BACKGROUND CHARACTERISTICS

A total of 29 patients (Table 1) were identified for inclusion in this study, 14 of which received 4F-PCCs and 15 of which received andexanet alfa as initial reversal. The majority of included patients were taking apixaban (n=21, 72.4%) and the most common indication for anticoagulation in both groups was atrial fibrillation (n=17, 58.6%). The groups were similar at baseline with the exception of antiplatelet use, which was more common in the 4F-PCC group; the most common antiplatelet agent prescribed was aspirin. Patients in both groups had comparable baseline hemoglobin levels, and no patients presented with acute major bleeding. While a variety of surgery types were represented (Table 4), patients were most commonly admitted for general or trauma surgery procedures (n=24, 82.8%) with the most common surgery being exploratory laparotomy. Amongst patients who received 4F-PCCs, the median dose administered was 31.3 units/kg (IQR [25.9, 48.2]) based off of actual body weight, while the low dose regimen was most commonly utilized in patients who received andexanet alfa, which was appropriate based on timing of last dose. Two patients in each group were excluded due to evidence of ICH on imaging.

3.2. OUTCOMES

While hemostatic effectiveness appeared similar between the two groups, only patients in the andexanet alfa group required additional reversal agent administration. The pri-

mary outcome of interest (Table 2), effective hemostasis, was observed in 7 patients in the 4F-PCC cohort compared to 4 in the andexanet alfa cohort, which was not statistically significant (50% vs. 26.7%, p=0.196). There was no difference observed in either the number of patients with a stable hemoglobin at 48 hours. Need for any blood product and total blood products required was also not different across cohorts. However, only patients in the andexanet alfa cohort required additional reversal agent or FFP administration (0% vs. 40%, p=0.017). The most common procedure requiring additional reversal was exploratory laparotomy, with two patients receiving FFP and one patient receiving both FFP and 4F-PCC. FFP was also administered to a patient undergoing ascending aortic aneurysm replacement, as well as one undergoing a sacral wound debridement. The second patient who received additional reversal with 4F-PCC underwent a laparoscopic appendectomy. In these patients, 4F-PCC was dosed at a median of 2234 units, which correlated to approximately 24 units/kg. Despite higher baseline antiplatelet use amongst the 4F-PCC group, only one patient received reversal with desmopressin (DDAVP); this patient was in the andexanet alfa group.

One thromboembolic event was identified amongst the cohort of patients who received andexanet alfa (Table 3). This patient underwent a laparoscopic appendectomy and was found to have an acute PE two days after andexanet alfa administration. The patient was on rivaroxaban 20mg daily for a past history of venous thromboembolism. While this patient was not on any form of anticoagulation at the time of PE diagnosis, a majority of patients (n=26, 89.7%) had some degree of anticoagulation resumed during hospitalization. The degree of anticoagulation resumed initially was most often prophylactic (75.6%) and typically occurred within 2 days of reversal agent administration. No additional thromboembolic events were identified in either cohort.

Disposition outcomes (Table 3) were similar between the two groups with no statistically significant difference in hospital length of stay or 30-day mortality. Of the 3 deaths, none occurred intra-operatively or within a week of procedure.

4. DISCUSSION

Patients systemically anticoagulated with DOACs present a unique pharmacotherapeutic challenge for anticoagulation reversal in the setting of surgery or invasive procedure. While the ANNEXA-4 trial demonstrated excellent or good hemostatic efficacy in the majority of patients enrolled, patients requiring intervention within 12 hours of randomization were strictly excluded. Although retrospective studies of andexanet alfa in this population have demonstrated similar results, like ANNEXA-4, they have also lacked a comparator group. In a single-center study of 44 patients who received andexanet alfa prior to emergent surgical intervention, 78.9% were identified as achieving excellent or good hemostasis. However, nearly half (45.5%) of patients included received reversal for a neurologic procedure, which may limit generalizability to other surgical popula-

Table 1. Baseline Characteristics

	4F- PCC (n=14)	Andexanet alfa (n=15)
Age (years) - median, [IQR]	73.5 [65, 84]	69 [65.5, 74.5]
Male sex - n, (%)	9 (64.3)	12 (80.0)
DOAC - n, (%) Apixaban Rivaroxaban	8 (57.1) 6 (42.9)	13 (86.7) 2 (13.3)
Indication for DOAC - n, (%) Atrial fibrillation DVT/PE	9 (64.3) 5 (35.7)	8 (53.3) 7 (46.7)
Antiplatelet use - n (%)	7 (50.0)	2 (13.3)
Baseline hemoglobin (g/dL) - median, [IQR]	11.8 [10, 13]	12.1 [10, 13.5]
Type of procedure - n, (%) General/trauma Cardiac Vascular Neurologic	13 (92.9) 0 (0.0) 1 (7.1) 0 (0.0)	11 (73.3) 1 (6.7) 0 (0.0) 3 (20.0)
Duration of procedure (hours) - median, [IQR]	2.9 [2.1, 3.4]	4.1 [2.1, 7]
Patients reversed intra-operatively -n, (%)	0 (0%)	11 (73.7%)
Time from reversal administration completion to incision time (hours) -median, [IQR]	0.83 [0.5, 1.2]	4
Confirmed recent DOAC administration - n, (%) Confirmed on MAR DOAC Anti-Xa Ordered Patient Endorsed	13 (93.8) 5 (31.3) 3 (18.9) 7 (43.8)	10 (58.8) 2 (11.8) 3 (17.6) 5 (9.4)
Time from last dose to reversal (hours) - median, [IQR]	19.5 [11.25, 24.25]	18 [12, 22.5]

4F-PCC: four factor prothrombin complex concentrate, DOAC: direct oral anticoagulant, DVT: deep vein thrombosis, PE: pulmonary embolism

Table 2. Hemostasis

	4F-PCC (n=14)	Andexanet alfa (n=15)	p-value
Effective hemostasis at 48 hours - n, (%)	7 (50.0)	4 (26.7)	0.196
Patients requiring additional reversal agent(s) - n, (%) 4F-PCC- n, (%) Fresh Frozen Plasma (FFP)- #, (%)	0 (0.0) 0 (0.0) 0 (0.0)	6 (40.0) 2 (13.3) 5 (33.3)	0.017
Patients requiring any non-FFP blood product - n, (%)	3 (18.8)	7 (41.2)	0.259
Patients receiving any blood product(s) - n, (%)	3 (18.8)	8 (47.0)	0.085
Total number of blood products per patient - median, [IQR]	1 [1,2]	2.5 [2,10]	0.873
Stable hemoglobin at 48 hours - n, (%)	7 (50.0)	7 (46.7)	0.858
Total blood products (units) - median, [IQR]	1 [1,2]	3 [2,10]	0.222
Patients requiring surgical re-intervention - #, (%)	0 (0.0)	0 (0.0)	1.00

4F-PCC: four factor prothrombin complex concentrate, FFP: fresh frozen plasma, pRBC: packed red blood cells

tions with higher risk of coagulopathy, such as cardiac, vascular, or thoracic procedures. Within this cohort, a 34.1% 30-day mortality rate and 27.3% rate of thromboembolic complications were observed.⁷

The off-label use of 4F-PCC in this setting has been supported by numerous trials, including a recent meta-analysis.⁸ However, use in the surgical population is limited to retrospective studies, one of which was published in 2020 that included 62 patients primarily undergoing intraabdominal or orthopedic procedures. The mean dose of

4F-PCC administered was 26.6 ± 8 units/kilogram of body weight and no repeat doses were required. 26% of patients required transfusion of at least one unit of blood product, but bleeding was reported in only 5% of the cohort.⁹ A more recent study published in 2024 included twenty patients undergoing emergent surgery with anticipated blood volume loss of 50 milliliters or more. Patients were treated with fixed dose 2000 IU 4F-PCC for a median dose of 27 IU/kg; no patients received repeat doses. The primary outcome

Table 3. Outcomes

	4F-PCC(n=14)	Andexanet alfa (n=15)	p-value
New VTE- n, (%) Deep vein thrombosis (DVT)- #, (%) Pulmonary embolism (PE)- #, (%)	0 (0.0) 0 (0.0) 0 (0.0)	1 (6.7) 0 (0.0) 1 (6.7)	1.00
Time to thrombosis- days	N/A	2	
Anticoagulation resumed during admission- n, (%)	12 (85.7)	14 (87.5)	1.00
Time from reversal until any anticoagulation resumption (hours)- median, [IQR]	29 [18, 41]	39 [21, 50]	0.406
Hospital length of stay (days)- median, [IQR]	14.5 [7.5, 23]	8 [6.5, 13]	0.112
30-day mortality- n, (%)	2 (14.3)	1 (6.7)	0.598

Table 4. Procedure Types

	4F- PCC (n= 14)	Andexanet alfa (n-15)
General/ Trauma	- Laparoscopic appendectomy (n=4) - Exploratory laparotomy, ileocolic resection, resection of midline hernia defects and repair of hernias, lysis of adhesions and washout of abdominal infection - Exploratory laparotomy, lysis of adhesions, ileocectomy, end ileostomy, and mucous fistula - Total colectomy with end ileostomy - Exploratory laparotomy, transverse colectomy, mucous fistula, and liver biopsy - Colectomy, ileoproctostomy, sigmoidoscopy - Laparoscopic small bowel resection with anastomosis and gastrostomy tube placement - Exploratory laparotomy, partial descending colectomy, ostomy creation - Exploratory laparotomy, total colectomy, pre-peritoneal left inguinal hernia repair - Exploratory laparotomy, diverting loop ileostomy	- Exploratory laparotomy, sigmoidectomy, and end colostomy - Laparoscopic appendectomy (n=2) - Exploratory laparotomy, subtotal colectomy, small bowel resection and abdominal washout, evacuation of intra-abscesses, and open abdomen - Exploratory laparotomy with diverting loop sigmoid colostomy - Exploratory laparotomy and small bowel resection - Wide sharp debridement and excisional biopsy of necrotic tissue (skin, subcutaneous tissue, deep fascia, and muscle) - Exploratory laparotomy, lysis of adhesions, small bowel resection, and wound washout - Exploratory laparotomy, splenectomy - Perineal necrotizing wound debridement - Neck exploration
Cardiac	N/A	Aortic ascending and hemiarch replacement, left atrial appendage closure
Vascular	Explant of infected aorto-bi-iliac bypass, ligation of infrarenal aorta, ligation of right common iliac, ligation of left renal artery and vein	N/A
Neurologic	- Right sided burrhole for subdural hematoma, craniotomy - Right sided burrhole for subdural hematoma	- Craniectomy and right sided decompressive hemicraniotomy - Thoracic level 12 to lumbar level 3 laminectomies for decompression; evacuation of epidural abscess - Intrathecal baclofen pump replacement - Left frontal craniotomy for tumor resection - Right hemicraniectomy for hematoma evacuation

of normal or mildly abnormal hemostasis was observed in 80% of the cohort.¹⁰

To our knowledge, this is the first study comparing outcomes with andexanet alfa to 4F-PCC reversal strategies exclusively prior to urgent or emergent surgery or procedure. While hemostatic effectiveness at 48 hours appeared similar between the two groups, only patients in the andexanet alfa group required additional reversal agent administration. The median dose of 4F-PCC administered in the two patients requiring additional reversal was approximately 24 units per kilogram. Five patients in the andex-

anet alfa arm also required administration of FFP. Both of these interventions may serve as surrogate markers of coagulopathy or incomplete reversal with andexanet alfa, and their use was statistically significant compared to patients initially reversed with 4F-PCCs. Strengths of this study include patient groups that were comparable in size and baseline characteristics, including procedure type, procedure duration, and median baseline hemoglobin.

Additionally, more than 75% of our patient population had confirmation of recent DOAC administration via EHR or patient report; the remaining patients were included based

on clinical suspicion, including prescription fill history and coagulopathy on hemostatic labs. The latter is reflective of clinical practice, as patients occasionally may be unable to confirm last doses due to clinical condition or being unreliable historians. One notable difference within our patient populations was the difference in baseline antiplatelet use, which was statistically significantly higher in the 4F-PCC group compared to the andexanet alfa group. Despite a higher potential for coagulopathy in patients on both an anticoagulant and concomitant antiplatelet agent, this was not reflected in our observed results.

The most notable limitations of this study are its small sample size which likely led to it being underpowered, as well as its retrospective nature. Additionally, there was risk of selection bias since reversal agent selection was left to clinician discretion within limited restrictions based on our institutional protocol. Given the urgent or emergent nature of procedures in this study, opportunity for interdisciplinary team discussion between ordering surgeon or interventionist and verifying pharmacist regarding potential risks, benefits, and limitations of both reversal strategies may have been limited.

Additionally worth addressing is the difference in reversal administration timing; 100% of patients who received 4F-PCC were reversed less than an hour prior to incision time, as compared to almost three quarters of patients whose andexanet alfa dose finished intra-operatively. These differences are most likely due to the urgent or emergent nature of the procedures coupled with the significant difference in administration times of the two agents, with 4F-PCC typically being administered as a twenty minute IV piggyback and andexanet alfa given as a bolus followed by a continuous 120-minute IV infusion. Amongst patients who received the complete dose of andexanet alfa prior to surgery, the median time from dose completion to incision was 4 hours. The remaining duration of procedure after andexanet alfa infusion was not collected. Given andexanet alfa's short duration of action and rebound Xa levels two hours after infusion completion, these instances may have contributed to the need for additional reversal, as observed in the patient undergoing sacral wound debridement who required supplemental FFP. Furthermore, additional 4F-PCCs and blood products were often administered at provider discretion rather than pre-specified laboratory parameters, as permitted per institutional protocol, which may have confounded transfusion results. Of note, while potentially permissible per institutional protocol with pharmacist administrator approval, andexanet alfa was not re-dosed within our patient cohorts, so we are unable to comment on safety nor efficacy of repeat administration of this agent.

Other limitations of note include minimal representation of cardiovascular and vascular interventions, which may potentially limit generalizability to these types of procedures. Intraoperative reports and estimated blood loss were not collected, largely due to the heterogeneity of included procedures. Baseline and changes in anti-Xa levels were not collected and assessed despite this being an endpoint in ANNEXA-4, as this is not standard practice at our

institution; while DOAC anti-Xa levels can detect presence of drug, they do little to estimate overall degree of coagulopathy and interpretation of these levels has yet to be formally labeled a standard of care. Although viscoelastic testing is available at our institution, we did not collect results from these tests as they were not routinely used, turnaround time may have impaired ability to act on results in real time, and lack of widespread availability at other institutions may limit external validity.

From a safety standpoint, we identified one thromboembolic event in the andexanet alfa group, reflective of 6.7% of that patient population. This event occurred at two days post reversal, comparable to the 3.5-day time to thrombosis observed in the andexanet alfa arm of the ANEXA-I trial.¹¹ This thromboembolism rate is slightly lower than that previously documented in the literature and may be in part due to the small sample size included, as well as lack of collection of arterial thrombotic events such as myocardial infarction and ischemic cerebrovascular accidents. Most importantly, the collection of thromboembolic events was retrospective in nature. Given that diagnostics were ordered based on clinical suspicion alone rather than for routine surveillance, the overall incidence of thromboembolic events is likely underestimated in both cohorts.

Finally, worth further discussion is heparin resistance which has been reported after andexanet alfa administration, particularly in patients requiring systemic heparinization intra-operatively, such as in those undergoing cardiopulmonary bypass.¹² In cases such as these, massive doses of heparin may be required in order to achieve appropriate degree of anticoagulation. In some instances where adequate anticoagulation is not achieved with large heparin doses, administration of antithrombin or use of less favorable agents, such as direct thrombin inhibitors may be required. The proposed mechanism of action of this phenomenon is through andexanet alfa's binding of anti-thrombin III in addition to factor Xa. This sequela not explicitly detected in the original ANNEXA-4 trial given that surgical populations where heparinization may have been immediately required were excluded, and only 67.4% of patients resumed anticoagulation during their admission, nearly a third of which (30.1%) had resumption delayed 6 days or greater post andexanet alfa administration.

Within our cohort, one case of intra-operative heparin resistance was identified in a cardiothoracic surgery patient who received andexanet alfa. In total, the patient required 190,000 units of heparin (1900 units/kg), 1220 units of AT3, and 4 units of FFP before sufficient activated clotting times (480 per institutional protocol) allowed for initiation of cardiopulmonary bypass. We recognize that for this patient, administration of FFP may have been for AT3 content to overcome heparin resistance as opposed to inadequate hemostasis, which may have skewed results in the andexanet alfa arm. Regardless, this adds to a growing body of evidence suggesting the risk of heparin resistance in patients who receive anticoagulation reversal with andexanet alfa. Providers should be made aware of this potential complication, particularly for patients who require systemic heparinization during a procedure.

5. CONCLUSION

Although rates of effective hemostasis appeared similar between andexanet alfa and 4F-PCCs amongst patients on apixaban or rivaroxaban presenting with acute need for surgery or invasive procedure, additional measures were often required to achieve these effects in the andexanet alfa group. Additional prospective, comparator studies within surgical populations are warranted to confirm these findings, particularly amongst those undergoing vascular and cardiovascular procedures.

CONFLICTS OF INTEREST

None of the authors have any relevant conflicts of interest to disclose.

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