

Terapie anticoagulanti e gestione delle complicanze

REAL-WORLD EMERGENCY DEPARTMENT USE OF ANDEXANET ALFA FOR FACTOR XA INHIBITOR REVERSAL: AN ITALIAN COHORT

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Background and Aims. Andexanet alfa (AA) has been used for several years as a targeted reversal agent for factor Xa inhibitors in life-threatening or uncontrolled bleeding. Observational studies had already identified an approximately 10% thrombotic-event risk, subsequently confirmed by ANNEXA-I trial, which also triggered a regulatory debate after withdrawal from the North American market. In Europe, however, AA remains authorised, and Italian emergency department (ED) data are scarce. We aimed to describe real-world ED use, safety and clinical profile of AA in patients requiring urgent reversal of factor Xa inhibitors.

Methods. We performed a retrospective analysis of consecutive DOAC-treated patients managed in the ED of Ospedale di Circolo (Varese) from january 2022 up to december 2025 and receiving a specific antidote as reversal agent. This analysis focuses on patients treated with AA. Demographic characteristics, indication for anticoagulation, bleeding site or procedural indication, timing of administration, dose, follow-up imaging, 30-day outcomes, thrombotic and recurrent bleeding events, anticoagulation resumption and mortality were collected.

Results. Among 68 DOAC reversal cases using an antidote, 47 patients received AA. Median age was 80 years (IQR 76–86) and 26 patients (55.3%) were male. The reversed factor Xa inhibitor was apixaban in 30 cases (63.8%), rivaroxaban in 12 cases (25.5%) and edoxaban in 5 off-label cases (10.6%). Atrial fibrillation was the main indication for anticoagulation (40/47, 85.1%). Among patients with documented bleeding site, intracranial bleeding predominated (29/41, 70.7%), followed by gastrointestinal bleeding and other sites (6 cases each); 20 patients (42.6%) had a traumatic event. According to the primary indication, AA was used for life-threatening bleeding (41/47, 87.2%), whereas in 6 additional cases it was administered before urgent surgery in the absence of a documented active bleeding site, as off-label-use. Low-dose and high-dose regimens were used in 27 (57.4%) and 20 (42.6%) patients, respectively. Antidote administration occurred within 3 hours from ED access in 33/47 patients (70.2%). Red-cell transfusion was required in 11 patients (23.4%) and urgent surgery was indicated in 11 (23.4%). Follow-up imaging, when available, was stable or improved in 32/41 patients (78.0%). One recurrent bleeding event occurred within 30 days. Thrombotic events occurred at a mean of 4 days after AA administration and before anticoagulation resumption, with 4 events recorded among 43 evaluable patients (9.3%), consisting of 2 strokes, 1 myocardial infarction and 1 multiple site ischemia associated with endocarditis (one event occurred in an off-label use case). Overall mortality was 12/47 (25.5%). Anticoagulation was resumed in 23/46 evaluable patients (50.0%).

Conclusions. In this Italian ED cohort, AA was used mainly in elderly, high-risk patients with factor Xa inhibitor–associated intracranial bleeding. The observed thrombotic-event rate was consistent with the known safety profile from observational studies and ANNEXA-I trial, without suggesting an unexpected safety signal. In a setting where European authorisation remains unchanged, these data support the continued, carefully selected ED use of AA as a potentially life-saving reversal strategy, while emphasizing the need for early reassessment of antithrombotic therapy, structured follow-up and larger Italian registries.