

Terapie anticoagulanti e gestione delle complicanze

MONOCENTRIC EXPERIENCE OF DOACS REVERSAL MANAGEMENT AT L SACCO HOSPITAL, MILAN: A REAL-WORLD RETROSPECTIVE STUDY

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Background and Aims. The increasing use of direct oral anticoagulants (DOACs) has made the management of major bleeding and non-deferrable urgent surgery a relevant clinical challenge. Specific reversal agents are available for selected DOACs, such as andexanet alfa (AA) for factor Xa inhibitors, whereas four-factor prothrombin complex concentrate (4F-PCC) remains the most widely used non-specific option. At L. Sacco Hospital (Milan, Italy), a multidisciplinary institutional protocol based on ISTH recommendations is applied. This study aims to evaluate whether our institutional DOACs reversal strategy—based on 4F-PCC or AA—is consistent with current evidence and published case series in terms of safety and clinical outcomes.

Methods. We conducted a retrospective, single-center observational study including all consecutive DOACs reversal requests managed by the Transfusion Medicine Service (January 1, 2023 – December 31, 2025). Patients undergoing non-deferrable invasive procedures received 4F-PCC (25–50 IU/kg). Patients with intracranial hemorrhage (ICH) on apixaban or rivaroxaban received AA, while those on edoxaban or with major bleeding at other sites received 4F-PCC (25–50 IU/kg). Safety outcomes included in-hospital mortality and thrombotic events. Hemostatic effectiveness was assessed using published criteria (effective/ineffective for bleeding; ineffective/partially effective/effective for surgery), as in Khorsand et al, 2021, and Piran et al, 2018.

Results. A total of 41 reversal episodes were managed: 36 with 4F-PCC and 5 with AA. In the 4F-PCC group, hemostatic effectiveness was 82.35% in urgent surgery and 68.42% in major bleeding ($p<0.0001$). In-hospital mortality in the 4F-PCC group was 19%, with a trend toward higher mortality in bleeding vs surgical cases (31.58% vs 5.88%, $p=0.055$). The majority of 4F-PCC use was observed in patients undergoing abdominal and urogenital surgery. Bleeding site and age were not associated with mortality. Thrombotic events occurred in 4/36 patients. Mortality increased with worsening hemostatic effectiveness (21.4% effective, 50% partially effective, 100% ineffective), although data were limited by low number. In the AA group, the small sample size and diverse clinical indications precluded meaningful comparisons between reversal strategies. However, follow-up brain CT scans showed hematoma stability or reduction in 80% with 20% in-hospital mortality.

Conclusions. In this real-world monocentric cohort, outcomes after DOACs reversal appeared more related to baseline patient risk and clinical presentation than to the reversal strategy. Higher mortality was observed in bleeding vs post-surgical patients, while post-sugical mortality was lower tahn previously reported. Hemostatic effectiveness in bleeding was consistent with the pooled estimates reported from Piran et al. (Blood Advances), while in-hospital mortality was comparable to that reported in the literature and prior case series. Any differences in outcome may reflect population heterogeneity and the reason for admission (major bleeding and its site vs urgent surgery). Overall, findings support the applicability of our institutional protocol in real-world practice. A key limitation is the lack of rapid DOAC level assessment, limiting confirmation of anticoaugulant activity. Prospective or larger studies are needed to identify the optimal reversal strategy across different patient subgroups.