A three-year prospective study of the presentation and clinical outcomes of major bleeding episodes associated with oral anticoagulant use in the UK (ORANGE study)

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Supplementary information

Details of data collection and verification

Upon identifying an eligible case, hospital research staff would complete and submit a case report form as soon as possible after the acute event, using information from patients' case notes exclusively (i.e. not through patient contact). The first outcome within 30 days – hospital discharge, inter-hospital transfer or death in hospital – would be noted in a follow-up report. Hospitals were prompted by the central registry for any outstanding returns 30 days after the date of major bleeding onset. Emails were sent to query all incomplete cases, with reminders sent after five weeks and a call to the clinician after another three weeks. No patient identifiable information (i.e. names, addresses, dates of birth, hospital or National Health Service numbers etc.) were submitted. Hospitals kept their own logs of patients' identifiers in order to ensure non-duplication of reports.

Case eligibility was first checked by the study data coordinator and hospital researchers were contacted for clarification where necessary. Where ambiguity remained, case details were referred to the first and last authors of this paper for further clinical review in order to confirm case identification.

Dataset variables

The study collected information on: patients' baseline characteristics (age, sex and hospital); type of OAC and indication(s), as well as co-administration of prescription antiplatelet drugs or heparin; co-morbidities required to calculate HAS-BLED and CHA_2DS_2–VASc scores; (2) bleeding site which was categorised into intracerebral, subarachnoid, subdural/epidural, upper gastrointestinal, lower gastrointestinal, or "Other", i.e. neither ICH nor gastrointestinal (patients reported to have more than one bleeding site would be assigned to the clinically most severe, in the afore-stated order of descending priority); provocation of bleeding (categorised into spontaneous, trauma (excluding fall), fall or surgery/procedure-related). Follow-up data were collected up to 30 days, death, or discharge, whichever occurred first. These included: complications following from the major bleeding episode such as cardiac arrest; admission to intensive care units; acute respiratory distress syndrome with or without mechanical ventilation; organ failure, inclusive of sepsis and hospital-acquired pneumonia; recurrence of bleeding; and arterial or venous thrombotic events.

Justification of Sample Size

Published evidence estimated that of all major bleeds on OACs, ICH and fatal bleeding made up 20% and 10% of cases respectively. Approximately 750 cases of major bleeding per year were predicted to present to our study hospitals. At the start of the study, DOACs made up 5% of cases; with increasing uptake, we expected this to increase over the study period to reach 10% overall. Thus, with a total sample of 2250 patients, and assuming 10% will be on DOAC, the study will have 80% power to detect: (1) a difference in ICH proportions of 8%, and (2) a difference in mortality rates of 5.5%, at the 5% level of significance.