Summary APACHE-AF

Background: In patients with atrial fibrillation who survive an anticoagulation-associated intracerebral haemorrhage (ICH), a clinical dilemma is whether restarting or permanently avoiding anticoagulation is the best long-term strategy to prevent recurrent stroke and other vascular events. We aimed to estimate the rates of the composite of non-fatal stroke or vascular death in such patients when treated with apixaban and when anticoagulation was avoided, to inform the design of a larger trial.
Methods: APixaban versus Antiplatelet drugs or no antithrombotic drugs after anticoagulation-associated intraCerebral HaEmorrhage in patients with Atrial Fibrillation (APACHE-AF) was a prospective, randomised, open-label, blinded endpoint, parallel group trial at 16 hospitals in the Netherlands. We included patients who survived ICH, while treated with anticoagulation because of atrial fibrillation, between 7 and 90 days after the haemorrhage. Participants were randomly assigned to apixaban or avoiding anticoagulation (1:1) by computer. We stratified for the intention to start or withhold antiplatelet therapy in participants randomised to avoiding anticoagulation. We applied a minimisation protocol for age (≤75/>75 years) and ICH location (lobar/non-lobar). We followed participants for the primary composite outcome of non-fatal stroke or vascular death, whichever came first, for a minimum of 6 months and calculated annual event rates in each treatment arm. We estimated the effect of apixaban on the occurrence of the primary outcome using Cox proportional hazards modelling, adjusting for an aggregated risk variable based on minimisation and other relevant covariates. APACHE-AF is registered with ClinicalTrials.gov (NCT02525693) and the Netherlands Trial Register (NL4395).
Findings: Between January 15, 2015 and July 6, 2020 we recruited 101 patients (median age, 78 years, IQR 73–83; 55 men) a median of 46 days (IQR 21–74) after ICH. 50 were assigned to apixaban and 51 to avoiding anticoagulation (of whom 26 started antiplatelet therapy). None were lost to follow-up. Over a median of 1·9 years (IQR 1·0–3·1; 222 person-years) non-fatal stroke or vascular death occurred in 13 (26%) participants allocated to apixaban (annual event rate 12·6%, 95% CI 6·7–21·5) and in 12 (24%) allocated to avoiding anticoagulation (annual event rate 11·9%, 95% CI 6·2–20·8; adjusted hazard ratio 1·05, 95% CI 0·48–2·31; p=0·90).
Interpretation: Patients with atrial fibrillation who had an ICH while taking anticoagulation treatment have a high subsequent annual risk of non-fatal stroke or vascular death, both when allocated to apixaban and when allocated to avoiding anticoagulation. Our data underline the need for randomised controlled trials sufficiently large to allow identification of subgroups in whom the effect of restarting anticoagulation may be either beneficial or hazardous.
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