Safely Addressing Patients with Atrial Fibrillation to Early Anticoagulation after Acute Stroke

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Background: It has been widely reported that anticoagulants (ACs) are underused for primary and secondary prevention of ischemic stroke in patients with atrial fibrillation (AFib). Furthermore, precise evidence-based guidelines about the best timing for AC initiation after acute stroke are currently lacking. *Methods and Results:* In this retrospective, observational study, we analyzed prescription trends in AFib patients with acute ischemic stroke who were hospitalized in four neurologic stroke units of our region (Lombardia, Italy). In-hospital antithrombotic prescription was performed in highly heterogeneous patterns. A prestroke treatment with AC was the leading factor enhancing AC prescription during hospitalization. The other factors promoting AC were male gender, younger age, lower prestroke disability and stroke severity, and smaller stroke volumes. AFib subtype influenced AC prescription only in AC-naïve patients. Interestingly, Congestive heart failure, Hypertension, Age higher than 75 years, Diabetes, previous Stroke or TIA or thromboembolism, Vascular disease, Age 64–75 years, female Sex (CHA$_2$DS$_2$-VASc) and Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile INRs, Elderly, Drugs and alcohol (HAS-BLED) scores were not associated with AC prescription. However, patients who were treated with AC, including early treatment (<48 hours), showed a low rate of bleeding. *Conclusions:* Our findings potentially suggest that, although apparently neglecting the common risk stratification tools, our neurologists were able to select the more suitable candidates for prompt AC treatment. Further studies are needed to develop new scoring systems to aid ischemic and hemorrhagic risk estimation in the secondary prevention of stroke. **Key Words:** Acute ischemic stroke—anticoagulants—atrial fibrillation—stroke unit.
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Introduction

Atrial fibrillation (AFib) is responsible for at least 25% of ischemic strokes,[1] being the major cause of cardioembolic stroke[2] and, in its silent form, of a high percentage of cryptogenic strokes.[3] In ischemic stroke patients, AFib is strongly associated with higher clinical severity, larger infarction size, and higher rates of hemorrhagic transformation and mortality.[4,5]

The efficacy of anticoagulants (AC) treatment has been widely demonstrated for primary and secondary prevention of ischemic stroke in patients with AFib,[6,7] also in older patients without significant increase in the risk of major bleedings.[8] Despite evidence, it is known that in clinical practice ACs are underprescribed: prescription rates vary from 37% to 71% of AFib patients in different settings.[9-12] AC treatment underuse in the secondary prevention of stroke in AFib patients could be partially due to some *gray areas* in current guidelines. In fact, straight recommendations about the correct timing and pattern of prescription are lacking.[13-15] ACs are not recommended in the early poststroke phase due to increased bleeding risk[16]; however, recent analyses have identified 4-14 days after the index event as the best time frame for AC initiation.[17] Also, the evaluation of hemorrhagic risk could be difficult especially in older patients with a lot of comorbidities.[9,15,18]

The aim of this study was to explore patterns of antithrombotic prescription in acute ischemic stroke patients with AFib hospitalized in four stroke units of our region, Lombardia. We investigated clinical and neuroimaging factors influencing AC prescription in these patients. We also explored the relationship between AC treatment and outcome measures (mortality, stroke recurrences, bleedings).

Materials and Methods

Patients

The study considered patients hospitalized in the stroke units of the following hospitals: National Neurological Foundation IRCCS "Casimiro Mondino," Pavia; "Fondazione Macchi—Ospedale di Circolo," Varese; "Humanitas" Institute, Rozzano; and Hospital of Legnano, Legnano. All these stroke units are managed by trained stroke neurologists and cooperate in feeding a regional registry,[19] which was approved by the ethics committees of all of the institutes. In all the cooperating centers, the admission rate is >300 stroke patients per year.

All the patients discharged with diagnosis of ischemic stroke and AFib between January 1, 2011 and December 31, 2013 were enrolled. Only patients with at least one acute ischemic lesion confirmed by neuroimaging (computed tomography or magnetic resonance imaging) and consistent with acute neurologic symptoms were included. Written informed consent for the handling of personal data was obtained from all subjects.

Patients' demographics and clinical data were independently collected from medical charts by two stroke-trained neurologists. The following variables were collected:

– *Demographics*: age, gender, race, enrollment center, and prestroke disability (modified Rankin scale, mRS)[20];
– *Vascular risk factors and comorbidities*: AFib subtype (sustained: persistent or permanent; paroxysmal; new onset),[13] hypertension, diabetes, previous stroke or transient ischemic attack, carotid stenosis (≥60% according to the European Carotid Surgery Trial criteria),[21] other sources of cardioembolism (congestive heart failure, left atrial or ventricular thrombus, prosthetic valve, recent myocardial infarction, dilated cardiomyopathy),[22] intra- or extracranial aneurysms, alcoholism, hepatopathy, chronic kidney disease, behavioral or cognitive disorders, stroke severity on admission and discharge (NIHSS score),[23] and Congestive heart failure, Hypertension, Age higher than 75 years, Diabetes, previous Stroke or TIA or thromboembolism, Vascular disease, Age 64–75 years, female Sex (CHA$_2$DS$_2$-VASc)[24] and Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile INRs, Elderly, Drugs and alcohol (HAS-BLED) score[18];
– *Antithrombotic treatments*: antiplatelets (AP) and ACs, including oral vitamin K-dependent or direct oral anticoagulants (DOACs) or low molecular weight (LMW) heparin, were recorded for all the following items: prestroke treatments, in-hospital treatments (including details about timing of administration), treatments prescribed at discharge;
– *Recanalization procedures*: intravenous or intra-arterial thrombolysis, surgical or endovascular interventions (endarterectomy or stenting) performed during hospitalization;
– *In-hospital complications*: hypertensive fits, seizures, deep venous thrombosis, acute myocardial infarction, falls; and
– *Clinical outcome measures*: discharge status; stroke recurrences (defined as newly onset neurologic symptoms consistent with neuroimaging evidence of a new ischemic lesion); and intra- and extracranial bleedings. Intracranial bleedings were classified according to the European Cooperative Acute Stroke Study criteria,[25] and were defined as symptomatic if associated with NIHSS score ≥4 worsening or death. Systemic bleedings were considered severe if associated with loss of ≥1 g/dL of hemoglobin within 24 hours, and not severe otherwise.

Neuroimaging

Neuroimaging data were collected by an independent trained observer from the digital archives (Carestream PACS, Carestream Health, Inc. Rochester, NY, USA) of all participating centers.