Atrial fibrillation treatment

Compared to vitamin K antagonists (VKAs) (e.g. warfarin), the novel oral anticoagulants (NOACs) dabigatran, rivaroxaban & edoxaban are at least as effective in preventing ischemic stroke and systemic embolization in a patient with atrial fibrillation.

Atrial fibrillation (AF) is often treated with medications to slow the heart rate to a near normal range (known as rate control) or to convert the rhythm to normal sinus rhythm (known as rhythm control).

Electrical cardioversion can also be used to convert AF to a normal sinus rhythm and is often used emergently if the person is unstable.

Ablation may prevent recurrence in some people.

Deciding when to initiate oral anticoagulation in patients with non-valvular atrial fibrillation is a longstanding, common, and unresolved clinical challenge. Although the risk of early recurrent ischemic stroke is high in this population, early oral anticoagulation is suspected to increase the risk of potentially harmful intracranial hemorrhage, including haemorrhagic transformation of the infarct. This assumption, and current treatment guidelines, are based on historical, mostly observational data from patients with ischaemic stroke and atrial fibrillation treated with heparins, heparinoids, or vitamin K antagonists (VKAs) to prevent recurrent ischaemic stroke. Randomised controlled trials have subsequently shown that direct oral anticoagulants (DOACs; ie, apixaban, dabigatran, edoxaban, and rivaroxaban) are at least as effective as VKAs in primary and secondary prevention of atrial fibrillation-related ischaemic stroke, with around half the risk of intracranial haemorrhage. However, none of these DOAC trials included patients who had experienced ischaemic stroke recently (within the first few weeks). Clinicians therefore remain uncertain regarding when to commence DOAC administration after acute ischaemic stroke in patients with atrial fibrillation.

Prospective observational studies and two small randomised trials have investigated the risks and benefits of early DOAC-administration initiation (most with a median delay of 3-5 days) in mild-to-moderate atrial fibrillation-associated ischaemic stroke. These studies reported that early DOAC treatment was associated with a low frequency of clinically symptomatic intracranial haemorrhage or surrogate haemorrhagic lesions on MRI scans, whereas later DOAC-administration initiation (ie, >7 days or >14 days after index stroke) was associated with an increased frequency of recurrent ischaemic stroke. WHERE NEXT?: Adequately powered randomised controlled trials comparing early to later oral anticoagulation with DOACs in ischaemic stroke associated with atrial fibrillation are justified to confirm the acceptable safety and efficacy of this strategy. Four such randomised controlled trials (collectively planned to include around 9000 participants) are underway, either using single cutoff timepoints for early versus late DOAC-administration initiation, or selecting DOAC-administration timing according to the severity and imaging features of the ischaemic stroke. The results of these trials should help to establish the optimal timing to initiate DOAC administration after recent ischaemic stroke and whether the timing should differ according to stroke severity. Results of these trials are expected from 2021 [1)].

Trends

The aim was to identify sex-specific factors linked with oral anticoagulant initiation in a cohort of patients with atrial fibrillation using administrative data from Quebec (Canada) between 2014 and 2017. Cohort entry defined as new users, that is, no claims in last 12 months, a cohort of 32 050 patients was stratified in two groups, that is, women and men. Multivariable regression models were used to identify factors of initiations for low- and standard-dose direct oral anticoagulants (DOACs) versus warfarin, and low- versus standard-dose DOACs. In both sexes, warfarin initiation decreased and DOAC initiation increased, with year of initiation as major factors of DOACs use. In 2017, the increase was of 2- to 4-fold and 3- to 8-fold for low- and standard-dose DOACs (vs. warfarin), respectively. The proportion of patients starting on a low-dose DOAC was higher in women than men. Older age for both sexes and CHADS2 score ≥2 (only women) were major factors of low-dose dabigatran and rivaroxaban versus warfarin use. The only significant factor of standard-dose DOAC versus warfarin use was age of 65-79 for women or men treated with apixaban by 1.8- and 1.4-fold, respectively. Factors that made women and men less likely to receive a standard-dose DOAC versus warfarin were higher CHADS2 (for dabigatran and rivaroxaban), HAS-BLED and frailty scores, prior coronary disease, major bleeding, and chronic kidney disease (CKD) status. The choice of a low- versus standard-dose DOAC was mainly driven by age and CKD, and higher CHADS2 score (for dabigatran and apixaban) for both sexes [2].

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Seiffge DJ, Werring DJ, Paciaroni M, Dawson J, Warach S, Milling TJ, Engelter ST, Fischer U, Norrving B. Timing of anticoagulation after recent ischaemic stroke in patients with atrial fibrillation. Lancet Neurol. 2018 Nov 8. pii: S1474-4422(18)30356-9. doi: 10.1016/S1474-4422(18)30356-9. [Epub ahead of print] Review. PubMed PMID: 30415934.

2)
Lenglet A, Qazi JZ, Boivin Proulx LA, Legault C, Dorais M, Perreault S. Trends of use and factors that determine the choice of oral anticoagulants in women and men with atrial fibrillation. Pharmacol Res Perspect. 2022 Dec;10(6):e01012. doi: 10.1002/prp2.1012. PMID: 36413058.