DSEN ABSTRACT

Safety, Effectiveness and Cost-effectiveness of Direct Oral Anti-coagulants in Patients with Atrial Fibrillation

Summary

A systematic review and network meta-analysis of the efficacy and safety evidence pertaining to the use of anticoagulants for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation. Key subgroups of age, stroke risk, and time spent in the therapeutic range.

Key messages

At the study-level, all the DOACs, with the exception of dabigatran 110 mg, significantly reduced all-cause stroke/systemic embolism compared to adjusted-dose warfarin. Except for apixaban, none of the DOACs significantly reduced all-cause mortality. Apixaban and dabigatran 110 mg significantly reduced the risk of major bleeding relative to adjusted-dose warfarin.

Data suggest that there may be subgroups for which use of DOACs may be more or less beneficial – decisions will depend on relative preferences to avoid strokes over major bleeds.

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What is the issue?

- Approximately 250,000 Canadians are affected by atrial fibrillation (AF). Canadians with AF are five times more likely to have a stroke and twice as likely to die as individuals without AF.
- Anti-coagulant strategies for AF patients include warfarin and the direct oral anticoagulants (DOACs).
- While DOACs have been demonstrated to be effective in preventing stroke in AF patients, the relative effectiveness and associated bleeding risks of the DOACs, both among themselves and in comparison to warfarin, is not clear.

What was the aim of the study?

- To review the evidence on the DOACs (dabigatran, rivaroxaban and apixaban) in patients with non-valvular AF, to prevent stroke and systemic embolism when compared to warfarin therapy.
- Key components include: a full assessment of clinical and cost-effectiveness and safety, specific consideration for age, stroke risk and time-in-therapeutic international normalized ratio range (TTR) subgroups.

How was the study conducted?

- A systematic review identified 5 randomized controlled trials evaluating non-inferiority of DOACs compared to adjusted-dose warfarin. Three large trials were assessed as high quality (ROCKET AF, RE-LY, ARISTOTLE) and included in the analysis.
- The main outcomes were: all-cause stroke/systemic embolism, major bleeding, intracranial bleeding, major gastrointestinal bleeding, all-cause mortality, and myocardial infarction.
- Bayesian network meta-analyses were conducted to combine trial results. Subgroup analyses were conducted to adjust for sources of heterogeneity.

What did the study find?

- The limited number of studies coupled by study heterogeneity and use of sub-group data means there is uncertainty regarding any conclusions; nevertheless, data suggest that there may be subgroups for which use of DOACs may be more or less beneficial. Subgroup data based on age, stroke risk and TTR presented in the full technical report and related publications.
- Choice of DOAC will depend on relative preferences to avoid strokes over major bleeds. Rigorously conducted comparative studies or network meta-regression analyses of patient-level data are required to confirm these findings.

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CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

ccNMA Canadian Collaboration for Drug Safety, Effectiveness & Network Meta-Analysis

Link to Publications: Cameron et al,2014; Coyle et al, 2013; Wells et al, 2012.