

Safety of direct oral anticoagulants (DOACs) vs. warfarin for people aged ≥ 75 years with atrial fibrillation: a cohort study

Introduction: Warfarin significantly reduces the risk of stroke in people with atrial fibrillation (AF), but historically has been underused in older people due to complicated dosage regimens. DOACs offer an attractive alternative to warfarin and were shown to be non-inferior in randomised controlled trials, however older people were underrepresented in these trials and there have been few studies investigating outcomes specifically in this high risk group (1).

Aim: To compare the risk of major, non-major, gastrointestinal, and intracranial bleeding between warfarin and DOACs in people aged ≥ 75 years with AF.

Methods: A cohort of patients aged ≥ 75 years with a diagnosis of AF was extracted from the Clinical Practice Research Datalink (CPRD). Patients could enter the study on the date of their first prescription for warfarin or a DOAC between 1/1/2013 and 27/12/2017. Patients were censored on the date of the outcome, death, or leaving the general practice. Switching between anticoagulants and unexposed periods were measured using prescription mapping. Crude and adjusted hazard rates of the risk of bleeding were calculated using a Cox proportional hazards model with oral anticoagulant prescribing as a time varying covariate.

Results:

The cohort included 10,149 patients in the warfarin group and 10,237 in the DOAC group. The groups had similar characteristics and the average age was 81 in the warfarin group and 82 in the DOAC group. Table 1 summarises the results. Whilst major and non-major bleeding was similar between all DOACs and warfarin, rivaroxaban was associated with higher risk and apixaban lower risk when analysed separately. Risk of gastrointestinal bleeding was higher with all DOACs and rivaroxaban than warfarin but apixaban was not significantly different. Few intracranial events occurred (n=131).

Table 1: Adjusted hazard ratios (95% confidence intervals) for bleeding outcomes with DOACs compared with warfarin

	Major bleeding	Non-major bleeding	Gastrointestinal bleeding	Intracranial haemorrhage
All DOACs	1.11 (0.98-1.27)	1.00 (0.91-1.10)	1.19 (1.03-1.38)	0.76 (0.50-1.14)
Rivaroxaban	1.34 (1.15-1.55)	1.29 (1.16-1.44)	1.46 (1.23-1.73)	0.89 (0.55-1.44)
Apixaban	0.84 (0.69-1.01)	0.73 (0.64-0.85)	0.84 (0.68-1.05)	0.70 (0.39-1.23)

Conclusion: The results indicate that DOACs as a group are not significantly different to warfarin, however when analysed separately, apixaban may be safer. While the study relies on prescription data and hence it is not known if patients were taking the medications, the large cohort studied is representative of older people who are prescribed these medications in UK primary care

References:

(1) Mitchell A, Watson MC, Welsh T, McGrogan A. Effectiveness and safety of direct oral anticoagulants versus vitamin K antagonists for people aged 75 years and over with atrial fibrillation: A systematic review and meta-analyses of observational studies. *Journal of Clinical Medicine*. 2019; 8 (554).