

Direct Oral Anticoagulants or Warfarin for A-fib?

A recent study evaluated the effectiveness of three direct oral anticoagulants and warfarin in patients with atrial fibrillation. Which agents came out on top?

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PRACTICE CHANGER

Use direct oral anticoagulants instead of warfarin in patients with atrial fibrillation; they are just as effective at preventing ischemic stroke and systemic emboli as warfarin, and apixaban and dabigatran have lower bleeding rates.

STRENGTH OF RECOMMENDATION

B: Based on a single prospective cohort study.¹

A 66-year-old man with a history of hypertension and type 2 diabetes is hospitalized for palpitations and dizziness and is diagnosed with atrial fibrillation (A-fib). His heart rate is successfully regulated with a β -blocker. He has a CHA₂DS₂-VASc score of 3, making him a candidate for anticoagulation. Which agent should you start?

Thromboembolism in patients with A-fib often results in stroke and death, but appropriate use of antithrombotic therapy can reduce risk. Evidence-based guidelines recommend that patients with A-fib at intermediate or high risk for stroke (CHADS₂ score \geq 2, or prior history of cardioembolic stroke or transient ischemic attack) receive antithrombotic therapy with oral anticoagulation, rather than receive no therapy or therapy with antiplatelets.^{2,3}

The American College of Chest Physicians also recommends use of the direct oral anticoagulant (DOAC) dabigatran instead of warfarin for those patients with nonvalvular A-fib with an estimated glomerular filtration rate \geq 15 mL/min/1.73 m².³

A meta-analysis of large randomized controlled trials (RCTs) investigated individual

DOACs: dabigatran (a direct thrombin inhibitor) and the factor Xa inhibitors rivaroxaban, apixaban, and edoxaban. The results revealed similar or lower rates of ischemic stroke and major bleeding (except gastrointestinal bleeds; relative risk, 1.25) when compared with warfarin (at an international normalized ratio [INR] goal of 2-3).⁴ In addition, three separate meta-analyses that pooled results from large RCTs involving dabigatran, apixaban, and rivaroxaban also concluded that these medications significantly reduced incidence of embolic stroke and risk for major bleeds and hemorrhagic stroke, compared with warfarin.⁵⁻⁷

However, less is known about the comparative effectiveness and safety of the DOACs when they are used in clinical practice, and it is not clear which, if any, of these agents is superior to others. Moreover, only about half of the patients in the United States with A-fib who are eligible to take DOACs are currently managed with them.⁸

STUDY SUMMARY

Different DOACs, different benefits

This large cohort study used data from three Danish national databases to assess the effectiveness of three DOACs compared with warfarin. The nearly 62,000 patients had been recently diagnosed with A-fib without valvular disease or venous thromboembolism. Subjects were prescribed either standard doses of dabigatran (150 bid; N = 12,701), rivaroxaban (20 mg/d; N = 7,192), or apixaban (5 mg bid; N = 6,349) or dose-adjusted warfarin to an INR goal of 2 to 3 (N = 35,436). Patients were followed for an average of 1.9 years.

Ischemic stroke, systemic emboli. In the first year of observation, there were 1,702

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reports of ischemic stroke or systemic emboli. The incidence of ischemic stroke or systemic embolism was the same or better for each of the three DOAC treatments than for warfarin (2.9-3.9 vs 3.3 events per 100 person-years, respectively). Ischemic stroke or systemic emboli events occurred less frequently in the rivaroxaban group than in the warfarin group at one year (hazard ratio [HR], 0.83) and after 2.5 years (HR, 0.80). The rates of ischemic stroke and systemic emboli for both apixaban and dabigatran were not significantly different than that for warfarin at either end-point.

Bleeding events (defined as intracranial, major gastrointestinal, and traumatic intracranial) were lower in the apixaban group (HR, 0.63) and dabigatran group (HR, 0.61) than in the warfarin group at one year. Significant reductions remained after 2.5 years. There was no difference in bleeding events between rivaroxaban and warfarin.

Risk for death. Compared with warfarin, the risk for death after one year of treatment was lower in the apixaban (HR, 0.65) and dabigatran (HR, 0.63) groups, and there was no significant difference in the rivaroxaban group (HR, 0.92).

WHAT'S NEW

No agent “has it all,” but DOACs have advantages

This comparative effectiveness and safety analysis reveals that all of the DOACs are at least as effective as warfarin in preventing ischemic stroke and systemic emboli, that rivaroxaban may be more effective, and that apixaban and dabigatran have a lower risk for bleeding than warfarin.

CAVEATS

Lacking INR data

This study was a nonrandomized cohort trial. And, while propensity weighting helps, the researchers were unable to completely control for underlying risk factors or unknown confounders.

INR data for patients on warfarin were not provided, so it is not clear how often patients were out of therapeutic range, which could affect the stroke and bleeding results in the warfarin group. This, however, is seen with routine use of warfarin. This study reflects the challenge of maintaining patients in warfarin's narrow therapeutic range.

CHALLENGES TO IMPLEMENTATION

It comes down to cost

Cost could be a barrier, as health insurance coverage for DOACs varies. Patients with high-deductible health insurance plans, or who find themselves in the Medicare “donut hole,” may be at a particular disadvantage. **CR**

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