Original Investigation

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Apixaban to Prevent Recurrence After Cryptogenic Stroke in Patients With Atrial Cardiopathy

The ARCADIA Randomized Clinical Trial

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Key Points

Question Is anticoagulation superior to antiplatelet therapy for prevention of recurrent stroke in patients with cryptogenic stroke and evidence of atrial cardiopathy?

Findings In this randomized clinical trial that included 1015 patients, the rate of recurrent stroke did not significantly differ between the apixaban group (annualized rate, 4.4%) and the aspirin group (annualized rate, 4.4%).

Meaning In patients with cryptogenic stroke and evidence of atrial cardiopathy without atrial fibrillation, apixaban did not significantly reduce recurrent stroke risk compared with aspirin.

Abstract

Importance Atrial cardiopathy is associated with stroke in the absence of clinically apparent atrial fibrillation. It is unknown whether anticoagulation, which has proven benefit in atrial fibrillation, prevents stroke in patients with atrial cardiopathy and no atrial fibrillation.

Objective To compare anticoagulation vs antiplatelet therapy for secondary stroke prevention in patients with cryptogenic stroke and evidence of atrial cardiopathy.

Design, Setting, and Participants Multicenter, double-blind, phase 3 randomized clinical trial of 1015 participants with cryptogenic stroke and evidence of atrial cardiopathy, defined as P-wave terminal force greater than 5000 μV × ms in electrocardiogram lead V_1, serum N-terminal pro-B-type natriuretic peptide level greater than 250 pg/mL, or left atrial diameter index of 3 cm/m^2 or greater on echocardiogram. Participants had no evidence of atrial fibrillation at the time of randomization. Enrollment and follow-up occurred from February 1, 2018, through February 28, 2023, at 185 sites in the National Institutes of Health StrokeNet and the Canadian Stroke Consortium.

Interventions Apixaban, 5 mg or 2.5 mg, twice daily (n = 507) vs aspirin, 81 mg, once daily (n = 508).

Main Outcomes and Measures The primary efficacy outcome in a time-to-event analysis was recurrent stroke. All participants, including those diagnosed with atrial fibrillation after randomization, were analyzed according to the groups to which they were randomized. The primary safety outcomes were symptomatic intracranial hemorrhage and other major hemorrhage.

Results With 1015 of the target 1100 participants enrolled and mean follow-up of 1.8 years, the trial was stopped for futility after a planned interim analysis. The mean (SD) age of participants was 68.0 (11.0) years, 54.3% were female, and 87.5% completed the full duration of follow-up. Recurrent stroke occurred in 40 patients in the apixaban group (annualized rate, 4.4%) and 40 patients in the aspirin group (annualized rate, 4.4%) (hazard ratio, 1.00 [95% CI, 0.64-1.55]). Symptomatic intracranial hemorrhage occurred in 0 patients taking apixaban and 7 patients taking aspirin (annualized rate, 1.1%). Other major hemorrhages occurred in 5 patients taking apixaban (annualized rate, 0.7%) and 5 patients taking aspirin (annualized rate, 0.8%) (hazard ratio, 1.02 [95% CI, 0.29-3.52]).

Conclusions and Relevance In patients with cryptogenic stroke and evidence of atrial cardiopathy without atrial fibrillation, apixaban did not significantly reduce recurrent stroke risk compared with aspirin.

Trial Registration ClinicalTrials.gov Identifier: NCT03192215

Editorial
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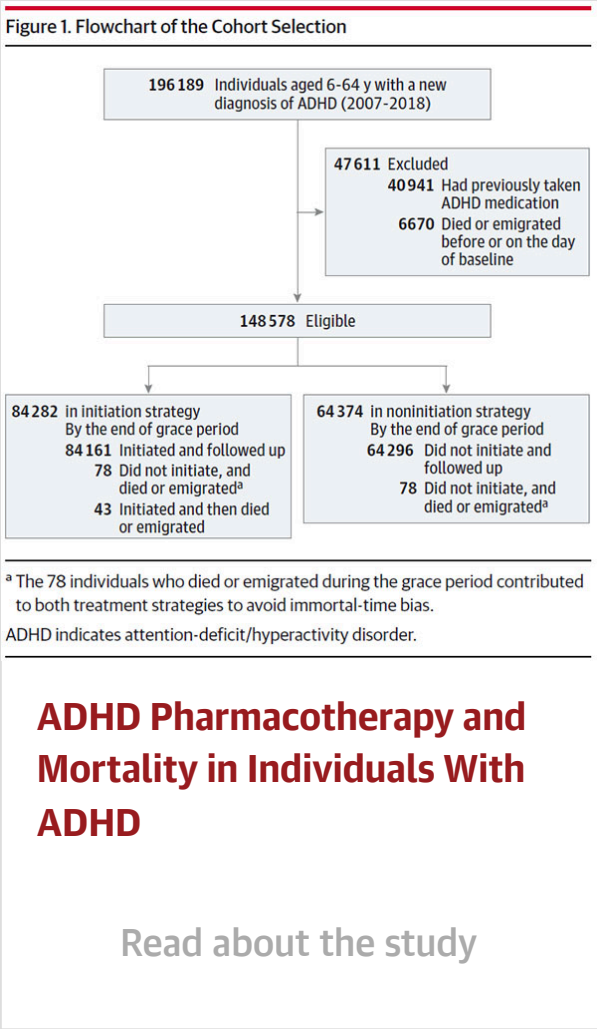

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