

Anticoagulation for Stroke Prevention in Elderly Patients with Atrial Fibrillation: Risk-Benefit Ratio Remains Highly Favorable

The benefits of oral anticoagulation may be obscured in elderly patient with atrial fibrillation due to multiple factors reasons. However, a new study by Van Walraven et al¹ showed that oral anticoagulants remain beneficial in preventing ischemic stroke even in elderly patients with atrial fibrillation.

Alberto Maud, MD
Kamakshi Lakshminarayan, MD PhD
Adnan I. Qureshi, MD

Address Correspondence to:
Alberto Maud, MD,
Minnesota Stroke Initiative,
University of Minnesota,
12-100 PWB MMC 295,
516 Delaware St. SE,
Minneapolis, MN 55455.

maudx006@umn.edu

Atrial fibrillation (AF) is an independent risk factor for stroke, and subsequent death and disability. AF independently increases the stroke risk 5-folds in an age dependent manner.² AF affects 5% of the population over 70 years, and the prevalence approaches up to 10% for individuals over 80 years.³ It is expected that AF will increase its prevalence in the future because of aging of the population.⁴ Adjusted-dose warfarin to achieve an International Normalized Ratio (INR) between 2 and 3 is proven to significantly reduce the risk of stroke associated with AF.²

The Birmingham Atrial Fibrillation Treatment of Aged, a prospective, randomized, open label trial, compared the efficacy of warfarin (INR 2-3) with aspirin 75 mg daily, for the prevention of stroke in AF patients without previous stroke, aged 75 years or greater. The primary end point was fatal or non fatal disabling stroke, intracranial hemorrhage, or clinically significant systemic arterial embolism. This trial showed superiority of warfarin over aspirin for prevention of stroke in a population of elderly AF patient. The frequency of ischemic stroke, systemic arterial embolism and hemorrhagic stroke was 52% lower in the anticoagulated

patients.⁵ The Warfarin versus Aspirin for Stroke Prevention in Octogenarians with Atrial Fibrillation trial specifically addressed the efficacy of adjusted doses of Warfarin (INR 2-3) versus 300 mg of aspirin in patients between 80 and 90 years old. Primary end point was combined death, thromboembolism, major bleeding and withdrawal from assigned treatment. There were more outcome events in the aspirin group, interestingly because of aspirin toxicity.⁶

Despite the benefits, elderly people are less likely to be treated with long term oral anticoagulants. The high prevalence of co-morbid factors e.g., impaired cognition with limited compliance, use of concomitant medications, and frequent falls are the most common limiting factors associated with no use of oral anticoagulants in elderly patients with AF. In a prospective study of warfarin prescription at the time of the treatment decision among consecutive patients admitted and discharged with AF showed that hemorrhage, falls, and patient's refusal or history of non adherence to therapy constituted nearly 80% of the physician-cited reasons for not prescribing warfarin.⁷

The Atrial Fibrillation Investigators studied the effect of age on stroke prevention therapy in patients with atrial fibrillation. In this secondary analysis of patient-level randomized trial data, the investigators determined if patient age significantly influenced the effect of oral anticoagulants and antiplatelets on the risk of ischemic stroke, serious bleeding, or cardiovascular events.¹

Patient-level data from almost all published clinical trials in which patients with nonvalvular AF were randomized to at least 2 of the following treatment: full-dose of oral anticoagulants, antiplatelets, or either placebo or control were included in this analysis. Patient age was analyzed as a continuous variable trying to determine if the association of treatment with outcome varied with patient age.

The analysis include 8,932 patients, with a mean age of 70.9 (standard deviation [SD], 9.4) years. A total of 19.6% of the patients were 80 years old or older. The proportion of men varied extensively among studies but overall 63% were men in the aggregate data. The frequency of cerebrovascular risk factors including hypertension, diabetes mellitus, and congestive heart failure, was relatively consistent across studies. The mean follow up term was 2 years (SD, 1.2; range, 1.2 to 3.8 years). Patient age was independently associated with the risk of each outcome, including ischemic stroke (hazard ratio, 1.45 per decade increase in age; 95% confidence interval [CI], 1.26 to 1.66), serious hemorrhage (hazard ratio, 1.61; 95% CI 1.47 to 1.77), and cardiovascular event (1.43; 95% CI, 1.33 to 1.53).

From the Zeenat Qureshi Stroke Research Center, University of Minnesota, Minneapolis, MN

Oral anticoagulants remain overwhelming beneficial for preventing stroke and cardiovascular events in elderly patients with AF despite a slight decrease of the relative risk reduction of oral anticoagulant. Moreover, there was a marked decrease of stroke risk reduction from antiplatelet treatment in the elderly patients with AF. There was no significant interaction between oral anticoagulants or antiplatelets and patient's age regarding serious hemorrhage or cardiovascular death. This finding contradicts the common belief that advanced age is a risk factor for hemorrhagic events associated with long term use of antithrombotics.

These results support that elderly age alone is not a contraindication to the use of oral anticoagulant in patient with AF. The prominent reduction in the efficacy of antiplatelet treatment with increasing patient age makes the oral anticoagulants even a more attractive treatment choice for stroke risk reduction in the elderly patients with AF.

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