






Anticoagulant plus antiplatelet treatment increased the risk of bleeding in atrial fibrillation

Shireman TI, Howard PA, Kresowik TF, *et al.* Combined anticoagulant-antiplatelet use and major bleeding events in elderly atrial fibrillation patients. *Stroke* 2004;**35**:2362–7.

Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ Internal medicine ★★★★★☆☆ Haematology ★★★★★☆☆
Cardiology ★★★★★☆☆

Q What is the effect of concomitant anticoagulant and antiplatelet treatment on the risk of major bleeding in older patients with atrial fibrillation (AF)?

METHODS

	Design: retrospective cohort analysis within the US National Stroke Project.
	Setting: USA.
	Patients: 10 093 patients ≥65 years of age (mean age 77 y, 51% men) who were admitted to hospital for AF and had warfarin discharge treatment. Exclusion criteria: transfer to another acute care hospital, death during hospitalisation, or discharge against hospital advice.
	Risk factors: age, sex, comorbid conditions (coronary or valvular heart disease, diabetes, previous cerebrovascular event, hypertension, and congestive heart failure), bleeding risk factors (previous bleeding, anaemia during the index hospital admission, ulcer, risk of falls, alcohol use, hepatic disease, dementia, cancer, and concurrent medications), and warfarin use before admission.
	Outcomes: antiplatelet drug use after hospital discharge and hospital admission for acute bleed within 90 days.

MAIN RESULTS

1962 patients (19.4%) were prescribed an antiplatelet at discharge (aspirin [90%], aspirin plus clopidogrel or ticlopidine [6%], or ticlopidine alone [4%]). Bleeding events increased from 1.3% in warfarin only users to 1.9% in warfarin plus antiplatelet users (relative risk 1.45, 95% CI 0.998 to 2.09, absolute risk increase 0.6%)*. Factors associated with major bleeding within 90 days of discharge were female sex, age, anaemia, history of bleeding, and combined warfarin plus antiplatelet use (table). Coronary heart disease (odds ratio [OR] 2.41, CI 2.13 to 2.73) and concurrent use of non-steroidal anti-inflammatory drugs (OR 1.41, CI 1.09 to 1.82) or other medications (OR 1.28, CI 1.16 to 1.43) increased the likelihood of being prescribed antiplatelets. Women (OR 0.80, CI 0.72 to 0.88) and patients with previous warfarin use (OR 0.63, CI 0.57 to 0.70), dementia (OR 0.76, CI 0.62 to 0.93), cancer (OR 0.56, CI 0.38 to 0.83), a discharge antibiotic (OR 0.80, CI 0.71 to 0.90), or terminal status (prognosis <6 mo) (OR 0.77, CI 0.64 to 0.92) were less likely to be prescribed antiplatelets.

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CONCLUSION

In older patients with atrial fibrillation, combined anticoagulant plus antiplatelet treatment increased the risk of major bleeding by 50%.

*Numbers calculated from data in article.

Commentary

As the prevalence of coronary disease and AF escalate in our ageing population, clinicians increasingly must weigh the risk of using both antiplatelet and anticoagulation therapies in an individual patient.

The retrospective analysis by Shireman *et al* found that 19% of elderly patients discharged on warfarin after hospital admission for AF simultaneously used an antiplatelet agent; that this was associated mostly with sex, coronary disease, and absence of bleeding risks; and that it was independently associated with a 0.6% absolute increase (and 53% increase in odds) of major bleeding at 90 days.

The study provides interesting descriptive data regarding current practices in older patients, but it does not provide insights to fundamental clinical questions. Assessing cardiac and stroke outcomes, in addition to bleeding, would have allowed an interpretation of the risks in the context of the benefits. Also, the follow up period was too short to assess these long term prevention strategies. Characteristics of the 11 000 excluded patients in whom warfarin was withheld, the occurrence of haemorrhage in patients discharged on antiplatelets alone, and risks with different warfarin or antiplatelet doses would have been more informative.

Randomised trials provide better but still incomplete guidance regarding dual therapy. Importantly, the magnitude of coronary disease benefit with moderate intensity anticoagulation is greater than it is with antiplatelet therapy (warfarin v aspirin: 21% odds reduction of mortality, infarction, or stroke).¹ Accordingly, a clear indication should exist if adding aspirin to warfarin. Data from 3 randomised trials (about 3000 patients) suggest an incremental but small coronary disease benefit and no difference in bleeding risk when aspirin is added to moderate intensity anticoagulation.¹ Thus, the available evidence is not robust, and a reasonable strategy continues to rely on individual patient characteristics to determine the benefit-risk ratio of adding aspirin to warfarin. It should be remembered that it is not justified to lower the dose of warfarin to mitigate bleeding when aspirin is added, since this strategy is associated with more ischaemic events.^{1,2}

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1 Anand SS, Yusuf S. Oral anticoagulants in patients with coronary artery disease. *J Am Coll Cardiol* 2003;**41**:62–95.

2 Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. *Lancet* 1996;**348**:633–8.

Risk factors for major bleeding in older patients within 90 days of hospital discharge for atrial fibrillation*

Risk factors	Adjusted odds ratio (95% CI)	Relative risk (CI)	ARI (CI)
Female	1.40 (1.002 to 1.95)	1.39 (1.002 to 1.93)	0.5% (0.003 to 1.2)
Age†	1.03 (1.002 to 1.05)	1.03 (1.002 to 1.05)	0.04% (0.003 to 0.06)
Anaemia	2.52 (1.64 to 3.88)	2.47 (1.63 to 3.74)	1.9% (0.8 to 3.6)
History of bleeding	2.40 (1.71 to 3.38)	2.36 (1.69 to 3.28)	1.8% (0.9 to 3.0)
Warfarin plus antiplatelets	1.53 (1.05 to 2.22)	1.52 (1.05 to 2.19)	0.7% (0.06 to 1.5)

*Abbreviations defined in glossary; relative risk, ARI, and CI calculated from data in article.

†Each 1 year increase in age was associated with a 3% increase in bleeding rate.