Warfarin plus aspirin prevented ischemic heart disease in high-risk men


Question
Can low-intensity oral anticoagulation with warfarin and low-dose aspirin, together or individually, prevent ischaemic heart disease (IHD) in high-risk men?

Design
Randomized, placebo-controlled trial using a factorial design.

Setting
108 U.K. practices belonging to the Medical Research Council's General Practice Research Framework.

Patients
5685 men (mean age 57.5 y) at high risk for IHD on the basis of smoking, family history of premature IHD, body mass index, blood pressure, total cholesterol and plasma fibrinogen levels, and plasma factor VII coagulant activity. Exclusion criteria were history of possible peptic ulceration, myocardial infarction (MI), or stroke or use of drugs incompatible with trial medications.

Intervention
1277 men were allocated to warfarin and aspirin, 1268 to warfarin alone, 1268 to aspirin alone, and 1272 to placebo. Warfarin was started at 2.5 mg/d and adjusted monthly to maintain an International Normalized Ratio of approximately 1.5. Aspirin, 75 mg/d, was given in a controlled-release formulation.

Main outcome measures
Total IHD (coronary death and fatal and nonfatal MI), fatal IHD (coronary death and fatal MI [death within 1 month]), and nonfatal IHD.

Main results
344 IHD events occurred in the factorial component of the trial. Men who received warfarin and aspirin had fewer total IHD events (P = 0.005) and fewer nonfatal IHD events (P = 0.014) than men who received placebo only (Table). Men who received warfarin (alone or with aspirin) had fewer total IHD events (P = 0.04) and fewer fatal IHD events (P = 0.01) than men who did not receive warfarin. Men who received aspirin (alone or with warfarin) had fewer total IHD events (P = 0.04) and fewer nonfatal IHD events (P = 0.004).

Conclusions
In high-risk men, warfarin combined with low-dose aspirin reduced ischemic heart disease events. Combined treatment was more effective than either warfarin or aspirin alone.

Reference