Anticoagulation in atrial fibrillation in older people

There is controversy and apprehension regarding the routine use of oral anticoagulants in atrial fibrillation, especially in elderly people. Based on current evidence, however, patients with non-rheumatic atrial fibrillation who have no obvious contraindications to warfarin should receive prophylactic anticoagulant therapy for prevention of embolic stroke. Patients unable to tolerate warfarin would benefit from aspirin. It is poor clinical practice to await transient ischaemic attacks or a stroke before considering anticoagulation, and it should be remembered that cost–benefit values need to include the cost of rehabilitation and long-term care.

ATRIAL FIBRILLATION AND STROKE

In clinical practice, atrial fibrillation is one of the most common arrythmias seen in older people. It is the primary cardiovascular disorder predisposing patients to systemic embolization. The incidence of atrial fibrillation increases with age; it is seen in <1% of the 40–65 year age group, in 2–5% of the 65–74 year age group, and in >5% of patients above the age of 75 years.

The Framingham Heart Study (Kannel et al, 1982) found that the annual risk of strokes in patients with atrial fibrillation increases five-fold with advancing age from 6.7% in patients aged 50–59 years to 36.2% in patients aged 80–89 years. Patients with lone atrial fibrillation below the age of 60 years had no increased risk of stroke, yet non-rheumatic atrial fibrillation in patients with hypertension, congestive cardiac failure or thromboembolism was associated with an increased risk of stroke of >7% per year.

THE TRIALS

The past decade has witnessed a remarkable advance in our understanding of the stroke risk posed by atrial fibrillation and the prevention of risk offered by warfarin anticoagulation.

The Copenhagen Atrial Fibrillation Aspirin and Anticoagulation Study (AFASAK) was the first published randomized trial in non-rheumatic atrial fibrillation using anticoagulant therapy (Petersen et al, 1989). AFASAK showed a significant reduction in thromboembolic strokes with a minimal increase in haemorrhagic complications in the warfarin group. This benefit did not extend to aspirin.

The Boston Area Anticoagulation Trial for Atrial Fibrillation (BAATAF) Investigators (1990) was an unblinded study of patients with paroxysmal or chronic non-valvular atrial fibrillation. The trial was stopped early because interim analyses of the data showed a favourable effect of warfarin. Although 46% of the placebo group used aspirin, it had no demonstrable clinical benefit. This trial, in addition, showed no difference in stroke for chronic or paroxysmal atrial fibrillation.

The Veterans Affairs Stroke Prevention in Atrial Fibrillation (SPINAF) trial (Ezekowitz et al, 1992) was a double-blind placebo-controlled study looking at primary and secondary prevention of strokes with patients randomized to warfarin, aiming for a target international normalized ratio (INR) of 1.4–2.8, and placebo. Interim analyses showed a marked decrease in cerebral infarctions in the warfarin group.

The first Stroke Prevention in Atrial Fibrillation (SPAF I) (1991) randomized patients with chronic or paroxysmal atrial fibrillation to warfarin, aspirin or placebo. The study found an overall reduction of systemic embolization and ischaemic stroke. The trial was then continued as SPAF II (1994) which was designed to compare aspirin with warfarin.

The Canadian Atrial Fibrillation (CAFA) trial (Connolly et al, 1991) was a double-blind placebo controlled trial of low-dose warfarin, target INR of 2 to 3 in atrial fibrillation. The trial was stopped prematurely after the AFASAK report and the preliminary report of the SPAF I came out. The European Atrial Fibrillation Trial (EAFT) (1993) also found that there was significant reduction in incidence of strokes in patients on warfarin. A target INR below 2 is much less effective than an INR between 2 and 3.

RISK FACTORS FOR STROKE

All studies except the CAFA study attempted to identify clinical risk factors for ischaemic stroke in patients enrolled in their studies. The independent risk factors for stroke identified with multivariate analyses were increasing age, previous stroke or transient ischaemic attack, history of hypertension or diabetes, and recent congestive cardiac failure. Independent echocardiographic predictors are global left ventricular dysfunction and left atrial size.

ASPIRIN AND ATRIAL FIBRILLATION

The estimates of efficacy for aspirin therapy from the AFASAK and the SPAF I were quantitatively different. The SPAF II trial was conducted to make a direct comparison between aspirin and warfarin. On the basis of its evidence, warfarin was more effective than aspirin in all age groups and its superiority was more with increased age and other risk factors. Warfarin reduced the absolute risk of ischaemic

stroke and systemic embolism by 1.2% in patients in the age group over 75 years.

RISK OF BLEEDING

Annual frequency of major bleeding events was 1.0% receiving placebo and 1.3% per year in warfarin-treated patients in a meta-analysis of the five primary prevention trials (Laupacis et al, 1994).

Physicians are concerned about the risk of haemorrhagic complications, although studies have shown that warfarin is a safe drug if candidates are selected carefully. The Sixty Plus Reinfarction Study (Wintzen et al, 1982) found that most bleeding episodes occurred at a prothrombin time more than twice the control; thus patient age should not be considered a primary factor in assessing the risk of long-term anticoagulation therapy. It is believed that low-dose anticoagulation is associated with a lower risk of bleeding in elderly people.

In the AFASAK, SPAF and BAATAF studies, the annual incidence of serious bleeding varied from 0.5% to 3.2%, and the incidence of fatal bleeding ranging from 0% to 0.2%. Considering the very significant increase in the risk of stroke in patients with non-rheumatic atrial fibrillation, the benefits of anticoagulation outweigh the risks, especially in the elderly age group. Appropriate candidates for anticoagulation need to be identified, keeping in mind the contraindications. Other contraindications include recent history of bleeding or coagulopathy, peptic ulcer, history of falls, dementia, malignancy, alcoholism and severe liver disease. Despite this, the majority of elderly patients will still be eligible for anticoagulation. Compliance in some older people can be a practical problem but measures can be taken to ensure that the drugs are taken regularly and in the correct dose. HM

I Gupta/G Bennett/P Gompertz

Specialist Registrar and Lecturer/Reader and Consultant Physician/Consultant Physician

Department of Health Care of The Elderly

St. Bartholomew's and The Royal London School of Medicine

London E1 4DG

Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators (1990) The effect of low dose warfarin on the risk of stroke in patients with non-rheumatic atrial fibrillation. *N Engl J Med* **323:** 1505–11

Connolly SJ, Laupacis A, Gent M et al (1991) Canadian Atrial Fibrillation Anticoagulation Study. *J Am Coll Cardiology* **18:** 349–55

European Atrial Fibrillation Trial Study Group (1993) Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stoke. *Lancet* **342:** 1255–62

Ezekowitz MD, Bridgers SL, James KE et al (1992) Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. *N Engl J Med* **327:** 1406–12

Kannel W, Abbott R, Savage D et al (1982) Epidemiologic features of chronic atrial fibrillation: The Framingham Study. *N Engl J Med* **317:** 1018–22

Laupacis A, Boysen G, Connolly S et al (1994) Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analyses of pooled data from five randomised controlled trials. *Arch Intern Med* **154:** 149–57

Petersen P, Boysen G, Godtfredsen J et al (1989) Placebo controlled, randomized trial of warfarin and aspirin for prevention of thromboembolic complication in chronic atrial fibrillation: The Copenhagen AFASAK study. *Lancet* **i:** 175–8

Stroke Prevention in Atrial Fibrillation Investigators (1991) Stroke Prevention in Atrial Fibrillation Study: final results. *Circulation* **84:** 527–39

Stroke Prevention in Atrial Fibrillation Investigators (1994) Warfarin *vs* aspirin for prevention of thromboembolism in atrial fibrillation. Stroke Prevention in Atrial Fibrillation II Study. *Lancet* **343:** 687–91

Wintzen AR, Tijssen JG, De Vries WA et al (1982) Risks of long-term oral anticoagulant therapy in elderly patients after myocardial infarction: Sixty Plus Reinfarction Study Group. *Lancet* **i:** 64–8

Wolf PA, Abbott RD, Kannel WB (1991) Atrial fibrillation as an independent risk factor for stroke. The Framingham Study. *Stroke* **22:** 983–8

KEY POINTS

- Atrial fibrillation is a common cause of thromboembolic stroke.
- The incidence of stroke increases in the presence of associated risk factors including age.
- Warfarin has been proved to be beneficial and safe in patients with non-rheumatic atrial fibrillation in terms of reduction of risk of future strokes.
- Warfarin should be prescribed to all such patients if they can tolerate it and in the absence of any contraindications.