

Anticoagulation and Bleeding Risk - Guidelines for Medical Professionals

Introduction

Atrial Fibrillation is a common condition increasing in prevalence with increasing age. It is estimated that 600,000 people are currently affected in the United Kingdom however even this figure may be an under estimate. Although this can be unfortunately symptomatic in some it also has an increased risk of ischaemic stroke in almost all. In patients over 65 it attracts a five-fold increase in ischaemic stroke risk in non-valvular Atrial Fibrillation. Accordingly 15-20% of all ischaemic stroke patients are seen to be suffering from Atrial Fibrillation. Of patients found to have Atrial Fibrillation but receiving no form of anticoagulation 35% will suffer a stroke. Asymptomatic cerebrovascular events may also contribute to vascular dementia and cognitive decline in these patients.

When looking at stroke risk two important studies should be particularly noted. The Stroke Prevention in Atrial Fibrillation (SPAF) study showed that stroke rates in paroxysmal Atrial Fibrillation had similar sorts of figures to persistent Atrial Fibrillation. The second is the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial that demonstrated that the rhythm control group suffered the same incidence of stroke as the rate control group in patients not receiving anticoagulation.

From this we can see that patients who suffer from all forms of Atrial Fibrillation should be considered for some form of anticoagulation. The need for this is reflected in the Quality and Outcome Framework where the appropriate diagnostic test (the ECG) and intervention with antithrombotic therapy is awarded 10 points.

Stroke Prevention

In a meta-analysis of 13 trials it was found that adjusted dose Warfarin significantly reduced the risk of ischaemic stroke compared with placebo. No significant increase in the risk of intracranial haemorrhage was seen between the anti-coagulation group and those in the control groups. This meta-analysis further showed a reduction in all-cause mortality in the anti-coagulated group. In this review Warfarin was more effective than Aspirin in reducing the risk of ischaemic stroke.

An updated meta-analysis of 29 trials compared controls, dose-adjusted Warfarin and Aspirin and revealed a stroke reduction in the anti-coagulated group of 64% compared to 22% with the use of anti-platelet agents. This overview again showing therefore that formal anti-coagulation is more efficacious than anti-platelet therapy.

Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) Study

Concerns about the use of formal anti-coagulation in a practical primary care setting were reported in 2007 in the BAFTA study results. This study demonstrated that anti-coagulation with a controlled Warfarin dose achieving an INR between 2-3 was more effective than Aspirin at 75mg in the older (over 75 years) patient in a primary care setting. The study also demonstrated that there was no significant difference in major bleeding events between the two groups.

In view of the high risk of stroke in the older population and the effectiveness of anti-coagulation in reducing this risk there is an argument to use life-long anticoagulation

more often in this older group unless there is a clear contraindication.

In patients with non-valvular Atrial Fibrillation when Aspirin is compared to placebo it reduces stroke by 22% which is very similar to the effects of Aspirin on stroke prevention in patients regarded at high risk of stroke. Most of the evidence supporting Aspirin's use in Atrial Fibrillation comes from the SPAF study where two cohorts of patients were studied, those unable to receive formal anticoagulation and thus given Aspirin or placebo, and the others being those who could be anti-coagulated where the comparison was between Warfarin and Aspirin. In the first group there is a clear relative risk reduction of 94% however in the second group Aspirin only offered a meagre relative risk reduction of 8%. From this it is clear that Aspirin cannot be seen as an adequate alternative to Warfarin in the high-risk patient.

Risk Stratification - CHADS2

Risk factors for stroke include diabetes, hypertension, congestive cardiac failure, being over 75 and impaired left ventricular systolic function.

The CHADS2 criteria are based on a combination of two previous risk assessment schemes to grade people into low, moderate and high risk. This is scored with a point each for **C**ongestive Heart Failure, **H**ypertension, **A**ge over 75 and **D**iabetes and two points for previous history of **S**troke or TIA. People are regarded as low risk with a score of 0, intermediate risk with a score of 1-2 and high risk if greater than 3.

The current opinion would suggest that the risk benefit point for the patient when being graded through the CHADS2 scheme would be a score of 2 or above.

Summary

Atrial Fibrillation is an increasing issue with

the increasing age of our population. The causative link between Atrial Fibrillation and ischaemic stroke is well demonstrated. It is clear that Warfarin is currently the most efficacious agent in reducing this risk in the intermediate and high-risk patients. The BAFTA study has shown that this is a safe agent in the older population with risks below that generally anticipated by clinicians. If formal anti-coagulation is not acceptable due to concurrent risks in the individual patient then Aspirin can be considered.

CHAD 2 score	Adjusted annual stroke rate (%)	NNTs	Risk of major bleed (per 100 patient years)
0	1.9	53	Warfarin 2.2
1	2.8	36	
2	4.0	25	Aspirin 1.5
3	5.9	17	
4	8.5	12	
5	12.5	8	
6	18.2	5	

- i) Flaker GC, Belew K, Beckman K, et al; AFFIRM Investigators. Asymptomatic Atrial Fibrillation: demographic features and prognostic information from the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005; 149: 657-63.
- ii) Lip GY, Edwards SJ. Stroke prevention with aspirin, warfarin and ximelagatran in patients with non-valvular Atrial Fibrillation: a systematic review and meta-analysis. *Thromb Res* 2006; 118: 321-33.
- iii) Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular Atrial Fibrillation. *Ann Intern Med* 2007; 146: 857-67.
- iv) Mant J, Hobbs FDR, Fletcher K, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with Atrial Fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet* 2007; 370: 493-503.
- v) Stroke Prevention in Atrial Fibrillation Investigators. A differential effect of aspirin in prevention of stroke on Atrial Fibrillation. *J Stroke Cerebrovasc Dis* 1993; 3: 181-88.

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