

SCIENTIFIC LETTER

Warfarin for non-valvular atrial fibrillation: still underused in the 21st century?

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Atrial fibrillation (AF) is associated with an increased risk of stroke, particularly in the elderly.¹ Warfarin is associated with a 70% relative risk reduction of stroke compared with placebo, with only a moderate increase of major bleeding. Warfarin is more beneficial than aspirin for patients at higher risk from thromboembolism (stroke rate > 6%/year), but offers only modest protection compared with aspirin in patients at lower risk (stroke rate ≤ 2%/year).

Guidelines recommend that patients with non-valvular AF and higher stroke risk should be treated with warfarin.^{1,2} Nevertheless, in clinical practice the drug is underused.³ Most previous studies on the appropriateness of warfarin were performed before 1995, only a few years after publication of the randomised stroke prevention trials and thus without a sufficient time lag to incorporate their results into practice.

Our study was designed to assess the current appropriateness of antithrombotic treatment for patients with AF discharged from a teaching hospital in Turin, Italy.

METHODS.

We identified 313 consecutive patients with chronic AF as a secondary diagnosis (*International classification of diseases*, ninth revision, clinical modifications, diagnosis code 427.31) from the discharge file of S Giovanni Battista Hospital of Turin during the six month period from 1 January to 30 June 2000.

Exclusion criteria were: (1) AF as main diagnosis, since cardioversion should be considered and anticoagulation employed according to a specific protocol¹; (2) mitral stenosis or a prosthetic heart valve, because anticoagulant treatment is standard; (3) age > 90 years; (4) discharges from surgical units, because of contraindications to warfarin use or complications (for example, recent surgery, AF as a transient arrhythmia after open heart surgery).

Intermittent AF (at least two ECG documented episodes either before entry or during hospitalisation) without reversible causes (for example, thyrotoxicosis, pneumonia) was also considered.

The appropriateness of anticoagulation treatment was assessed according to three different schemes of risk stratification.^{2,4,5}

Patients were considered to have a contraindication to warfarin if any of the following were documented: haemorrhagic tendency (that is, platelets < 100000/mm³, international normalised ratio (INR) prolongation, etc); intracranial haemorrhage (history or current); major bleeding within six months (that is requiring transfusion or hospitalisation); creatinine concentration > 3.0 mg/dl (>265 μmol/l); hepatic cirrhosis; severe psychiatric disease, dementia or unreliable patient; diastolic pressure > 100 mm Hg despite antihypertensive treatment; a history of two or more falls; chronic alcoholism; allergic reaction to warfarin or previous discontinuation because of bleeding; life expectancy < 12 months; and difficulty/refusal to allow monitoring of INR values.

Multiple logistic regression models (including age, sex, number of clinical risk factors, and speciality of department) were used to estimate odds ratios (ORs) for predictors of warfarin use.

RESULTS

About 80% of the patients were more than 70 years old and/or had another risk factor for stroke. Contraindications to warfarin were present in 33.9% (106/313) of patients (13.2% of the patients were taking warfarin on admission and it was not suspended during the hospital stay).

Of 168 patients for whom prophylaxis was recommended according to the Scottish Intercollegiate Guidelines Network,² less than 50% were discharged with the optimal regimen of prophylaxis (75/168); about 30% were treated with antiplatelet agents (54/168), and more than 20% (39/168) did not receive any prophylaxis. When considering only patients who were not on warfarin treatment at admission, warfarin prescription during hospitalisation becomes even lower (< 30%). These figures were consistent among the three schemes applied (48% discharged on warfarin and 23% without antithrombotic treatment according to both ACCP (American College of Chest Physicians) and SPAF (stroke prevention in atrial fibrillation) criteria, and, respectively, 28% and 29% on aspirin).

Among 168 patients at high risk of stroke, and without contraindications to anticoagulants, warfarin use was positively associated with the number of clinical risk factors (OR 1.62, $p = 0.017$ for each risk factor: diabetes, coronary artery disease, previous stroke/transient ischaemic attack (TIA), hypertension, heart failure), but its use significantly declined with age (OR 0.90, $p = 0.002$ for each year). The relative importance of the clinical conditions in determining the use of warfarin tends to become weaker with increasing age (fig 1).

Secondary prevention with warfarin (previous stroke/TIA) was performed in 30/62 (48.4%) of the patients, but only in 29.3% of those not previously on warfarin. A higher proportion of patients who were admitted for acute stroke or TIA received warfarin (61.3%, $p = 0.039$). No significant difference in the choice of antithrombotic treatment for patients with paroxysmal versus chronic AF could be detected.

In patients incorrectly not treated with anticoagulants, the reasons were identified only in a minority of cases (10.8%); almost always advanced age was the reason, even when no contraindications were found.

Patients correctly treated were given written indications for INR controls at discharge in only 64% of cases. The INR value on admission was below the recommended range (INR 2) in 42.2% of patients already receiving treatment ($n = 45$).

Patients not treated with warfarin during hospitalisation were given antiplatelet drugs in about 58% of cases, even with no contraindications to their use. The use of aspirin was positively associated with age, with an increase in the probability of being treated of 1.06 for each year of age ($p = 0.036$), but not with the number of clinical risk factors.

Abbreviations: ACCP, American College of Chest Physicians; AF, atrial fibrillation; INR, international normalised ratio; OR, odds ratio; SPAF, stroke prevention in atrial fibrillation; TIA, transient ischaemic attack

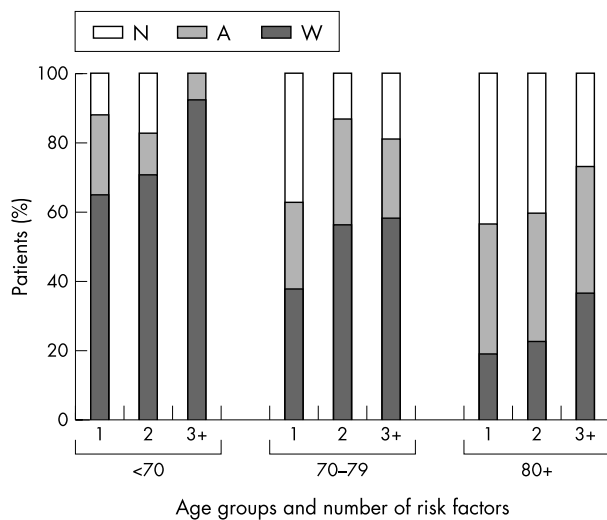


Figure 1 Prophylaxis at discharge. Percentage of patients treated with warfarin (W), antiplatelet drugs (A), or no drugs (N) at discharge by age and number of risk factors (1, 2, or ≥ 3).

DISCUSSION

Our data confirm that the use of anticoagulant drugs is suboptimal in hospitalised patients with chronic AF, both for primary and secondary prevention. In the year 2000 the potential for adjusted dose warfarin to reverse the increased risk of cardioembolic stroke associated with AF does not seem to change clinical practice.

The benefit of anticoagulant treatment is greater in older patients¹; nevertheless, age seems the major concern in starting warfarin treatment. Furthermore, the percentage of patients treated with warfarin increases according to the number of risk factors only in the younger age group (fig 1).

Other studies have found a negative age gradient in the use of warfarin, because of concerns about bleeding complications, especially intracranial haemorrhage, and the perceived differences in the estimated risk of systemic embolism in individual patients. Furthermore, physicians attach a greater negative value to haemorrhagic strokes than to ischaemic ones, even when the health outcomes are the same and despite the demonstrated reduced risk of bleeding with an appropriate range of anticoagulation in the elderly (INR 2.0–3.0). Physicians' fear of causing haemorrhagic stroke and other iatrogenic events, instead of maximising expected benefits, may also account for the tendency to use subtherapeutic INRs.³

The rate of anticoagulation in younger patients (< 70 years) with high stroke risk was better than previously reported, even if still low.

Aspirin was also underused, even if our percentage of patients treated was higher than previously reported, suggesting an increasing use in clinical practice. Even if less effective, it might be selected because of its less complicated regimen, without the burdens imposed on both patients and physicians by warfarin. In our hospital more than 20% of high risk patients were discharged without any prophylaxis; these data suggest that aspirin was not considered as an alternative in individuals who could benefit from it. Lack of reporting in clinical records of reasons for not using warfarin treatment, even when it was indicated, further outlines the scarce attention paid to the importance of deciding upon anticoagulant treatment.

Innovative educational projects must be implemented to increase awareness that strokes in patients with AF have a poorer outcome than in patients with sinus rhythm, and that anticoagulation is effective for preventing strokes of all severity.

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