Barriers to Anticoagulation in Patients With Atrial Fibrillation
Changing Physician-Related Factors

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The opinions in this editorial are not necessarily those of the editors or of the American Heart Association.

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Atrial fibrillation (AF) is not a benign cardiac arrhythmia but instead confers a 5-fold increased risk of stroke compared with age-matched people in sinus rhythm. AF patients also have a worse outcome after stroke, with elevated mortality and stroke recurrence rates, longer hospital stays, and lower discharge rates to their own homes. Current estimates suggest that AF afflicts ≈2.2 million Americans, whereas in the United Kingdom ≈740 000 individuals are thought to have AF, with >46 000 new cases being diagnosed each year. Given the increasing prevalence of AF and the associated thromboembolic complications, there are significant numbers of patients who require chronic oral anticoagulation (OAC).

Current guidelines recommend that AF patients at moderate to high risk of stroke should be commenced on chronic anticoagulation with a vitamin K antagonist (VKA). These recommendations are based on data from meta-analyses of 13 randomized controlled trials which have demonstrated significant reductions in stroke and mortality with the use of warfarin. Despite the overwhelming evidence of the benefit of warfarin thromboprophylaxis in patients with AF, such therapy remains significantly underused. OAC care varies considerably from country to country and physicians tend to undertreat more than overtreat. Physicians’ dilemma of whether to prescribe warfarin is reflected in the recent Euro Heart Survey of AF patients, which revealed that only 67% of patients eligible for VKAs were actually prescribed it, with >46 000 new cases being diagnosed each year. The increasing prevalence of AF and the associated thromboembolic complications, there are significant numbers of patients who require chronic oral anticoagulation (OAC).

Current guidelines recommend that AF patients at moderate to high risk of stroke should be commenced on chronic anticoagulation with a vitamin K antagonist (VKA). These recommendations are based on data from meta-analyses of 13 randomized controlled trials which have demonstrated significant reductions in stroke and mortality with the use of warfarin. Despite the overwhelming evidence of the benefit of warfarin thromboprophylaxis in patients with AF, such therapy remains significantly underused. OAC care varies considerably from country to country and physicians tend to undertreat more than overtreat. Physicians’ dilemma of whether to prescribe warfarin is reflected in the recent Euro Heart Survey of AF patients, which revealed that only 67% of patients eligible for VKAs were actually prescribed it, although actual ‘real-life’ prescription of OAC may be significantly lower than this.

So, why are eligible patients with AF not prescribed OAC? Warfarin itself is plagued by a number of inherent problems, the most important being the narrow therapeutic international normalized ratio (INR) window (target INR 2.5, range 2.0 to 3.0) which must be maintained, given that there is an increased risk of hemorrhagic stroke with INRs >3.0 and thromboembolic complications at INRs <2.0. A recent systematic review revealed that patients who receive long-term OAC achieve a therapeutic INR only 55% of the time. Furthermore, even a 10% increase in time out of therapeutic range is associated with an increased risk of mortality and thromboembolic events. Warfarin is also influenced by food, alcohol, and drug interactions and requires regular monitoring. Availability of adequate INR monitoring is an important and necessary component in the decision-making process and requires the necessary infrastructure to facilitate this. Consequently, it is not always possible to offer OAC therapy to everyone who is eligible.

In the current issue of Stroke, Gattellari and colleagues investigated the psychological barriers to the use of anticoagulation in patients with nonvalvular AF among 596 Australian family physicians using a questionnaire, which asked about their experience of patients’ suffering adverse events while on OAC and their ‘anticipated responsibility’ for these events. In addition, physicians were also presented with 8 case histories to assess their likelihood of prescribing OAC and/or antiplatelet treatment.

Personal experience of the prescription of warfarin influenced physicians’ feelings of ‘responsibility’ for strokes or intracranial hemorrhage, a finding supported by previous surveys of physicians’ OAC prescription. Physicians were more likely to feel ‘responsible’ for a stroke occurring while not on OAC than a hemorrhage occurring while on OAC. Physicians’ reluctance to prescribe warfarin is often due to a perceived greater risk of bleeding, overestimation of the associated risks, underestimation of the stroke risk, and clinical uncertainty or inexperience of warfarin.

The bleeding risk associated with warfarin is an important consideration and is the most common reason among physicians for not prescribing warfarin. Indeed, the survey by Gattellari et al revealed that physicians were far less likely to prescribe warfarin when there was an increased risk of bleeding due to history of falls, recent gastrointestinal bleeding, recurrent nose-bleeds, and previous intracranial hemorrhage, despite the patient being at high risk of stroke. Physicians with more years in medical practice were more likely to maintain a preference for warfarin when presented with increased bleeding risk in the case histories, which the authors conclude is a result of experience reducing their fears of OAC. Furthermore, patients are often willing to accept a much higher risk of bleeding for an associated reduction in the risk of stroke compared with physicians.

The following risk factors have been identified as increasing the risk of bleeding in patients taking warfarin: increased age, female sex, hypertension, anemia, previous MI, cerebrovascular disease, concomitant use of antiplatelet therapy,
history of previous bleeding, and concomitant medication use.\textsuperscript{24} Three bleeding risk stratification models have been proposed,\textsuperscript{24} but complex algorithms and the need for further prospective validation of these systems means that these schemas are not currently widely used but they may be a useful adjunct in the warfarin prescription decision-making process.

Increasing age is associated with a reduction in the likelihood of being prescribed warfarin in AF patients\textsuperscript{22} mainly because of the perception that there is an increased risk of bleeding in older people (due to polypharmacy, comorbidities, increased likelihood of falls, decline in cognitive function, inability to attend for regular INR checks) and second, the lack of data of the risk/benefit profile of warfarin thromboprophylaxis among the elderly from randomized controlled trials. However, the Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) trial, an RCT comparing dose-adjusted warfarin, with a target INR of 2.5 (range 2.0 to 3.0, compared with 75 mg aspirin, in elderly >75 years), in the primary-care setting, has recently demonstrated that warfarin was associated with a significant reduction in fatal or nonfatal disabling stroke (ischemic or hemorrhage, or significant arterial embolism; OR 0.48, 95\% CI, 0.28 to 0.80, NNT 50), with no difference in the risk of significant bleeds (ICH and all other major hemorrhages) between the warfarin and aspirin groups (0.87, 0.43 to 1.73 and 0.96, 0.53 to 1.75 for ICH and all major hemorrhages, respectively).\textsuperscript{25} These are extremely important data, given that the prevalence of AF and stroke events is greater among the elderly and these are the people more likely to benefit from OAC but less likely to receive it.

Perhaps the most alarming result from the survey by Gattellari et al\textsuperscript{18} is that as the bleeding risk and stroke risk increased in the case scenarios, the likelihood of prescribing warfarin decreased dramatically because of the uncertainty and lack of knowledge of the risk-benefit of warfarin displayed by a large proportion of GPs. Despite obvious and multiple risk factors for stroke, guidelines for the antithrombotic management of AF were not adhered to. This finding is supported by the Euro Heart Survey on AF\textsuperscript{13} which showed that the prescription of OAC was quite high over all stroke-risk categories, meaning that many AF patients at low-risk of stroke were exposed to an increased risk of bleeding, the inconvenience of regular INR monitoring, and lifestyle restrictions unnecessarily\textsuperscript{13} and that known risk factors for stroke did not promote OAC prescription in multivariate analyses.\textsuperscript{15}

Physicians may not adhere to the guidelines because they are either not aware of them or their knowledge of them is poor, or alternatively it may be because the guidelines are deficient in terms of evidence-based information (eg, the risks associated with the type of AF, uncontrolled hypertension, and ‘combination’ therapy for patients with vascular disease). Furthermore, the complexity of some risk stratification schemes and the importance of certain stroke risk factors may limit their applicability and physicians knowledge of them, although the CHADS\textsuperscript{2} scheme, for example, is short and the acronym denotes the risk factors and the weight of their importance. We echo the recommendation of the Euro Heart survey on AF\textsuperscript{13} for one standardized and simple-to-use stroke risk stratification scheme to facilitate appropriate and wider prescription of OAC therapy in AF patients.

In addition to physician-reluctance, there are patient-related barriers to warfarin prescription, the most pertinent of which are patients’ often limited knowledge about the disease, its treatment, and the risk-benefit ratio of warfarin thromboprophylaxis,\textsuperscript{26} and their preferences for treatment. Patient education and/or self-monitoring of the INR, pictorial representations of the risk and benefits of warfarin, involving the patient in the decision-making process, and consideration of their preferences for treatment have all been shown to increase the likelihood of compliance with associated benefits in outcomes.\textsuperscript{27}

There are a number of steps physicians should take when deciding whether to initiate warfarin therapy. First, assess the risk of stroke according to current clinical guidelines\textsuperscript{7,8} and the associated risk of bleeding individually for each patient. Second, physicians should educate the patient about the need for OAC, the risk and benefits associated with treatment, and the importance of maintaining a therapeutic INR. Third, patient preferences for treatment should be taken into consideration, to ensure compliance. Finally, the risk profile should be reviewed regularly, including detection and optimal management of common risk factors, such as hypertension.\textsuperscript{28,29} These factors together with the advent of ‘new’ oral anticoagulants will hopefully help to improve the prescription of, and compliance with, OAC among eligible AF patients and reduce stroke rates and the associated morbidity and mortality.

**Disclosures**

None.

**References**

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