EDITORIALS

Advancing age and bleeding risk are the strongest barriers to anticoagulant prescription in atrial fibrillation

In clinical practice many patients with atrial fibrillation (AF) at high thromboembolic risk fail to receive adequate oral anticoagulation (OAC) [1]. The complex management of anticoagulant therapy (frequency international normalised ratio (INR) monitoring because of narrow therapeutic window, interaction with food and alcohol, concomitant medications and comorbidities), the overestimation of bleeding risk and the underestimation of stroke risk, may partially explain physicians’ reluctance to prescribe anticoagulation.

In the current issue of Age and Ageing, Pugh and Mead [2] report a systematic review on physicians’ attitudes concerning anticoagulant treatment among AF patients. Through surveys (questionnaire, clinical vignette and interview) on hypothetical case scenarios, they have identified the barriers to effective anticoagulant prescription, as follows: increasing age, bleeding risk or previous bleeding, fall risk, co-morbidities (e.g. chronic alcoholism or cognitive impairment) and lack of compliance. In particular, advanced age has been reported as the most striking reason for withholding anticoagulation, while risk of falls and previous bleeding are also disproportionate barriers to warfarin prescription.

Pugh and Mead [2] found that physicians were reluctant to anticoagulate elderly patients, especially those over 80 years old, even if otherwise healthy and without contraindications to warfarin. However, the risk of stroke attributable to AF increases with advancing age [3] and older AF patients (aged >85 years) are more likely to receive antiplatelet drugs rather than OACs [4]. Nonetheless, age alone should not be a contraindication to OACs as elderly AF patients may stand to benefit most from anticoagulation [3]. Indeed, the Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) trial (all patients aged ≥75 years) demonstrated that warfarin was more efficacious than aspirin in the prevention of stroke, with a similar risk of major haemorrhage [5]. A recent review of 12 AF thromboprophylaxis trials [6] confirmed that the benefit of OAC for ischaemic stroke reduction remained even with advancing age, whereas the relative benefit of anti-platelet drugs decreased significantly as age increased.

Overestimation of the risk of bleeding by physicians is a key barrier to OAC prescription [2]. Physicians are often reluctant to start OAC in warfarin-naïve patients, since the risk of haemorrhage is higher during the first few months of therapy [7]. Supporting evidence from a large-scale (140,185 patients) retrospective study found that AF patients prescribed warfarin were significantly more likely to have prior warfarin-experience during the previous year than those not prescribed warfarin [8].

Since risk of bleeding is one of the major reasons why physicians withhold or stop OAC, it is essential to minimise this risk. This can be achieved in several ways including ensuring patients are not prescribed concomitant anti-platelet or non-steroidal anti-inflammatory drugs, establishing and maintaining a therapeutic INR (range 2.0–3.0), improving patient education (regarding food, drug and alcohol interactions, importance of compliance), reducing the risk of falls and ensuring patients who are cognitively impaired are cared for by another responsible adult who can administer their medication.

Physicians need to complete a comprehensive and objective assessment of the patients’ risk of stroke and bleeding before deciding upon appropriate thromboprophylaxis. It is essential that physicians are aware of appropriate validated stroke and bleeding risk stratification schemes, such as CHA2DS2-VASC [9] and HAS-BLED [10], which can be easily employed in everyday clinical practice to aid OAC treatment decisions. Regular review of both bleeding and stroke risk factors is imperative to ensure patients receive optimum care.

One limitation of the current review by Pugh and Mead [2] is the exclusion of qualitative evidence. Qualitative research can provide a valuable insight into both patient and physician barriers to OAC. For example, narratives from one study suggest that physicians may find it difficult to use guidelines and apply the findings of clinical trials in practice [11], while another suggests that physicians may not adhere to guidelines because of lack of awareness, poor knowledge or perception that they are not applicable to every patient [12] and because of confusion given the overlap of stroke and bleeding risk factors. Guidelines need to provide consistent, clear advice. Further, qualitative research surrounding physician barriers to prescribing OAC may provide greater insights into physician training needs.

Physicians’ experience with warfarin use, especially previous adverse events, may influence their feelings of responsibility in the prescription of OACs. One survey
found that physicians felt more responsible for a stroke occurring while on OAC, than a haemorrhage occurring while on OAC [13]. However, this evidence is in direct contrast with other studies that suggest that adverse events associated with an action have more influence on physicians’ attitude than those resulting from inaction [14, 15]. Perhaps these contradictory findings highlight the problem with relying on evidence from clinical vignettes, as the latter study was a retrospective analysis of real-life prescribing. The dramatic memory of bleeding events and the deeper regret associated with action could have a significant impact on physicians’ future decision making, in agreement with the principle of non-maleficence [15]. Evidently quantitative evidence can lack depth of explanation and these conflicting findings could be further examined with qualitative research.

Patients’ attitudes and beliefs about medication play an important role in the decision-making process. A prospective observational study demonstrated that patients at high risk of developing AF are often willing to accept a much higher risk of bleeding, to reduce the potential risk of future stroke, compared with physicians [16]. However, another study has shown that risk of intracranial haemorrhage does attenuate the number of patients willing to take OAC [17], suggesting that patients trade-off risks when making decisions regarding OAC.

The importance of the patient–physician relationship is also underlined by current European Society of Cardiology (ESC) guidelines that highlight the need for more discussion with patients regarding the risks and benefits of OAC treatment and greater consideration of patients’ treatment preferences [18, 19], particularly with the advent of novel anticoagulants. Increasing patients’ knowledge about AF, treatment options and the risks and benefits of thromboprophylaxis can help improve therapeutic control [20]. An ongoing randomised controlled trial, targeting warfarin-naïve AF patients, will further examine the impact of a psychological theoretically driven intensive educational intervention on time in therapeutic range (TTR) versus usual hospital care [21]. This trial has been specifically designed to address patients’ barriers to adherence. Improving patients’ knowledge and addressing patients’ barriers within routine clinical consultations is essential, particularly with the imminent arrival of new anticoagulants.

Novel OACs [22], which do not require INR monitoring, have fewer or no drug, food and alcohol interactions, and similar or better efficacy and safety profiles compared with warfarin, may simplify the management regimen, increase patients’ compliance and lessen physicians’ anxiety over the risks of OACs, resulting in more widespread prescription of OAC. Regardless of the novel OAC used, patient factors will be particularly pertinent, where antithrombotic treatments are not monitored, and patient education may become particularly important to ensure adherence to recommendations [19].

In conclusion, the prescription of anticoagulant therapy in AF is still impeded by physician barriers. The risk of bleeding appears to be the most important barrier to prescribing, alongside advancing age. Comprehensive stroke and bleeding risk assessment and regular review of patients’ risk factors may help physicians feel more confident in making OAC decisions and to overcome their barriers to OAC prescription. Further, qualitative research may offer more insight into real-life prescribing barriers, and potentially overcome the discrepancy between evidence-based recommendations and clinical practice.

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Diabetes, the glycaemic index and older people

Older people differ from younger people but most of what is known about diabetes is derived from studies that have not involved older people. This is highlighted in the developing story about glucose metabolism and older people. There is a very high prevalence of type 2 diabetes in those over the age of 60 years. More than 20% of people over 60 years have type 2 diabetes and another 20% will have impaired glucose tolerance. Indeed isolated post-challenge hyperglycaemia defined as a 2 h level glucose >11.1 mmol/l by OGTT despite a fasting glucose of 7.0 mmol/l is also common in this group [1]. Isolated post-challenge glucose levels increase with age by about 0.3–0.5 mmol/l per decade. This is not benign; in all ages all-cause mortality increases as the post-challenge glucose rises.

In addition HbA1c levels are positively associated with age in non-diabetic people even when people with impaired glucose tolerance are excluded [2]. Previously the normal range for HbA1c was derived from non-diabetic healthy volunteers aged 13–39 years. Now data from large population-based cohorts established by NHANES 2001–04 and Framingham Offspring Study has compared HbA1c levels from people over 70 years with people below 40 years. This shows that HbA1c levels are significantly increased in older people. They also demonstrated that the 2 h post-glucose load increased with age in non-diabetic people.

Why should this be and does it matter? In older people, as part of normal ageing, intracellular body water is reduced, body fat increases and muscle mass is reduced and this can lead to the development of insulin resistance [3]. At the same time hepatic glucose output is normal in older people but pancreatic islet cell function declines and insulin levels are lower. Insulin secretion declines at a rate of around 0.7% per year with age in those without diabetes and this decline doubles in those with impaired glucose tolerance [4]. Those older people who develop type 2 diabetes are more likely to have near normal fasting glucose levels but significant post-prandial hyperglycaemia [5, 6].