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The same patient in various European countries

Use of anticoagulants for atrial fibrillation in older subjects across different countries: Cyprus, France, Netherlands, Norway



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ABSTRACT

Atrial fibrillation (AF) is the most common arrhythmia in older adults, and those with AF have an increased risk of developing stroke. Although the use of anticoagulants for stroke prevention is strongly recommended, many older people are not appropriately treated. Vitamin K antagonists (VKA) have been the only available oral anticoagulants for such patients, but recently, new oral anticoagulants have been approved for stroke prevention in AF as an alternative to VKA. Some characteristics make them an attractive treatment option; however, many gaps in evidence remain, especially in the population of older patients. This paper explores the use of anti-thrombotic treatment for the prevention of stroke in AF in old subjects in four different European countries. VKA seems to be the standard therapy in older patients, although anti-platelet drugs are still used widely in some countries. In many European countries, warfarin is replaced by coumadin derivatives. The use of new oral anticoagulants seems to be quite limited in older subjects and some degree of discrimination exists in access to these new drugs. European Society of Cardiology (ESC) 2010 and 2012 guidelines seem to be triggering a wide change in attitudes and practices. Many countries are incorporating such guidelines into official recommendations, and specific country recommendations on the use of new anticoagulants have been published, partly due to the high economic impact of these drugs. Geriatricians still have a marginal role in the prescription of anticoagulants, which in most countries usually lies on cardiologists. General practitioners are key for follow-up, as the role of anticoagulation clinics remains relevant only in The Netherlands. Most old patients have limited knowledge of anticoagulant treatment options, thus, their involvement in decision-making is low.

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1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in older adults, and those with AF have an increased risk of developing stroke. Although the use of anticoagulants for stroke prevention has been strongly recommended by the European Society of Cardiology (ESC) guidelines for some years based on high quality evidence [1], many older people are not appropriately treated for many reasons [2], including misperceptions about stroke and bleeding risk, polypharmacy, and multimorbidity [3]. Some patients are still

treated with aspirin, which is no longer recommended for AF thromboprophylaxis and carries its own risks.

Traditionally, a vitamin K antagonist (VKA), such as warfarin or coumadin, is prescribed for stroke prevention in patients with AF. VKAs are effective in reducing the risk of stroke but have several limitations due to food restrictions, drug interactions, a narrow therapeutic window and the need for careful monitoring. In the recent years, novel oral anticoagulants (NOACs) have been approved for stroke prevention in AF as an alternative to VKA. With new mechanisms of action, few drug or food interactions and no need for therapeutic drug monitoring, they are an attractive alternative to VKA, also among older patients [4]. However patient adherence, lack of a reversal agent, cost, and a suspected increased risk of adverse effects in older adults suggest that a cautious

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approach is needed, and the role of NOACs in very old multimorbid patients with polypharmacy remains uncharted [5].

This paper explores the current strategies of anticoagulation therapy for stroke prevention in older people in different European countries and it might contribute to illuminate areas for improvement.

2. Epidemiology: use of anticoagulants and anti-platelet agents

What are the rates of anticoagulation in older patients with AF? Do they change across the country? Are they lower in geriatric patients? Are there specific studies in geriatric settings (geriatric clinics, acute geriatric care, nursing homes)? Are they changing in recent years?

Are anti-platelet agents used in older patients? Is double anti-platelet therapy (aspirin plus clopidogrel) used? Are new anticoagulants approved and used for AF? Which ones? How are they being adopted?

2.1. Cyprus

Cyprus is a small European country, with a population just over 1 million, and a very fragmented health care system, where the public health system cares for the financially challenged people with low income, and older people (retirees), and with a National Health Care system in construction, that has been heavily hit by the recent financial crisis. Academic medical research in Geriatrics is not carried out, and few data are available to answer many of these questions.

Actual anticoagulation rates are unknown, and there are no studies performed in geriatric patients with AF in Cyprus. Anti-platelet agents are widely used as anti-thrombotic drugs for the prevention of stroke in AF older patients. Double anti-platelet treatment with aspirin and clopidogrel is reserved for patients with previous MI following PTCA, and not used in AF patients.

NOACs approved for use in AF in Cyprus include dabigatran and rivaroxaban. Rivaroxaban has an age-related restriction related to renal function: when creatinine clearance is below 50 mL/min, rivaroxaban is prohibited. The use of new anticoagulants is limited due to their high cost.

2.2. France

Atrial fibrillation affects between 600,000 and 1 million persons in France, half of them over 75 years old [6]. Hospitalisations of patients presenting with AF are rapidly growing [6,7]. On the other hand, haemorrhage of VKA treated patients is the most frequent cause of hospitalisation for adverse drug events and is responsible of around 4000 deaths each year [8].

A prospective observational study conducted in 2002 gathered data on 5893 outpatients with documented permanent AF seen by 770 randomly selected private physicians, general practitioners or cardiologists. The percentage of patients treated with VKAs was 76.4%, whereas 19.1% were treated with anti-platelet drugs; however, only 63.5% of the patients aged 80 years or above were treated with VKA [9]. High age was a highly significant predictor of non-prescription of anticoagulants, and aspirin was often prescribed to older patients. A small study conducted in an acute geriatric ward in 2008 reported that 30% of the patients with atrial fibrillation (mean age 89) were discharged with VKA, 45% with aspirin, and 25% with no anti-thrombotic treatment [10]. Clopidogrel is not recommended usually and not used for AF, neither alone nor in association.

Despite the absence of evidence concerning fluindione, this drug is (as a historical peculiarity) the preferred VKA in France. In a study conducted in 2003, only 3% of anticoagulated patients

were treated with warfarin, whereas 78% received fluindione and 18% acenocoumarol [11]. With fluindione, physicians often have to prescribe alternating doses (e.g., 0.5 tablet alternating with 0.75 tablet). However, the use of warfarin has probably increased and the use of acenocoumarol decreased the last few years [12].

Apixaban, dabigatran and rivaroxaban have been approved for AF patients in France, but are not recommended as the first line treatment. They are especially inadvisable for patients over 75 years old, because of the bleeding risk associated with renal insufficiency [13,14]. As a result, they are to our knowledge seldom used in geriatric settings.

2.3. Netherlands

There are good data on the prevalence of AF in the general Dutch community and in Dutch geriatric patients, but numbers on anticoagulation treatment rates are limited. In the population-based Rotterdam Study, the prevalence of AF was 5.5%. The prevalence rose with age from 0.7% in those aged 55–60 years to 17.8% in those over 85 years [15]. For the geriatric population, data from 2004 on 807 geriatric outpatients visiting a geriatric diagnostic day centre showed that 17.5% suffered from chronic or paroxysmal AF [16].

There are no published data on treatment rates in older persons. Dutch studies, as those performed in most countries, often show under-treatment. The Euro Heart Survey – in which Dutch clinics and patients are well represented (714 out of 5333 patients) – shows that that only 67% of eligible patients received OAC [17]. In our geriatric patient cohort mentioned above, we evaluated under-treatment by describing non-adherence to the general practitioner's guidelines. In 9.9%, there was non-adherence to the guideline, and 8.6% of suitable patients were not treated with anticoagulants at all. Then, 33.6% were treated only with a salicylate and 57.8% with OAC [16]. In a questionnaire survey of 86 GPs, 93 internists and 99 cardiologists enrolling 1596 subjects, 84% were at high risk for stroke and therefore were eligible for oral anticoagulation treatment, but only 64% of these patients actually received it [18].

Anti-platelet agents are still used in AF, mainly salicylates; addition of clopidogrel is unusual. In the EXAMINE-AF survey, compared with GPs and internists, cardiologists prescribed more often OAC (84% vs 76% and 70% respectively; $P < 0.001$), and less often anti-platelet drugs (12% vs 20% and 18% respectively; $P < 0.001$) [18]. In the Dutch GP guideline, acetylsalicylic acid was until very recently still mentioned as the preferred treatment option for patients with an annual stroke risk between 0–4%. In cardiology, geriatrics and internal medicine, the ESC guidelines have been adopted, but many GPs still consider acetylsalicylic acid to be safer regarding bleeding risk.

In the Netherlands, dabigatran and rivaroxaban have recently been approved for the prevention of stroke in AF. Reimbursement of both drugs, however, requires several conditions, including publication by the Dutch Order of Medical Specialists of a document for the guided introduction in the Dutch market, adjustment of guidelines by scientific boards to improve safety and therapeutic adherence, further research and improvements in transmural multidisciplinary care [19], including regional protocol between caregivers (hospital, ambulances) on how to act in the case of bleeding complications.

Only very recently, the new anticoagulants are being introduced. They have not yet been widely adopted in geriatric practice. The Guidance document of the Dutch Order of Medical Specialists states that the use of NOACs is not advised in patients with non-compliance, renal insufficiency, a high risk of bleeding complications, with insufficient care, who have stable INR with VKA, and

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