OPTIMIZING ANTICOAGULANT THERAPY IN NON-VALVULAR ATRIAL FIBRILLATION

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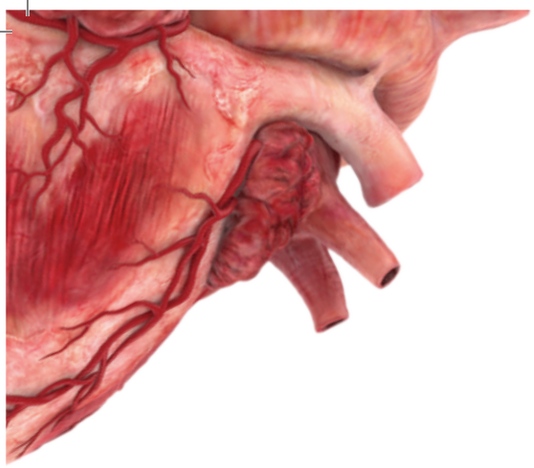
The prevalence of atrial fibrillation (AF) is estimated to be around 3% of the population above 20 years of age, and increases with age, hypertension, cardiovascular disease, diabetes and obesity. Besides a 1.5- to 2-fold increase in mortality in people suffering from AF, they also have an increase in morbidity from heart failure and stroke. In fact, 20-30% of all ischaemic strokes are thought to be secondary to AF. The CHA_2DS_2-VASc score is a useful tool to quantify the yearly risk of stroke. One should note that the risk of stroke is independent of whether the AF is paroxysmal, persistent or permanent.[1]

Guidelines published by the European Society of Cardiology[2] (ESC) give a class I A indication for the prescription of oral anticoagulants (OACs) to males with a CHA_2DS_2-VASc score ≥ 2 and females with a score ≥ 3. One should also consider giving OACs to males with a score of 1 and females with a score of 2 (IIa B indication). No anticoagulants should be given to males or females with no additional risk factors, and anti-platelet monotherapy is not recommended whatever the stroke risk. A careful analysis of the patient's bleeding risk should be carried out before prescribing these drugs. Naturally, OACs should be avoided in patients with active bleeding, and concomitant antiplatelets should only be prescribed if indication is strong.

Vitamin K antagonists (VKAs) such as warfarin have been used for many years to reduce the risk of stroke and mortality in patients with AF. VKAs are limited by their narrow therapeutic interval, with patients needing frequent monitoring and dose adjustments. They are only effective in stroke prevention when delivered with adequate time in therapeutic range (TTR). In the last few years Non-Vitamin K Oral Anticoagulants (NOACs) have made an appearance on the market. All NOACs (the Direct Thrombin Inhibitor Dabigatran, and the Factor Xa inhibitors Rivaroxaban, Apixiban, and Edoxaban) have the distinctive advantage over VKAs of having a predictable effect, and therefore no need for monitoring. Treatment doses are well-defined; and all are given as a twice-daily dose, except for Rivaroxaban, which is given as a once-daily dose. All four NOACs were given regulatory approval after each of them had been compared to dose-adjusted Warfarin in large randomised trials and were proved to be, at least, non-inferior to Warfarin in the prevention of stroke or embolism. Comparison between NOACs based on these trials is difficult as the populations studied were different; notably the mean $CHADS_2$ score was 2.1 for dabigatran (RE-LY trail[3]) and apixiban (ARISTOTLE trial[4]) while it was 3.5 for Rivaroxaban (ROCKET-AF trial[5]).

The recently updated ESC guidelines recommend NOACs to be prescribed instead of VKAs when this is feasible (figure 1). Unfortunately NOACs are not yet available on the Maltese National Health Service, but patients might be willing to buy these drugs for their convenience and better safety profile. There are circumstances where one may actively suggest that a patient switches from Warfarin to NOACs. These include: Patients who have had a stroke or a bleed while on Warfarin, patients with labile INRs, and patients with low TTR. Patient with mechanical heart valves or mitral stenosis should be on VKAs and NOT given NOACs. In cases where a patient



IT IS STILL WORRYING THAT [ACCORDING TO THE GARFIELD-AF REGISTRY]SLIGHTLY MORE THAN 25% OF PATIENTS WITH CHA2DS2-VASC SCORE ≥ 2 WERE NOT ON ANY ANTICOAGULANTS

Table 1. Summary of ESC 2016 anticoagulation guidelines for stroke prevention in non-valvular AF.

Recommendations	Class	Level
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a **NOAC is recommended in preference to a Vitamin K antagonist.**	I	A
AF patients already on treatment with a vitamin K antagonist may be considered for **NOAC treatment if TTR is not well controlled** despite good adherence, **or if preferred by patient** without contra-indications to NOAC (e.g. prosthetic valve).	IIb	A
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III (harm)	A

with AF is unable to tolerate anti-coagulation, percutaneous closure of the left atrial appendage might be considered.

According to recently published data from the Global Anticoagulant Registry in the FIELD-Atrial Fibrillation (GARFIELD-AF)[6] - an ongoing, prospective, observational, worldwide study of adults with recently diagnosed non-valvular AF from 1215 sites in 35 countries - uptake of NOACs has increased steadily over the last few years. This has resulted in a greater proportion of patients being on guideline-recommended therapy. However, it is still worrying that slightly more than 25% of patients with CHA_2DS_2-VASc score ≥ 2 were not on any anticoagulants.

Unfortunately, the author is not aware of any data on rates of anti-coagulation of AF patients in Malta. The setting up of a local AF registry would be an important tool to enable the health authorities to reduce the number of strokes in our country by ensuring adequate anti-coagulation of patients. It is strongly encouraged that all doctors recommend anti-coagulation, preferably with a NOAC, to all AF patients with one risk factor or more and no contra-indications.

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