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REVIEW

An Update on Anticoagulation in Atrial Fibrillation

John Amerena, MBBS, FRACP, FCSANZ [a*], **Daryl Ridley, MBBS, FRACP, FCSANZ** [b]

[a]Deakin University, Geelong, Vic, Australia
[b]University Hospital, Geelong, Vic, Australia

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Cerebrovascular accidents related to atrial fibrillation (AF) are potentially preventable with anticoagulation. Until recently, warfarin was the only proven anticoagulant to be effective in stroke prevention, however the novel, direct acting oral anticoagulants (DOACs) are now available, triggering a paradigm shift in treatment philosophy. Today, physicians need to consider in which patients anticoagulation should *not* be used rather than, as in the past, deciding in which patients it should be used. Although warfarin will continue to have a place in managing some patients with AF, in the future, the DOACs should be the predominant therapy for stroke prevention in patients with non-valvular AF.

Keywords Anticoagulation • Atrial fibrillation • Warfarin • Novel anticoagulants

Introduction

Atrial fibrillation (AF) is the commonest cardiac arrhythmia and its prevalence is expected to increase globally, and in Australia, over the next 20 years [1]. The incidence of AF increases with age, and is present in around 15% of the population aged above 80 years, so is by far the commonest cause of stroke in this age group. Identification of AF and appropriate institution of anticoagulation is therefore the largest potential way to prevent stroke in this population.

Ischaemic stroke is the most common cause of cerebrovascular accident in Australia and 75% of these strokes are directly related to atrial fibrillation [2]. The proportion of stroke from cardioembolic sources rises with age [3], so that 35% or more of stroke in patients over 80 years of age is cardiac in origin, mostly due to AF. Atrial fibrillation causes incomplete and sluggish emptying of the left atrial appendage (LAA) and this is the site where thrombus forms, although thrombus can occasionally be seen in the left atrium itself. These LAA thrombi tend to be large, and when they dislodge and embolise, stroke or peripheral embolisation are the common outcomes. Strokes associated with atrial fibrillation tend to be larger, and are more likely to be fatal or disabling [4]. Given this mechanism, strokes related to AF are potentially preventable with anticoagulation.

Valvular or Nonvalvular Atrial Fibrillation?

Atrial fibrillation is commonly classified as being either valvular or non-valvular in origin, which is an important distinction as it influences the choice of treatment options available for stroke prevention in these patients. The majority of patients with AF have non-valvular AF (NVAF) with the minority having AF associated with valvular heart disease. The definition of valvular/non-valvular AF has been a little confusing over recent years, as American and European definitions are somewhat different.

The current AHA/ACC definition of valvular heart disease states that valvular AF is that which is associated with rheumatic mitral stenosis, prosthetic heart valves (metallic or bioprosthetic) and mitral valve repair [5]. This is a fairly broad definition and many clinicians would not agree that mitral valve repair or a bioprosthetic valve is truly valvular heart disease, as, after an initial period of anticoagulation,

*Corresponding author at: 4th Floor Kardinia House Bellerine Str Geelong 3220., Email: johnamerena@gmail.com

these valvular conditions do not require anticoagulation in their own right.

According to these guidelines, anticoagulation with a vitamin K antagonist (VKA), such as warfarin, is recommended for stroke prevention in patients with valvular heart disease, whereas VKA or one of the direct acting oral anticoagulants (DOACs) can be used in patients with NVAF.

The latest definition from the European Society of Cardiology (ESC) in 2016 is simpler, and states that valvular heart disease is confined to moderate to severe mitral stenosis or metallic prosthetic heart valves, and that everything else should be considered non-valvular [6]. The ESC recommended that VKAs be used for anticoagulation in patients with valvular heart disease, and that a VKA or DOAC can be used in patients when the valvular heart disease does not require anticoagulation in its own right. This includes patients with a mitral valve repair or bioprosthetic valves after the initial implantation, and also patients with mitral regurgitation, tricuspid regurgitation, aortic incompetence and aortic stenosis which are not haemodynamically significant enough to require intervention.

This ESC definition has removed a lot of the confusion about what is valvular and non-valvular AF and we would encourage Australasian clinicians to follow these latest guidelines.

Who to Anticoagulate?

All patients with AF associated with valvular heart disease should be considered for anticoagulation with a VKA, as the stroke risk is high without anticoagulation. The decision to anticoagulate patients with NVAF for stroke prevention depends on their risk of stroke, and there are several risk scores that can be used to evaluate stroke risk in these patients.

The traditional stroke evaluation tool has been the $CHADS_2$ score which assigns points to various risk factors (see Table 1) and is good at evaluating the risk of stroke in relatively high risk patients but is not good at identifying patients who are at low risk of stroke and thus do not require anticoagulation [7].

Because of this lack of discrimination in low-risk patients, the CHA_2DS_2-VASc score has been developed [8], and has largely superseded the $CHADS_2$ score. The authors of these guidelines reviewed epidemiological and registry data looking at the risk of stroke related to various risk factors and have incorporated the $CHADS_2$ risk factors in the score and have upgraded age >75 years to the same level of risk as previous stroke, and have also included vascular disease, age >65 years and female gender as significant risk factors for stroke, although the magnitude of gender associated risk has been questioned recently. The score has been validated in large populations and is now the most widely used tool for stroke risk assessment in UK, Europe and Asia Pacific. The real advantage of the CHA_2DS_2-VASc score is that it is better at identifying truly low-risk patients who would not benefit from anticoagulation and thus not be treated inappropriately.

The current US guidelines advise that if the $CHADS_2$ score is >/ = 2 for men or women anticoagulation is recommended but that if the $CHADS_2$ score is 1, anticoagulation or aspirin can be considered depending on the individual patient characteristics and preferences [5]. In a patient with a $CHADS_2$ score of 0, neither anticoagulation nor aspirin is recommended in these American guidelines [5].

The most recent iteration of the European guidelines has recommended that, if men have a CHA_2DS_2-VASc score of >/ = 2, anticoagulation should be used for stroke prevention, but if the CHA_2DS_2-VASc score is 1, it should be considered, depending on patient characteristics and preferences [6]. For females, there has been a liberalisation of the recommendations for anticoagulation due to the recognition that female gender is a relatively weak risk factor for stroke. The latest guidelines advise that if a female has a CHA_2DS_2-VASc score of >/ = 3, anticoagulation is recommended, but if the score is 2, anticoagulation be considered. If the CHA_2DS_2-VASc score is 0 in men and women or is 1 in a woman, neither anticoagulation nor aspirin is necessary. Although these latest recommendations have been validated, the more liberal risk score for females has yet to be adopted in clinical practice in Australia. These guidelines have also stated that the DOACs are to be preferred over VKA for stroke prevention in NVAF. Australian guidelines for stroke prevention in NVAF are being currently written under the auspices of the CSANZ.

Table 1 **Risk score.**

Risk Score $CHADS_2$	Risk Factors	Risk Score CHA_2DS_2-VASc
1	Chronic heart failure	1
1	Hypertension	1
1	Age (≥ 75)	2
1	Diabetes	1
2	Stroke/TIA	2
	Vascular disease (CAD/MI)	1
	Age (65–74)	1
	Sex category (female gender)	1