

How to Approach the Patient with Non-Valvular Atrial Fibrillation and Cha2ds2-Vasc Score of 1



Tiago Luiz Luz Leiria*

Fellow-ship in Cardiac Electrophysiology at the Hôpital du Sacré-Coeur Montréal, Canada

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***Corresponding author:** Tiago Luiz Luz Leiria, Fellow-ship in Cardiac Electrophysiology at the Hôpital du Sacré-Coeur Montréal, Canada,

Opinion

Atrial fibrillation (AF) is a public health problem. It is estimated that one in four individuals will be affected by this arrhythmia throughout their lives. AF increases the risk of stroke five times, and this event is mainly responsible for the morbidity and mortality of this arrhythmia [1]. Oral anticoagulation with vitamin K antagonists (AVK), such as warfarin and phenprocoumon, have been shown to reduce the risk of stroke and systemic embolic events. More recently, the non-vitamin K oral anticoagulants (NOACs) have also proved effective for this same goal. In this paper we will review the most recent evidence on the real benefit of using oral anticoagulants in patients with atrial fibrillation associated with an additional risk factor for stroke.

How to Reduce the Risk of Stroke? What is the Evidence?

The relative risk reduction of stroke with AVK use is 62%; with an absolute risk reduction of 2.7% and 8.4% per year for primary and secondary stroke prevention respectively [2]. At the end of the first decade of the 21st century, four large randomized clinical studies [3-5] in patients with non-valvular AF tested a new class of drugs initially referred to as the novel oral anticoagulants (NOACS). These drugs are the factor Xa inhibitors (rivaroxaban, apixaban and edoxaban) and direct thrombin inhibitors (dabigatran – the only representatives of this class). More recently, because they are no longer considered to be new, they are referred to as non-vitamin K antagonists (Non-vitamin K antagonist Oral AntiCoagulant). The potential advantage of this new class of drugs reside in the fact that they do not have a large number of drug and food interactions, as in the AVK drugs. They also do not require the use of routine blood control of anticoagulation levels. Different from the AVK drugs, the administered dose of the NOACs is the same for most patients.

When prescribing NOACs we need to take into account only renal function (for dose adjustments) and the absence of absolute contraindications for its use, such as the presence of mechanical cardiac prosthesis. A meta-analysis including the four randomized clinical trials investigating the clinical application of NOACs in non-

valvular AF found a 19% relative risk reduction of stroke compared to warfarin [6]. A second meta-analysis [7], this time including studies of phase II and III, with more than 77,000 patients, showed that, compared to the AVK, the NOACs reduced not only the outcome of stroke and systemic embolism, but there was also a reduction of 14% in total mortality.

Which Patients Should be Anticoagulated? How to Predict the Risk of Stroke?

The risk of stroke and systemic embolism may be estimated according to the latest guidelines on the management of AF [8-10] with the use of the CHA2DS2-VASc score. This score takes into account the presence of the following risk factors: Heart failure (1 point), Hypertension (1 point), Age \geq 75 years (2 points), Diabetes (1 point), Thromboembolic events), Vasculopathy - previous myocardial infarction, peripheral artery disease, aortic plaque (1 point), Age 65-74 years (1 point), Gender Female category (1 point). According to the American and other international societies guidelines [9,10], patients who score 2 or more on the CHA2DS2-VASc score should receive prophylaxis for stroke using oral anticoagulants. In the European guideline [8], the recommendation is that this cut-off point is greater than or equal to 3 in women to initiate anticoagulation, and a value greater than or equal to two in men.

What is the Real Risk for af Patients and an Additional Risk Factor for Stroke? Are there Evidence for this Population?

There is a discussion in the literature on how best to proceed in patients who present a CHA2DS2-VASc = 1 score. According to the validation cohort of the CHA2DS2-VASc score [11], the annual event rate in this category of the score would be 2.01 per 100 patients per year. This figure is considered by some as a high value of adverse outcomes [12]. For, in a probabilistic trial [13], the cut-off point between the benefit of prevention and the risk bleeding (the “tipping point”) with AVK would be when the estimated risk

of annual thromboembolic events was greater than or equal to 1, 7% per year. Therefore, according to the results of the cohort of validation of the CHA2DS2-VASc score, patients with a score of 1 with an annual risk of approximately 2% would already benefit from the use of anticoagulation. In this same study [13], the author still suggests that due to the higher safety of NOACs in relation to AVK, mainly due to a lower rate of hemorrhagic stroke with the first group of drugs, that the that this “tipping point” for NOACs should be reduced, suggesting the existence of the benefit from NOAC use for those with an annual risk of 0.9%.

However, when different patient populations are stratified by the CHA2DS2-VASc score, do not exhibit the same annual risk of events. A study in Taiwan [14] suggests that the risk of stroke in patients with an additional risk factor (with the exception of sex) ranges from 1.96% year to 3.5% year. On the other hand, in a Swedish study [15], the risk of stroke in patients with a single risk factor was 0.5 to 0.7% per year, well below the suggested value, such as tipping point, where the risk of bleeding and the benefit of anticoagulation are balanced. A recent study [16] has also shown a great variability between stroke rates in patients with an additional risk factor in the different cohorts published in the literature. The variation in this study was 0.9% per year up to 6.64% per year. Another point to be emphasized is that the different risk factors included in the prediction scores of AF, when analyzed independently, do not behave in the same way [11]. Previous history of stroke and age predict a higher risk in most studies [11,14].

Evidence of the benefit of oral anticoagulation in patients with CHA2DS2-VASc = 1 can already be found in classical stroke prevention studies. In the SPAF study of 1991 [17], the prevalence of risk factors was low. The occurrence of previous stroke was 8%, age above 75 years 8%, diabetes 12% and ischemic disease 19%. Even with these characteristics, the use of anticoagulation was associated with an absolute reduction in stroke risk of 5.1% and relative risk of stroke of 67%. More recently, the RELY [5] and ARISTOTLE [3] studies included patients with non-valvular AF with an additional risk factor. One third of the patients in both studies had only one additional risk factor for stroke. In these two studies, the incidence of stroke in patients with an additional risk factor was similar to the incidence recorded in patients taking AVK.

How to Proceed?

In 2016, the Canadian Society of Cardiology, in its update on the management of AF [18], recommends that the presence of a risk factor be enough to indicate anticoagulation as stroke prevention, preferably with NOAC. It is worth noting that, according to this orientation, the risk of stroke should be calculated according to the use of a simplified CHADS265 score (heart failure, hypertension, age > 65 years, Diabetes, Systemic embolism). The other guidelines [8, 9,10] suggest the use of oral anticoagulants can be done in patients with a CHA2DS2-VASc = 1 score. However, the strength of this recommendation is lower than that indicated for patients with more risk factors. Another important fact in the therapeutic decision-making in cases with CHA2DS2-VASc = 1 is the knowledge

of the real local risk of stroke. As previously seen, this risk may have a wide variation [16]. Even so, when we analyze most of the data available in the literature, the mean risk of stroke in the presence of only one risk factor is around 1.2% to 1.67% per year. These values are higher than those suggested by the definition of tipping point and certainly higher than the risk of events recorded in patients with AF with CHA2DS2-VASc = 0 score. From the clinical point of view, the presence of associated comorbidities such as renal failure, coagulation abnormalities, hepatic dysfunction, among others, should be duly researched. This is necessary to avoid that the use of oral anticoagulation in patients with only one risk factor for stroke is not associated with loss of the preventive benefit of this therapeutic strategy.

Conclusion

The presence of a single risk factor for the occurrence of stroke may generate a misperception that the risk for this brain event is not high enough to warrant the use of oral anticoagulation. However, when stroke is due to AF they tend to be more severe, leave greater sequelae and be associated with higher mortality. According to the data presented, patients with AF and a score of CHA2DS2-VASc = 1 should receive oral anticoagulation preferably with the use of NOACs.

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