Waging Warfarin against ASA

Raviqubal S. Basi, MD, FRCPC and Kris B. Stewart, BSc, Pharm MD
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One of the challenges of managing a patient with atrial fibrillation (AF) is choosing an anticoagulation strategy that best fits the patient. Compared to the general population, AF increases the risk of stroke by 2.5 to 3.0 times and, in comparison to other causes of embolic stroke, AF results in strokes with greater disability and mortality. The risk of stroke is independent of the duration of AF and patients with paroxysmal AF are at as much risk as those who have chronic AF.

Which patients with AF are at the greatest risk for stroke?

This question has consistently yielded the same risk factors:

- advanced age,
- female gender,
- systolic dysfunction,
- hypertension and
- a history of prior transient ischemic attack (TIA) or stroke.

Some studies have also found diabetes and coronary artery disease to be significant risk factors, but this is a more inconsistent finding. It is also unclear whether treated hypertension bestows a lower risk when compared to untreated hypertension.

In clinical trials, ASA alone has lowered the risk of stroke by 22% to 45%.

How can the risk of stroke be reduced?

The mainstays of treatment in attempting to reduce the inci-

Table 1
Stroke risk index

Risk category	Stroke/year	Warfarin major bleed/yr	Consider
Prior CVA/TIA	10%	10%	Warfarin
Female > 75 or SBP > 160 or LVEF < 0.40	6%	3%	Warfarin
Treated HTN	3%	1%	ASA or warfarin
None of the above	1%	1%	ASA or none

CVA: Cardiovascular accident
TIA: Transient ischemic attack
SBP: Systolic blood pressure
LVEF: Left ventricular ejection fraction
HTN: Hypertension
ASA: Acetylsalicylic acid

dence of stroke are acetylsalicylic acid (ASA) and warfarin. In clinical trials, ASA alone has lowered the risk of stroke by 22% to 45% and, in a meta-analysis of six trials, was found to lower the risk by an average of 32%. Compared to placebo, warfarin decreases the risk of embolic stroke by 45% to 82%, with the highest reduction in risk seen in patients at the highest risk of embolic stroke (an average reduction of 50% is observed in all patients). In a meta-analysis of trials that compared ASA to warfarin directly, there was no significant difference in the reduction of stroke incidence.

What are the risks of ASA and warfarin in patients with AF?

Patients on either ASA or warfarin are at a greater risk of bleeding complications than patients on neither, but patients on warfarin have a substantially greater risk of major bleeding, including intracranial hemorrhage, than those on ASA alone. It appears that, in patients with AF, some of the same risk factors that confer an increased risk of ischemic stroke confer an increased risk of major bleeding. These risk factors include:

- advanced age,
- a history of prior stroke and
- systolic dysfunction.

Dr. Basi is a Clinical Assistant Professor of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan.

Dr. Stewart is a Resident, Department of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan.

For patients with these risk factors, the annual risk of stroke without warfarin may be 10% to 12%, but the annual risk of major bleeding on warfarin may also be 10% to 12%.

ASA or warfarin?

A variety of risk models have been developed to quantify an individual patient's risk of stroke and, consequently, the expected benefit of ASA or warfarin. Table 1 combines the stroke risk index derived from the stroke prevention in AF investigators and a retrospectively derived bleeding risk index for warfarin. ASA is at least as efficacious as warfarin in AF patients at a low risk for stroke. Conversely, in patients with AF and a history of prior TIA/stroke, the annual risk of recurrent TIA/stroke is so high that, given the increased risk of bleeding complications, warfarin is warranted. For patients at moderate risk for stroke, the decision must be more individual, taking into account the stroke risk for that patient's combination of risk factors and the risk of bleeding with warfarin.

ASA is at least as efficacious as warfarin in AF patients at a low risk for stroke.

Concluding thoughts

While managing patients with AF at the extremes of low and high risk for stroke is fairly straightforward, managing the patient at moderate risk for stroke leaves open either option–ASA or warfarin. Even in this group, because warfarin is probably more effective than ASA in stroke prevention (but at the price of significantly more major bleeding), patient preference is paramount.

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Resources

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