CARDIOLOGY Rounds®

As presented in the rounds of the Division of Cardiology, St. Michael's Hospital, University of Toronto

A Practical Guide to the Use of Novel Anticoagulants for Stroke Prevention in Atrial Fibrillation

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Three large, randomized clinical trials have compared warfarin for stroke prevention in atrial fibrillation (AF) to novel oral anticoagulants (NOACs) – dabigatran,[1] rivaroxaban,[2] and apixaban[3] – and a fourth large trial of edoxaban[4] has recently been published. All of these NOACs are either superior to warfarin (dabigatran 150 mg bid, apixaban) or noninferior (rivaroxaban, edoxaban, dabigatran 110 mg bid) in the reduction of stroke; all are associated with a significant reduction in intracranial hemorrhage compared to adjusted-dose warfarin, and are either noninferior to warfarin with respect to major bleeds (dabigatran 150 mg bid and rivaroxaban) or result in a significant reduction in major bleeding (dabigatran 110 mg bid, edoxaban, and apixaban). Canadian and international guidelines for the management of AF[5,6] have incorporated these agents into their recommendations, and Canadian guidelines recommend one of the novel agents in preference to warfarin for most patients with AF at moderate or high risk of stroke.[5] Despite these developments, these agents are relatively new and their incorporation into routine clinical practice is gradual and incomplete. Many practitioners are faced with uncertainties in the use of these new agents, and have many questions regarding their risks, benefits, and optimal use. This issue of *Cardiology Rounds* is intended to give an overview of a small selection of frequently asked questions that often come up at continuing health education sessions, workshops, symposia, and in conversations regarding stroke prevention.

In light of the data demonstrating their efficacy and safety in large-scale trials, the additional benefit of novel oral anticoagulants (NOACs) is their simplicity compared to warfarin: routine monitoring of anticoagulant effect is not required, and there are no relevant food and few drug-anticoagulant pharmacokinetic interactions. However, practitioners still need to become familiar with the pharmacology of these new drugs and strategies to understand and manage complexities associated with their use.

1) How good are the stroke risk prediction classifications (eg, $CHADS_2$ or CHA_2DS_2-VASc)?

It is critical to accurately identify patients at relatively high risk of stroke so that we may target anticoagulant therapy to those at greatest risk, while avoiding the administration of anticoagulants in patients who are at minimal risk.

Guidelines from the Canadian Cardiovascular Society (CCS) and others recommend systemic anticoagulation for the majority of patients with atrial fibrillation (AF).[5] The CHA_2DS_2-VASc risk stratification system[7] assigns a point for each of age ≥65 years, female sex, and vascular disease, in addition to the well known $CHADS_2$ risk factors (congestive heart failure, hypertension, age ≥75 years, diabetes, and prior stroke/transient ischemic attack

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[2 points]).[8] The vast majority (≥80%) of patients with AF will either be over 65 years of age - age is the second most important risk stratifier, after prior stroke - or have ≥1 clinical risk factors associated with stroke risk such as hypertension, diabetes, heart failure, vascular disease, or female sex. Therefore, a simple approach to stroke risk classification uses age first, since almost all patients >65 years have an annual stroke risk of ≥2%; in such patients the benefit from stroke prevention will outweigh the risk of life-threatening or fatal bleeding. Recent studies have confirmed that patients aged 65–75 years have approximately twice the stroke risk of patients <65 years. Although the absolute benefit of stroke risk reduction in patients between ages 65–75 may be considered relatively small, these younger patients have a very low risk of serious bleeding with the newer systemic anticoagulants, and the benefit of anticoagulation with the novel oral anticoagulants still outweighs the risk of bleeding.

Both $CHADS_2$ and CHA_2DS_2-VASc are useful in categorizing patients with respect to gradient of risk for stroke. Several recent articles and studies have supported CHA_2DS_2-VASc as a more sensitive stroke predictor over $CHADS_2$.[9-12] The authors of the AFNET (German Competence Network on Atrial Fibrillation) registry study[13] (N=8847) found that more than one-third of the strokes and thromboembolic events (145 of 403 events) over the 5-year follow-up period occurred in patients with $CHADS_2$ scores of ≤1 points; ie, oral anticoagulation not definitively recommended. Using the CHA_2DS_2-VASc scoring system, 54% of these patients were reclassified (≥2 points) to have a sufficiently high risk to recommend anticoagulation. The 2012 CCS guidelines[5] note that the greatest benefit of CHA_2DS_2-VASc is in the identification of truly low-risk AF patients – 8.5% of AF patients have a CHA_2DS_2-VASc score of 0 and a mean annual stroke risk of ≤0.5%[14,15] – who rarely require antithrombotic therapy.

In a study of patients with AF treated with antiplatelet agents, patients on acetylsalicylic acid (ASA) with $CHADS_2$ and CHA_2DS_2-VASc scores of 1 were at very low risk of stroke (1.1%/year), whereas those with a $CHADS_2$ score of 1 and a CHA_2DS_2-VASc score of 2 as well as were at more than twice the risk (2.3% /year).[16] The very low risk patients with a CHA_2DS_2-VASc score of 1 (as well as $CHADS_2$ score of 1) were mostly men aged < 65 years with either hypertension (87%), heart failure (8%), or diabetes mellitus (4%), and those with CHA_2DS_2-VASc scores of 2 were mostly aged 65–75 years, and were either female or had another risk factor. The significant predictors of risk in this generally low risk cohort were age >65 years or female sex.

2) Isn't the absolute benefit of anticoagulation in relatively low-risk patients small?

Although it is true that many low-risk patients with AF have an annual stroke risk of about 2%, compared to an average ~5% risk for all AF patients, it is important to note that this risk is cumulative. There are no good very long-term studies analyzing parameters such as the 10-year risk of stroke in generally low-risk ($CHADS_2$=1) patients aged >65 years; however, these patients have been observed to have a cumulative 5-year risk of 10% if treated with ASA alone. Dabigatran, for example, is associated with an estimated (extrapolated) risk reduction of 70% over ASA in such patients.[17] This adds up to an estimated 8% absolute reduction versus ASA in the rate of stroke and systemic embolism over an extended time frame of 5 years, and even larger over a more extended time frame. For apixaban, there was a 55% risk reduction in stroke and systemic embolism over ASA when the 2 were directly compared in the AVERROES study.[18] Similar data for rivaroxaban are not available, but the calculation would be expected to be consistent with its effect compared to warfarin. Similarly, the risk reduction of a NOAC over warfarin is likely to be cumulative, not even considering the increased discontinuation rates of warfarin over NOACs. For example, the RE-LY investigators[1] determined that dabigatran 150 mg bid reduced stroke risk over warfarin by 34%, an absolute reduction of 0.58% per year. Thus, taking the "long view," the absolute risk reduction of the new anticoagulants over warfarin, and particularly over ASA or no anticoagulation, is sufficiently large to warrant treatment.

3) In what situations should I consider the use of a NOAC?

The benefit:risk ratio for a NOAC is probably highest in patients at moderate or higher stroke risk who are not on currently receiving an anticoagulant. In addition to the benefits of the NOACs over warfarin for all patients, the first several months of warfarin therapy are associated with a substantially higher risk of bleeding complications than is seen in patients on long-term therapy.[19,20] The initiation of warfarin therapy is not straightforward, and requires frequent blood monitoring and dose adjustments, along with the heightened potential for under- or overanticoagulation until the stable dosing regimen is established. In contrast, the NOACs take effect almost immediately after the first dose, and stable blood concentrations and effect are established within 2–3 days.

A second important category is patients who are receiving warfarin but in whom maintaining the international normalized ratio (INR) in the therapeutic range is difficult. Arbitrary but commonly agreed upon standards suggest that optimum anticoagulation with warfarin is achieved only when the time in therapeutic range (TTR) is >65%. Patients may have difficulty complying with the requirement to undergo regular blood testing, observe a diet with relatively stable intake of vitamin K-containing foods, or have variable INRs despite close monitoring. Practitioners should follow closely the trajectory of INRs over time, not only paying attention to the most recent INR in making a determination of whether their patient is receiving optimum benefit from warfarin. Some patients will have stable INRs with TTR >65%, and are able to comply with the requirements for monitoring warfarin effect without difficulty. In such patients, there is a consensus that changing to new oral anticoagulant is not essential but can be considered. It seems reasonable to inform patients of the availability of the NOACs, and be guided in practice by a patient's values and preferences.

4) Are the new agents really better than warfarin?

All of the NOACs offer advantages with respect to warfarin, because of one or more of a significantly decreased risk of stroke, a decreased risk of life-threatening or intra-cranial hemorrhage, and the freedom from the complexities, risks, and inconvenience of the requirement for ongoing monitoring of therapeutic effectiveness with warfarin and its often unpredictable fluctuation of therapeutic effect (manifest as fluctuating INR). For some agents and doses, there are particular added benefits (Table 1), such as a significant reduction specifically in ischemic stroke (dabigatran 150 mg bid);[1] a significant reduction in major bleeding (dabigatran 110 mg bid and apixaban 5 mg bid),[1,3] and a statistically significant reduction in all-cause mortality (apixaban 5 mg bid).[3] It should be noted that each of the NOACs reduce all-cause mortality by a similar amount: dabigatran 150 mg bid by 12%, rivaroxaban 20 mg qd by 8%, and apixaban 5 mg bid by 11%; however, only the latter reduction was statistically significant.[1,3]

Although there has been much discussion about the unrealized benefit of warfarin if this drug is managed in carefully controlled settings (eg, anticoagulation clinics, advanced systems of care that allow close patient follow-up, and patient self-monitoring), there is substantial evidence that warfarin in the "real world" is difficult for patients and caregivers to use, maintain stable and effective level of anticoagulation, and maintain persistence of treatment over time.[20-22]

There is also substantial evidence from clinical trials and observational studies that warfarin is relatively ineffective if the INR cannot be maintained in the therapeutic range at least approximately 65% of the time. In a substudy of the ACTIVE W trial,[21] patients with "good" INR control (ie, time in the therapeutic range >65%) had significantly lower stroke rates than patients treated with the combination of ASA and clopidogrel; conversely, in the 50% of patients in whom the TTR was <65%, stroke rates were equivalent on warfarin versus the dual anti-platelet agent (Figure 1).[23]

5) The NOACs have only been available for a relatively short time. How can I be confident that they are indeed preferable to warfarin?

There are emerging data on the outcomes of patients treated with the NOACs and warfarin in community practice, after the publication of the abovementioned landmark clinical trials. Using the United States Food and Drug Administration Mini-Sentinel program, Southworth et al[24] compared patients with a recent prescription for dabigatran or warfarin were compared. The number of events of gastrointestinal hemorrhage per 100,000 days at risk in warfarin treated patients was 3.5, compared to 1.6 for dabigatran; respective intracranial hemorrhage rates were 2.4 per 100,000 days at risk for warfarin versus 0.8 per 100,000 days at risk for dabigatran. These latter event rates are very similar to those observed in the randomized clinical trial of warfarin versus dabigatran.

In a large Danish cohort of patients followed using administrative databases,[25] outcomes following warfarin and dabigatran 150 mg or 110 mg bid were similar to those observed in the large clinical trials, with a reduction in intracranial bleeding by both doses, slightly but not significantly reduced rates of major bleeding for both doses with respect to warfarin, and a reduction in hospitalization for both doses (all comparisons adjusted for comorbidities).

Discontinuation rates for warfarin have been reported to be ≥50% at 1–2 years after initiation, in community practice.[26] A recent study by Zalesak et al[22] investigating factors associated with warfarin discontinuation in AF patients found a 44% discontinuation rate for warfarin versus 26% for dabigatran, in 1775 and 3370 propensity matched patients, respectively. Patients with a low-to-moderate risk of stroke ($CHADS_2$ <2) were less persistent than patients with

Table 1: Outcomes in the major clinical trials of novel oral anticoagulants (NOACs) versus warfarin in patients with atrial fibrillation (AF)

Reduction of:	Study	NOAC (%)[a]	Warfarin (%)[a]	*P*
Ischemic stroke	RE-LY[1]	Dabigatran 110 mg: 1.34 150 mg: 0.92	1.20	0.35 0.03
	ROCKET AF[2]	Rivaroxaban 20 mg: 1.34	1.42	0.58
	ARISTOTLE[3]	Apixaban 5 mg bid: 0.97	1.05	0.42
Hemorrhagic stroke	RE-LY[1]	Dabigatran 110 mg: 0.12 150 mg: 0.10	0.38	<0.001 <0.001
	ROCKET AF[2]	Rivaroxaban 20 mg: 0.26	0.44	0.024
	ARISTOTLE[3]	Apixaban 5 mg bid: 0.24	0.47	<0.001
Major bleeding	RE-LY[1]	Dabigatran 110 mg: 2.71 150 mg: 3.11	3.36	0.003 0.31
	ROCKET AF[2]	Rivaroxaban 20 mg: 3.60	3.45	0.58
	ARISTOTLE[3]	Apixaban 5 mg bid: 2.13	3.09	<0.001
Mortality	RE-LY[1]	Dabigatran 110 mg: 3.75 150 mg: 3.64	4.13	0.13 0.051
	ROCKET AF[2]	Rivaroxaban 20 mg: 1.87	2.21	0.073
	ARISTOTLE[3]	Apixaban 5 mg bid: 3.52	3.94	0.047

[a]Outcome rates are per year for all studies.

greater stroke risk for both treatment cohorts. Similar Phase IV data are not yet available for rivaroxaban or apixaban.

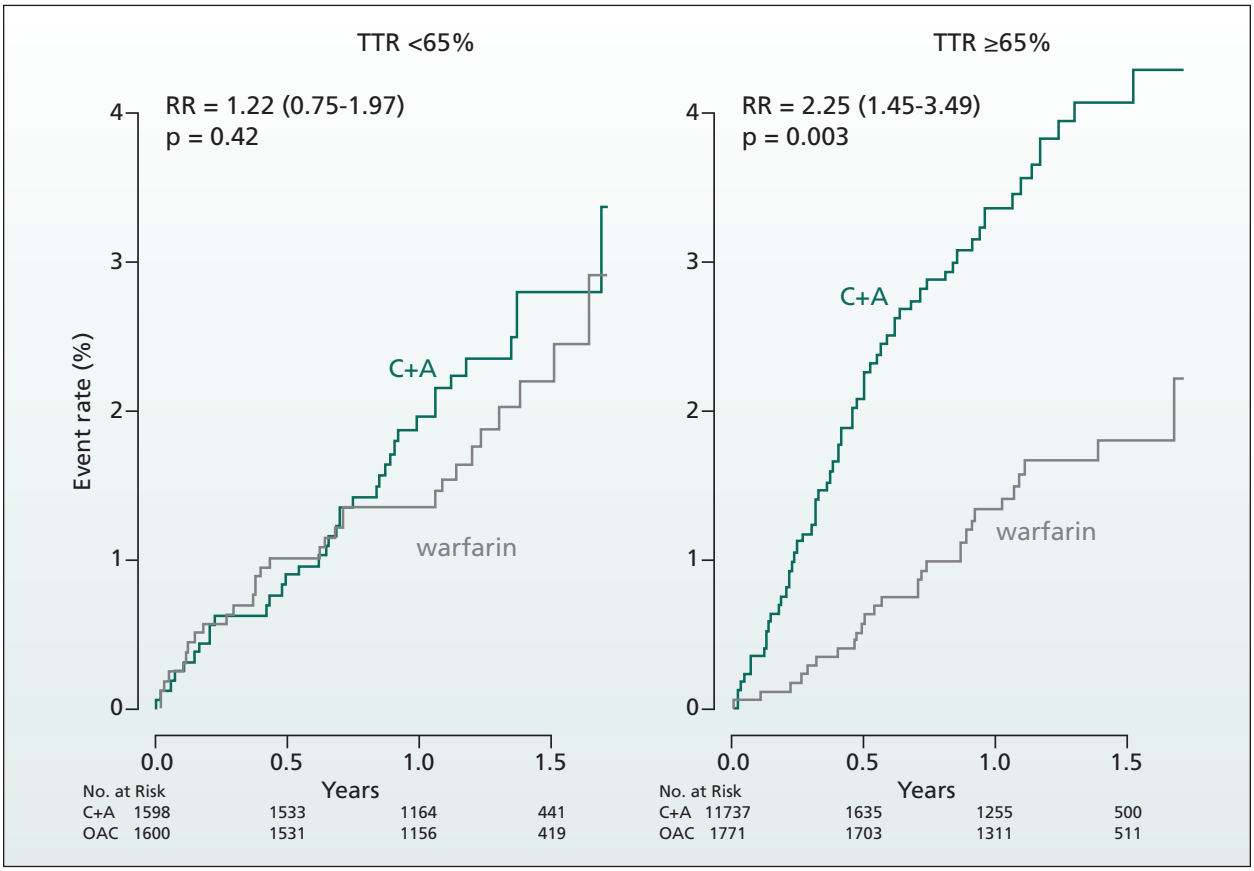
6) When a patient is on warfarin, I know exactly what their anticoagulation status is. How can I be confident that the NOAC is effective?

Physicians are understandably concerned that it is difficult to ascertain the extent of anticoagulation in patients on a NOAC. The accumulated evidence from clinical trials and post-marketing surveillance has suggested that NOACs are indeed as safe as or safer than warfarin even though anticoagulation status was not clinically monitored in these studies. The role of therapeutic drug monitoring for the NOACs, preferably with the HEMOCLOT Thrombin Inhibitor assay for dabigatran[27] or a factor Xa assay for apixaban or rivaroxaban[6] is evolving and not yet clear. For dabigatran, the widely available activated partial thromboplastin time (aPTT) test offers a rough guide to the anticoagulation status on dabigatran; if the aPTT is close to control values (generally less than 37-38 seconds), it is likely that there is no residual anticoagulant effect. If the aPTT is >2.0 times the control value (ie, ≥80 seconds), then it is likely there is excess anticoagulant effect. The aPTT can be useful to assess the potential safety of surgical interventions (to ensure there is no residual anticoagulant effect), or to assess the possibility of excess drug effect (in cases of minor bleeding). Current consensus indicates that the routine measurement of anticoagulation effect with the NOACs is unnecessary for safe clinical use.

7) The NOACs do not have an antidote. How big a concern is this?

Although in theory it is clearly preferable to have access to an agent that can readily reverse the anticoagulant effect, in practice there is no clear proof that the availability of an "antidote" can reduce mortality or severe morbidity from major bleeding. In the case of warfarin, transfusion requirements may be reduced.[28] Unfortunately, in cases of life-threatening bleeding and particularly intracranial hemorrhage, the availability of a specific "antidote" to warfarin (ie, four factor protein concentrate) has not been shown to reduce morbidity or

Figure 1: Effect of time in therapeutic range (TTR) on the cumulative risk of stroke in patients treated with warfarin or clopidogrel and acetylsalicylic acid (C+A)[9]



RR = relative risk

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mortality, presumably because of the time delay required to administer this agent.[29] A reasonable surrogate for the potential risk of the absence of an antidote is the probability of death if major hemorrhage actually occurs; in a recent study, the probability of death following major hemorrhage on dabigatran versus warfarin was compared, with a nonsignificantly (P=0.052) lower risk of fatality in the 30 days following a major bleed on dabigatran compared to warfarin.[30]

In a substudy of the RE-LY study, the risk of major bleeding in patients requiring urgent surgery (ie, within 30 days) was 17.8% following dabigatran 110 mg bid, 17.7% following dabigatran 150 mg bid, and 21.6% following warfarin therapy.[31] In the ARISTOTLE study, the risk of a major hemorrhage following any invasive procedure was 1.6% in the apixaban-treated patients versus 1.8% in the warfarin-treated patients.[32] These results suggest that standard conservative measures (eg, prompt drug discontinuation in cases of bleeding or impending surgical procedures, supportive measures, mechanical methods of controlling bleeding, and blood transfusions) are sufficient to deal with bleeding in the vast majority of cases, whether from NOACs or warfarin. Specific "antidotes" for both thrombin inhibitors or factor Xa inhibitors are under active investigation and will likely eventually become commercially available.

The CCS guidelines[5] place lower value on the availability of a specific antidote for warfarin, along with the accumulated experience with clinical use and a simple and a standardized test of the anticoagulant effect of warfarin, than on the improved efficacy and/or safety of NOACs.

8) What practical steps can I take to maximize efficacy and reduce risk with the NOACs?

It is extremely important to educate patients regarding the necessity of taking their NOAC exactly as prescribed. Since there is no "built-in" compliance measure as there may be with warfarin and the moni-

toring of INRs, patients need to be informed and educated regarding the necessity for strict adherence to the dosing regimen prescribed, and to avoid missed doses. For the drugs taken twice daily (dabigatran, apixaban), this includes instructions on what to do for missed doses (take the missed dose if within 6 hours, otherwise wait until the next scheduled dose); for the drug recommended to be taken once daily (rivaroxaban), emphasize the recommended timing of drug administration with a meal, preferably at dinner time. Missing a dose of a once-daily drug may result in a 48-hour period between doses, potentially leading to underanticoagulation.

Patients should be instructed about the potential for increased bleeding risk with ASA or nonsteroidal anti-inflammatory drugs taken in combination with an anticoagulant, and such drugs should be avoided unless absolutely indicated or required. In particular, ASA in patients on a NOAC should be reserved for cases of a definite indication for secondary prevention of coronary artery disease, and is not necessary or indicated for the primary prevention of coronary artery disease.

9) My patient is 70 years old and in good health except for AF. Does she really need an anticoagulant? Is ASA sufficient?

Of all the factors that are associated with increased risk of stroke in the presence of AF, age is the most potent risk factor. The risk of stroke is doubled in patients aged 65-75 years compared to younger individuals. Females are at higher risk than males, even correcting for other stroke risk factors. CCS[5] and European Society of Cardiology[6] guidelines recommend oral anticoagulation in patients over 65 years, particularly in women, even if they have no other risk factors for stroke (eg, hypertension, diabetes, prior stroke or transient ischemic attack, heart failure, or vascular disease). ASA is not highly effective at stroke prevention and carries a nontrivial risk of bleeding.

10) My patient seems to be free of AF clinically, and has been on an anticoagulant for some time. Does it have to be continued indefinitely?

Current guidelines uniformly recommend continuing an anticoagulant indefinitely in patients who have AF not due to a reversible cause, even if they appear to be in stable sinus rhythm. This is because AF will usually recur in most patients with a prior history, and can do so unpredictably. Importantly, asymptomatic episodes of AF are extremely common in patients who seem to be free of symptomatic recurrences, and thus routine electrocardiographic monitoring and the absence of symptoms do not ensure that AF has actually been eliminated or is absent. For these reasons, if an anticoagulant has been started for long-term stroke prevention, it almost always is indicated indefinitely (unless there is major bleeding or a new contraindication develops). Until further data become available, patients need to be informed that an anticoagulant prescription for stroke prevention in AF is typically for the rest of their lives, and particularly that ablation of AF, which can be very useful in selected patients, does not allow previously indicated anticoagulants to be discontinued.

Conclusion

Our understanding of the benefits and risks of the NOACs is evolving. Warfarin will remain a frequently used and useful anticoagulant for the foreseeable future. Optimal use of the NOACs will require an understanding of their pharmacology, detailed and careful patient education, and an awareness of post marketing surveillance data as it becomes available. The European Heart Rhythm Association has published a very useful practical guide on the use of NOACs;[33] and this guide details, in a straightforward checklist based approach, strategies to ensure safe and effective use of these agents during follow-up.

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Dr. Dorian has received grant support and honoraria from Bristol-Myers Squibb, Bayer, Boehringer Ingelheim, and Pfizer.

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This publication is made possible by an unrestricted educational grant from

Boehringer Ingelheim (Canada) Ltd.

AFib In One Page

January 9, 2013

1. Stroke Risk

a i. Determine your patient's $CHADS_2$ score:

$CHADS_2$ risk stratification does not apply to AFib patients with mitral stenosis. They should be anticoagulated.

	Findings	Points
C	Congestive Heart Failure	1
H	Hypertension	1
A	Age ≥ 75 years	1
D	Diabetes	1
S	Prior Stroke or TIA	2

ii. Determine your patient's recommended treatment:

$CHADS_2$ = 0 , most still require treatment
Stroke risk is 1.9%/year

- ≥ 65 yrs **or** combination of female sex and vascular disease → **OAC***
- Either female sex **or** vascular disease → **ASA**
- No additional risk factors for stroke → **No antithrombotic**

$CHADS_2$ 1 or more

$CHADS_2$ Score	Stroke Rate per 100 patient years (95% CI)	Recommended therapy
1	2.8 (2.0 – 3.8)	OAC*
2	4.0 (3.1 – 5.1)	OAC
3	5.9 (4.6 – 7.3)	OAC
≥ 4	≥ 8.5	OAC

*OAC = Oral Anticoagulant Therapy

b Determine your patient's risk of bleeding. One way to do this is the HAS-BLED score:

Hypertension SBP > 160 mmHg	**A**bnormal renal or liver function	**S**troke	**B**leeding history	**L**abile INR	**E**lderly age > 65 years	**D**rugs or ETOH	Max. score
1	1 or 2	1	1	1	1	1 or 2	9

Score ≥ 3 indicates high risk & warrants some caution/regular patient evaluation of antithrombotic therapy. The incidence of major bleeding with a HAS-BLED score of 0 to 1 is 1.0%/year, 2 is 1.9%/year, 3 is 3.7%/year, 4 is 8.7%/year, 5 is 12.5%/year.
RENAL: ESRD or Cr>200umol/L; LIVER: cirrhosis or bilirubin>2xULN with AST/ALT/ALP>3xULN. less than 60% of INRs in therapeutic range or frequent unstable INRs. DRUGS: antiplatelets/NSAIDs.

c Summary of Available Treatments:

Stroke Prevention	Major Bleeding	Comments
• Compared to warfarin, dabigatran 150 mg BID is superior in preventing stroke, while dabigatran 110 mg BID has similar efficacy • Compared to warfarin, rivaroxaban 20 mg once daily is at least as good at preventing strokes • Compared to warfarin, apixaban 5mg BID is superior in preventing stroke • Warfarin is superior to ASA. (Efficacy based on achieving a time in therapeutic range (INR 2-3) at least 60% of the time) • 2012 Canadian AFib Guidelines recommend apixaban, dabigatran or rivaroxaban over warfarin	• Compared with warfarin, dabigatran 150 mg BID and rivaroxaban 20 mg once daily are associated with similar rates of major bleeding but more GI bleeds • Compared with warfarin, dabigatran 110 mg BID is associated with less major bleeding and is the preferred dose for patients over 80 years or over 75 years with risk factors for bleeding • Compared with warfarin, apixaban 5mg bid is associated with less major bleeding • Apixaban, dabigatran and rivaroxaban are associated with less intracranial hemorrhage (ICH) than warfarin	• No clinical trials directly comparing the new anticoagulants (apixaban, dabigatran, rivaroxaban) to each other are available • 2012 Canadian AFib Guidelines suggest dialysis patients should not routinely receive OAC or ASA • Dabigatran and rivaroxaban should be avoided in signifi cant renal dysfunction (i.e., CrCl < 30 mL/min); Apixaban should be avoided if CrCl<25ml/min • Dabigatran is contraindicated in combination with strong P-gp inhibitors/inducers. Rivaroxaban and apixaban are contraindicated in combination with strong inhibitors of both P-gp and CYP 3A4. Refer to prescribing information for details • Discuss cost and coverage of new OACs with patient

*Adapted from the Canadian Cardiovascular **Pharmacists Network Stroke** Prevention in Atrial Fibrillation (SPAF) Pocket Reference*

2. Symptoms/Quality of Life (QOL)

a i. MD to determine impact of AFib using Severity of Atrial Fibrillation (SAF) class:

SAF	Impact on QOL	Example
0	Asymptomatic	
1	Minimal effect on QOL	Single episode of AFib without syncope or heart failure (CHF)
2	Minor effect on QOL	Mild awareness of symptoms or rare (less than a few per year) episodes
3	Moderate effect on QOL	Moderate awareness of symptoms on most days, or more severe symptoms
4	Severe effect on QOL	Highly symptomatic, or frequent episodes, or AFib related syncope or CHF

ii. Assess *apical* HR. If resting HR > 100 or SAF class is >2 follow preferred rate control strategy below:

- **MI or CHF** → Beta blocker (BB) → Titrate to resting apical HR < 100 and SAF Class 0-2. If not achieved → Add digoxin
- **No previous MI, no CHF** → Calcium Channel Blockers (CCB)† or BB → Titrate to resting apical HR < 100 and SAF Class 0-2. If not achieved → Add or sub CCB/BB Add digoxin

If still not achieved, may need rhythm control

†Use only non-dihydropyridine CCB for heart rate control (diltiazem, verapamil)

iii. Rate control drug dosing information:

Class	Medication	Starting Dose	Usual Range
Beta blocker (BB)	Bisoprolol Metoprolol Atenolol	2.5-5 mg daily 12.5-25 mg BID 25-50 mg daily	2.5-10 mg daily 25-150 mg BID 50-150 mg daily
CCB	Diltiazem CD‡ Verapamil SR‡	120 mg daily 120 mg BID	120-360 mg daily 120-240 mg BID
Digitalis	Digoxin‡	0.0625-0.125 mg daily	0.125-0.25 mg daily

‡Caution when combining CCB and digoxin

b Assess AFib pattern (paroxysmal, persistent, permanent):

Pattern	Definition	Action
Paroxysmal	AFib is self-terminating within 7 days	Educate and **REASSURE** patient that this rarely requires cardioversion§ or urgent intervention. **REFER** if rhythm control needed.
Persistent	AFib is not self-terminating within 7 days	If symptoms (SAF > 2) persist despite HR control, **REFER** for cardioversion§
Permanent	Longstanding AFib where a decision not to pursue sinus rhythm has been made	Focus on **RATE CONTROL** to achieve resting HR < 100. Rhythm control not indicated

§Pharmacologic or electrical

All management recommendations are in accordance with Canadian Cardiovascular Society Atrial Fibrillation Guidelines Canadian Journal of Cardiology 2012;28:125-136

Was this tool helpful to you? Do you have any suggestions for improvement? Please email your feedback to **afib@uhn.ca**