www.cardiologyrounds.ca 2008 volume XIII, issue 2

CARDIOLOGY Rounds®

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

Stroke Prophylaxis in Non-Valvular Atrial Fibrillation

By BRIAN K. COURTNEY, MD, MSEE, and PAUL DORIAN, MD, FRCPC

Atrial fibrillation (AF) is the most common cardiac arrhythmia; lifetime risk for the development of AF is 1 in 4 in people 40 years of age and older.[1] AF is also a powerful and independent risk factor for stroke. The availability of oral anticoagulation agents, such as warfarin or other vitamin K antagonists, provides a substantial opportunity to reduce the relative risk of stroke or other cardioembolic events by >60%. In comparison, antiplatelet agents such as acetylsalicylic acid (ASA) reduce the risk by only 20%-33%.[2] Unfortunately, several complications are also associated with warfarin use, such as the risk of increased bleeding and drug interactions. Despite risks and inconveniences, the evidence weighs strongly in favour of anticoagulation with warfarin for most patients, with a few notable exceptions. In light of the importance of optimal management for stroke prophylaxis and recent data regarding the efficacy of warfarin in certain high-risk populations, this issue of *Cardiology Rounds* reviews the strategies for simplifying the management of patients with AF.

Estimating the risk for stroke in patients with nonvalvular AF

The first step, which influences all other aspects of stroke prophylaxis in AF, is to assess the risk of stroke for each individual. This process allows both physician and patient to assess the potential benefit of anticoagulation therapy. Several scoring systems have been developed for predicting the risk of stroke in the setting of nonvalvular AF. These include the Stroke Prevention in Atrial Fibrillation (SPAF), Atrial Fibrillation Investigators (AFI), and $CHADS_2$ (Table 1) scoring systems, and they all appear to have similar predictive value;[3] however, these scoring systems apply specifically to nonvalvular AF. Patients with valvular lesions such as mitral stenosis, rheumatic heart disease, a history of valve repair or valve replacement are generally at higher risk for embolic events and are outside of the scope of this article.

Among these scoring systems for nonvalvular AF, the $CHADS_2$ scoring system has received the most widespread adoption and has been well validated. The $CHADS_2$ score is easy to remember (Table 1) and easy to calculate. Explicitly including the $CHADS_2$ score as part of each office visit or consultation for patients with AF provides a quick method to reassess whether anticoagulation is indicated. The score may need to be updated over time, as patients develop new risk factors, such as advanced age. Importantly, the $CHADS_2$ score provides a framework for discussions with the patient concerning the risks and benefits of stroke prophylaxis.

Once calculated, the score can be used to provide reasonable guidance to the annual risk for stroke per year. While each point on the $CHADS_2$ score adds to the risk for an embolic event, there is some disparity between the published results on absolute event rates in the absence of anticoagulation (Table 2). In the most frequently cited study on event rates (National Registry of Atrial Fibrillation, published in 2001),[4] over 1,700 patients with a diagnosis of AF were followed for >1 year; one-third of these patients were taking ASA and the rest received neither ASA nor warfarin. Events in this registry included transient ischemic attacks, strokes, and the International Classification of Diseases, Clinical Modification (ICD-9-CM) codes for new diagnoses of cerebrovascular disease.

St. Michael's Hospital
30 Bond St.,
Suite 7049, Queen Wing
Toronto, Ont. M5B 1W8
Fax: (416) 864-5941

Table 1: $CHADS_2$ scoring system

	Points
Congestive heart failure (ever)	1
Hypertension	1
Age >75 years	1
Diabetes mellitus	1
Stroke (or any other previous event suspicious for an embolic origin – eg, acute limb ischemia, renal infarct, acute mesenteric ischemia)	2

Note that "$CHADS_2$" is an acronym for the score components, as underlined in the table. Each of these risk factors is considered an independent risk factor for stroke according to Canadian Cardiovascular Society guidelines. The score ranges from 0-6.

A later meta-analysis[5] by the same research group revealed slightly lower event rates in a group of patients who used ASA alone as stroke prophylaxis. The Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) trial[6] had a control arm of elderly patients in whom physicians were uncertain as to the benefits and risks of oral anticoagulation over ASA; therefore, they excluded many patients at high risk of either stroke or bleeding. The event rates in the BAFTA trial for patients on ASA alone were lower than anticipated for $CHADS_2$ scores[4] ≥3 (5% vs an anticipated 9%). This lower than anticipated event rate may reflect improved control of blood pressure and lipids in the past decade, but may also reflect a selection bias for the study. Over 45% of patients screened for the BAFTA trial were excluded on the basis of either patient or physician preference for warfarin. Thus, the event rates in the BAFTA trial, as shown in Table 2, may underestimate the risks of embolization in patients not taking warfarin. Despite the disparities between these reports, the event rates of all patients with a $CHADS_2$ score of ≥1 are sufficiently high to warrant strong consideration for anticoagulation with warfarin.

While the $CHADS_2$ score includes factors considered high risk for stroke, other factors considered more "moderate" include female sex, age 65-74 years, and the presence of established coronary artery disease (Table 3). As will be discussed later, one of these more moderate risk factors may make it reasonable to consider the use of ASA or warfarin in patients who otherwise have a $CHADS_2$ score of 0.

A few additional rules of thumb may further help to simplify risk stratification.

- **Rule #1 – There is clear evidence that patients with persistent AF, paroxysmal AF, and atrial flutter all have a very similar risk for cardioembolic events.** Therefore, a level 1 recommendation from the American Heart Association (AHA)[7] is that the selection of a stroke prophylaxis regimen, if any, should be guided by the same process for all 3 of these conditions.
- **Rule #2 – Once a patient is found to have AF, it should be assumed that they have it for the rest of their lives, unless it occurred in the setting of a clearly reversible cause that has been treated successfully (such as a pulmonary embolism, alcohol binge, postoperative AF after cardiac surgery, or hyperthyroidism).** In other words, once warfarin is started, it is usually "started for life" in the absence of contraindications. Even in the setting of a clearly reversible cause of AF, the selected regimen for prophylaxis against embolism should continue for a sufficient period to allow any potential thrombi that have formed to clear (at least 4 weeks after resolution of the reversible cause). The possibility that the AF may have existed independent of a presumed reversible cause must also be considered before assuming that the patient's AF has resolved completely. Given the high prevalence of AF, many patients with reversible causes will still have recurrences of AF once the presumed reversible cause has resolved.
- **Rule #3 – Any patient with AF should be considered for stroke prophylaxis therapy regardless of whether he/she is rate-controlled or converted back into sinus rhythm (by either pharmacologic means or electrical [DC] cardioversion).**

Table 2: The $CHADS_2$ score and associated annual risk of embolic events for nonvalvular AF, in patients not on warfarin

$CHADS_2$ Score	Preferred method of prophylaxis	Gage et al (1/3 ASA, 2/3 none)[4]	Gage meta-analysis (all on ASA)[5]	BAFTA (2001-2004, age ≥75, on ASA)[6]
0	None or ASA	1.9%	0.8%	n/a
1	ASA or Warfarin	2.8%	2.2%	3.3%
2	Warfarin	4%	4.5%	
3	Warfarin	5.9%	8.6%	5.0%
4	Warfarin	8.5%	10.9%	
5	Warfarin	12.5%	12.3%	
6	Warfarin	18.2%	13.7%	

The preferred method of prophylaxis indicates recommendations for methods of stroke prevention in the absence of contraindications. Adapted from references as cited.
AF = atrial fibrillation; ASA = acetylsalicylic acid;
BAFTA = Birmingham Atrial Fibrillation Treatment of the Aged

Table 3: Moderate risk factors for embolic events

- Age 65-74 years
- Coronary artery disease
- Female gender

These factors are relevant only in patients with a $CHADS_2$ score of 0.

Consideration for the risk of bleeding on warfarin

Patients should be assessed for their risk of major bleeding before initiating either ASA- or warfarin-based

treatment. Many factors must be considered in estimating the bleeding risk for a patient on warfarin therapy. Most studies examining the use of warfarin have not included patients with a history of intracerebral hemorrhage, recent severe bleeding in the preceding 3-6 months, or previously demonstrated intolerance or bleeding while on warfarin. Recent studies suggest that cognitive impairment is also associated with increased bleeding risk.

Advanced age (≥80 years) is another reported significant risk factor for bleeding. A recent prospective cohort study of anticoagulation in elderly patients who were initiated on warfarin therapy, revealed a 4.7% risk/year of major hemorrhage in patients 65-80 years old, compared with 13.1% in older patients.[8] Furthermore, the same study suggested an increased risk of bleeding with increasing $CHADS_2$ scores (2.0%-4.3% for $CHADS_2$ <3 and >19% for patients with $CHADS_2$ ≥3).

These data on the risk of bleeding may lead to a negative opinion on the use of anticoagulation therapy in the elderly with elevated $CHADS_2$ scores. Fortunately, the BAFTA trial provides some further guidance for this population. BAFTA randomized elderly patients from referring physicians who were willing to have their patients treated with either ASA or warfarin. These patients had an annual rate of 1.9% for major hemorrhage while on warfarin, compared with 2.0% while on ASA. An increased $CHADS_2$ score was not associated with a higher risk of major hemorrhage in this study. However, the risk of stroke with AF increased substantially with age (2.8%/year for patients 75-79 years of age vs 5.6%/year for those ≥85 years of age). Therefore, the benefits of anticoagulation appear to outweigh the risks for most elderly patients with AF in this randomized controlled study.

Finally, there is good evidence indicating that the highest risks of bleeding with oral anticoagulation occur during the first 6 months of therapy. Patients who have demonstrated tolerance to anticoagulation in the past are at a significantly lower risk of major hemorrhage while on warfarin compared with new users of the drug.

Selecting a prophylactic regimen

In multiple trials, anticoagulation with warfarin or other vitamin K antagonists has clearly and consistently demonstrated superiority to ASA or any other antiplatelet regimen for the purposes of preventing cardioembolic events. The target international normalized ratio (INR) should be 2.0 to 3.0, unless another concomitant indication for anticoagulation warrants a higher INR. Warfarin confers a relative risk reduction of approximately 66% in preventing stroke and other cardioembolic events over not using either warfarin or ASA. Compared with the use of ASA, warfarin confers a relative risk reduction of slightly >50%.

In determining a strategy for stroke prophylaxis, it is important to recognize that the absolute benefits from anticoagulation are dependent on the baseline risk of embolic events. Patients with a $CHADS_2$ score of 0 and none of the moderate risk factors have a low annual risk of stroke and do not warrant anticoagulation with warfarin. The AHA has specifically issued a level III recommendation to reinforce the notion that young patients (<60 years old) with AF, but no other risk factors for thromboembolism, should not be offered warfarin as prophylaxis.[7] It is reasonable to consider ASA as stroke prophylaxis in this group, especially if they have other potential indications for ASA, such as an increased risk for coronary events.

If there is no specific reason against using warfarin, it is recommended that most patients with a $CHADS_2$ score of ≥1 be offered oral anticoagulation. The risk of a stroke is increased sufficiently to offset the increased risk of bleeding with warfarin in most of these patients, unless a strong concern for bleeding exists. There is a large group of people with AF whose $CHADS_2$ scores lie in the intermediate-risk range (scores 1-2); >60% of all thromboembolic strokes in patients not taking warfarin appear to occur in this subgroup. The AHA guidelines recommend either ASA or oral anticoagulation for all patients with a $CHADS_2$ score of 1 and oral anticoagulation for all patients with a score of ≥2.[7] If oral anticoagulation is contraindicated, then ASA is recommended as an alternative. In comparison, the Canadian Cardiovascular Society (CCS)[9] recommends warfarin therapy for all patients with a $CHADS_2$ score ≥1, unless the only $CHADS_2$ risk factor for stroke is diabetes, in which case the CCS is more liberal and recommends either warfarin or ASA.

Historically, the elderly have been undertreated with anticoagulation, especially given that they are at an increased risk of bleeding, experiencing higher rates of falls and malignancies, have increased susceptibility to intracerebral bleeding, and more polypharmacy (ie, increased risks of drug interactions). However, they are also at increased risk of stroke in the setting of AF. The BAFTA trial demonstrated a significant reduction in its primary outcome measure (stroke, intracranial hemorrhage or other arterial embolism) with warfarin over ASA in patients >75 years old (1.8% per year vs 3.8% per year). It remains to be seen whether the next AHA guidelines update will recommend that age >75 alone (eg, $CHADS_2$ score 1) is associated with a sufficiently high stroke risk to prefer warfarin over ASA.

In the absence of any of the $CHADS_2$ risk factors, the presence of ≥1 moderate risk factors prompted the AHA guidelines to provide a weaker recommendation (class IIa) for the use of ASA or warfarin, but both are mentioned as reasonable options. CCS guidelines for these more moderate risk factors are similar, with the exception that it does not list female sex as a risk factor.

Clopidogrel use in patients with AF

The Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE-W) trial[10] compared warfarin with a combination of ASA and clopidogrel. The combination of ASA and clopidogrel remained

inferior to treatment with warfarin and was associated with a similar risk of major hemorrhage (2.4% vs 2.2% per year). The risk of stroke was 41% lower with oral anticoagulation. Results are pending for the ACTIVE-A trial that compares ASA with the combination of ASA and clopidogrel, in patients for whom warfarin is not appropriate.

While clopidogrel does not appear to have a defined role in stroke prophylaxis for AF, the presence of simultaneous coronary artery disease and AF is common, especially in elderly patients with hypertension. A frequently encountered issue in clinical practice is whether or not patients already on warfarin can safely tolerate the additive risks of bleeding conferred by ASA and clopidogrel. This issue occurs in patients already anticoagulated with warfarin for AF, who then need prolonged dual antiplatelet therapy (ASA and clopidogrel) after stent implantation or acute coronary syndrome. A recent registry study in Europe suggests that triple therapy (ASA + clopidogrel + oral anticoagulation) may possibly be preferred over dual antiplatelet therapy alone. Major bleeding in the triple-therapy group was higher (14.9% vs 9% over a median follow-up of 20 months), but the frequency of embolism (1.9% vs 6.9%) and death (17.8% vs 27.8%) was significantly lower in patients on triple therapy. Nevertheless, this study has considerable selection bias and should not be considered definitive. The AHA guidelines acknowledge the lack of adequate data relating to these circumstances that prohibits making strong recommendations.

Strategies to reduce complications of oral anticoagulation

Once a decision is made to pursue oral anticoagulation, several measures can be taken to minimize the likelihood of complications while on therapy. To maintain warfarin therapy within the therapeutic window (INR 2.0-3.0) is a challenging task; in most trials using warfarin, the INR of patients is on target in only 60%-65% of measurements. Table 4 outlines some suggestions for reducing the likelihood of either subtherapeutic anticoagulation or increased bleeding with supratherapeutic INRs. Patient education and the use of a dedicated anticoagulation clinic can help avoid potential problems or identify them at an earlier point.

Anticoagulation before and after cardioversion

The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)[11] and the RAte Control versus Electrical cardioversion (RACE)[12] trials have established that there is no benefit to converting AF back into sinus rhythm in terms of preventing thromboembolic events. However, a substantial minority of patients with AF will be offered elective cardioversion, using either electrical or pharmacolog-

Table 4: Strategies for improving safety while on warfarin

Patient Education
- Encourage patient adherence by involving patients in the decision to start anticoagulation, with explanation of risks and benefits.
- Provide a patient information sheet on warfarin therapy, monitoring, and side effects.
- Inform the patient about the effects of dietary changes on the efficacy of warfarin and the potential for drug interactions that may require dose adjustments of warfarin or other medications.
- Stress the importance of consistent adherence at a regular time of day. Employed people may be less likely to adhere to anticoagulation than retired or unemployed people.[13]
- Suggest patients be aware of their international normalized ratio (INR) and assist the physicians in signaling need for dose adjustments if the INR is outside the desired range.

When available, use a dedicated anticoagulation clinic
- Often more convenient for patients and physicians
- Multidisciplinary approach with nurse practitioners, pharmacists and administrative support

Optimize management of other health conditions
- Ask patients if they have had routine screening for malignancies.
  - eg, colonoscopy
- Control hypertension
  - reduces risk of intracerebral hemorrhage

Personalize the monitoring schedule by increasing the frequency of INR testing under the following conditions:
- Initiation of therapy
  - The highest risk for major bleeding is during the first 6 months of anticoagulation.
  - While the schedule can be customized, AHA guidelines recommend at least weekly monitoring during initiation, then monthly once stable.
- Increased age
  - The higher risk of bleeding in elderly patients may warrant monitoring on a more frequent basis.
- Higher risks of stroke
  - To avoid subtherapeutic INR
- Other events
  - Acute illness
  - Changes in medications, including treatment with antibiotics

Encourage patients to have all their prescriptions filled at a single pharmacy
- Most pharmacies now have systems that may identify potential drug interactions with warfarin.

Screen for cognitive impairment
- Suspicion for cognitive impairment may indicate inability of a patient to safely comply with warfarin dosing and monitoring.

ical methods, in an attempt to reduce their symptoms or improve cardiac pump function.

Most physicians are aware of the possibility of pre-existing emboli in the left atrium that can dislodge upon the return of sinus rhythm. Fewer are aware that cardioversion itself may predispose patients to developing potential embolic thrombi in the left atrium during the period shortly after a return to sinus rhythm. This process is thought to occur as a result of "stunning" the atrial myocardium, and can occur with either electrical or pharmacological cardioversion.

The AHA provides guidelines for anticoagulation procedures in the pericardioversion period.[7] Any patient in whom AF may have been present for ≥48 hours (or where the duration of fibrillation is uncertain) should be anticoagulated for at least 3 weeks prior and at least 4 weeks following cardioversion. If cardioversion in such patients is desired on a more urgent (but nonemergent) basis, it is reasonable to consider screening for thrombi in the left atrium using transesophageal echocardiography. If no signs of thrombus formation are identified, the patient can be cardioverted after initiating unfractionated heparin; following cardioversion, at least 4 weeks of anticoagulation is recommended.

Patients with ≥48 hours of AF who require emergent cardioversion (eg, in the setting of heart failure, hemodynamic instability, angina, or myocardial infarction) should be anticoagulated as soon after cardioversion as possible, unless contraindicated. Cardioversion should not be delayed for the purposes of anticoagulation in these circumstances.

The strategies for prevention of thromboembolic events are less clear for patients with an episode of AF lasting <48 hours prior to cardioversion. The AHA guidelines indicate a class IIa recommendation for the use of a conventional assessment of the risks for thromboembolism (eg, the $CHADS_2$ score and the moderate risk factors previously mentioned) as a guide to determine whether ASA, warfarin, or neither should be used. However, some data suggest that anticoagulation with ASA or warfarin for at least the first 4 weeks would be reasonable. The indication for anticoagulation is strengthened by a $CHADS_2$ score of ≥1 (in which case anticoagulation would be continued indefinitely in the absence of a reversible cause) or AF where the duration is uncertain.

Future directions and conclusions

In spite of the acknowledged bleeding risks of warfarin therapy, and the logistical burden involved in monitoring INRs and adjusting warfarin dosing, oral anticoagulation is an invaluable tool to prevent the severe consequences of stroke or other cardioembolic events. There would be tremendous value in developing agents that provide the anticoagulant effects of warfarin without the need for ongoing monitoring and with fewer drug interactions. Such agents are currently being tested in large phase 3 randomized trials. In the meantime, treatment of patients with AF will require continued clinical vigilance using approaches that balance the risks and benefits of the tools available today.

Dr. Courtney is a trainee in the Adult Cardiology Training Program at the University of Toronto.

Dr. Dorian is a Professor of Medicine, Division of Cardiology, St Michael's Hospital and University of Toronto.

References

1. Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation.* 2004;110(9):1042-1046.
2. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med.* 2007;146(12):857-867.
3. Fang MC, Go AS, Chang Y, Borowsky L, Pomernacki NK, Singer DE. Comparison of risk stratification schemes to predict thromboembolism in people with nonvalvular atrial fibrillation. *J Am Coll Cardiol.* 2008;51(8):810-815.
4. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA.* 2001;285(22):2864-2870.
5. Gage BF, van Walraven C, Pearce L, et al. Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin. *Circulation.* 2004;110(16):2287-2292.
6. Mant J, Hobbs FD, Fletcher K, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet.* 2007;370(9586):493-503.
7. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation.* 2006;114(7):e257-e354.
8. Hylek EM, Evans-Molina C, Shea C, Henault LE, Regan S. Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. *Circulation.* 2007;115(21):2689-2696.
9. Canadian Cardiovascular Society Consensus Conference 2004: Atrial Fibrillation. *http://www.ccs.ca/download/consensus_conference/consensus_conference_archives/2004_Atrial_Fib_full.pdf.* Chapter 12. Accessed March 20, 2008.
10. Connolly S, Pogue J, Hart R, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. *Lancet.* 2006;367(9526):1903-1912.
11. Wyse DG, Waldo AL, DiMarco JP, et al; Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med.* 2002;347(23):1825-1833.
12. Hagens VE, Van Gelder IC, Crijns HJ; RAte Control Versus Electrical Cardioversion of Persistent Atrial Fibrillation (RACE) Study Group. The RACE study in perspective of randomized studies on management of persistent atrial fibrillation. *Card Electrophysiol Rev.* 2003;7(2):118-121.
13. Platt AB, Localio AR, Brensinger CM, et al. Risk factors for nonadherence to warfarin: results from the IN-RANGE study. *Pharmacoepidemiol Drug Saf.* Published online: February 13, 2008.

Abstracts of Interest

Can patients at elevated risk of stroke treated with anticoagulants be further risk stratified?

Baruch L, Gage BF, Horrow J, Juul-Möller S, Labovitz A, Persson M, Zabalgoitia M.

BACKGROUND AND PURPOSE: Patients with atrial fibrillation have a varied risk of stroke, depending on age and comorbid conditions. The objective of this study was to assess the predictive value of stroke risk classification schemes and to identify patients with atrial fibrillation who are at substantial risk of stroke despite optimal anticoagulant therapy.

METHODS: Seven recognized classification schemes – the American College of Chest Physicians 2001, American College of Chest Physicians 2004, Stroke Prevention in Atrial Fibrillation (SPAF), Atrial Fibrillation Investigators, Framingham, van Walraven, and CHADS(2) – were compared for their ability to predict ischemic stroke in patients receiving anticoagulant therapy. Data came from the Stroke Prevention using an ORal Thrombin Inhibitor in atrial Fibrillation III and V trials, which compared the efficacy of adjusted-dose warfarin and the direct thrombin inhibitor ximelagatran (36 mg twice daily) in preventing thromboembolic events in 7329 patients with chronic or paroxysmal nonvalvular atrial fibrillation who were at moderate or high risk of ischemic stroke. The main outcome measure was ischemic stroke, as determined by a central event adjudication committee.

RESULTS: During 11 245 patient-years of follow-up, 159 patients had an ischemic stroke (1.4%/year). As indicated by c statistics and hazard ratios, 3 of the classification schemes predicted stroke significantly better than chance: Framingham (c=0.64), CHADS(2) (c=0.65), and SPAF (c=0.61).

CONCLUSIONS: In a large cohort of atrial fibrillation patients at moderate or high risk of ischemic stroke treated with warfarin or ximelagatran, the CHADS(2), SPAF, and Framingham schemes had greater predictive accuracy than chance. This predictive ability may allow clinicians to target high-risk patients for more aggressive intervention.

Stroke. 2007;38(9):2459-2463.

Enhanced cardiovascular morbidity and mortality during rhythm control treatment in persistent atrial fibrillation in hypertensives: data of the RACE study.

Rienstra M, Van Veldhuisen DJ, Crijns HJ, Van Gelder IC; RACE Investigators.

AIM: To investigate the influence of hypertension on morbidity and mortality during rate and rhythm control in patients with persistent atrial fibrillation (AF).

METHODS AND RESULTS: In the RAte Control vs. Electrical cardioversion (RACE) study, 522 patients (256 with hypertension) were randomized to rate or rhythm control. The occurrence of cardiovascular morbidity and mortality was compared between patients with and without hypertension. Patients with hypertension were older (69 ± 8 vs. 67 ± 9 years, P=0.01), more female (P<0.001), had more diabetes (P=0.005), a higher CHADS(2) score (2.2 ± 1.0 vs. 1.0 ± 0.9, P<0.001), and higher systolic and diastolic blood pressures. Septal and posterior wall thicknesses were higher in hypertensives. Complaints related to AF were similar. After a median follow-up of 2.4 (range 0-3.4) years more endpoints occurred in hypertensives (25 vs. 15%). Randomized treatment strategy, i.e. rate or rhythm control, influenced the occurrence of the primary endpoint only in hypertensives. Hypertensives treated with rhythm control experienced most endpoints (incidence rates/100 person-years 13.3 vs. 7.2, relative risk 0.5 [0.3-0.9], P=0.02), mainly thromboembolic complications, adverse effects of antiarrhythmics, and pacemaker implantations.

CONCLUSION: In persistent AF patients with hypertension, a pharmacological rhythm control approach is associated with enhanced cardiovascular morbidity and mortality. Therefore, rate-control strategy should be considered in these patients.

Eur Heart J. 2007;28(6):741-751.

Upcoming meetings

30 April – 2 May 2008
Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke Conference 2008
Baltimore, Maryland
Contact: http://www.americanheart.org/presenter.jhtml?identifier=3049494
E-mail: scientificconferences@heart.org
Telephone: (888) 242-2453 or (214) 570-5935

1 – 3 May 2008
European Society of Cardiology (ESC) EuroPRevent 2008
Paris, France
Contact: ww.escardio.org/

30 August – 3 September 2008
ESC Congress 2008
Munich, Germany
Contact: www.escardio.org/

Disclosure Statement: *Dr. Courtney has no disclosures to announce in association with the contents of this issue.*
Dr. Dorian has received grant funding and consultant fees from AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, and sanofi-aventis.

Change of address notices and requests for subscriptions to *Cardiology Rounds* are to be sent by mail to P.O. Box 310, Station H, Montreal, Quebec H3G 2K8 or by fax to (514) 932-5114 or by e-mail to info@snellmedical.com. Please reference *Cardiology Rounds* in your correspondence. Undeliverable copies are to be sent to the address above. Publications Post #40032303

This publication is made possible by an educational grant from
Merck Frosst Canada Ltd.