Canadian Journal of Cardiology 32 (2016) 278–280

Editorial

Evidence-Based Anticoagulation Decision Making for Atrial Fibrillation—How We Are Doing? (Maybe Not So Well?)

Laurent Macle, MD,[a] and Jason G. Andrade, MD[a,b]

[a] Montreal Heart Institute, Université de Montréal, Montréal, Québec, Canada

[b] Vancouver General Hospital, University of British Columbia, Vancouver, British Columbia, Canada

See article by Angaran et al., pages 336-343 of this issue.

Atrial fibrillation (AF) is the most common sustained arrhythmia seen in clinical practice, affecting approximately 1% of the population. AF is frequently associated with reductions in functional status and health-related quality of life, as well as an increased risk of mortality and stroke.[1-4] Despite advances in treatment strategies, AF-related mortality has remained relatively static. Tellingly, only oral anticoagulation (OAC) therapy has been shown to improve survival.[5,6] As such, the appropriate use of OAC in the prevention of AF-associated thromboembolism is paramount in the management of AF.

Unfortunately, despite strong evidence of clinical benefit, OAC use is limited by nonprescription (~ 50% patients with an indication for treatment do not receive an OAC),[7,8] nonadherence (~ 30% 1-year OAC discontinuation rate),[9] or subtherapeutic drug levels (~ 25%-40% of patients taking warfarin have an international normalized ratio outside the therapeutic range).[10,11] This combination portends an unnecessarily increased risk of stroke, an event that entails high social and economic costs.[12,13] This is especially true in the case of AF-associated strokes, because they are often recurrent and relatively more severe compared with strokes from other causes, resulting in a significantly greater use of resources as well as long-term disability and mortality.[13-15]

However, despite the presence of major national and international society guidelines advocating the importance of objectively assessing stroke and bleeding risk through the use of well-validated risk prediction scores, the decision to initiate OAC therapy remains a relatively personal and subjective assessment of individual risks vs benefits.[16-18] As a result, the real-world implementation of OAC therapy is often skewed by subjective physician interpretation, leading to the risk/treatment paradox, whereby proven efficacious therapy (in this case OAC) is not necessarily more likely to be prescribed to higher-risk patients.[16,19]

It is within this context that Angaran et al. present the results of a practice audit of more than 470 Canadian primary care providers in this issue of the *Canadian Journal of Cardiology*.[20] This large real-world contemporary study of primary care specialists offers an important insight into current practice patterns for patients with AF. Despite a familiarity with the management of AF, these primary care physicians do not seem to use existing stroke and bleeding prediction schemes and do only a modest job at assessing risk.

Specifically, the authors observed a significant disconnect between the physicians' categorized assessments of stroke and bleeding risk (lower [< 3%/y], intermediate [3%-6%/y], and higher [> 6%/y]) and the subsequently derived empirical stroke risk estimate using the $CHADS_2$ (**C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack) and CHA_2DS_2VASc CHA_2DS_2-VASc (**C**ongestive Heart Failure, **H**ypertension, **A**ge [≥ 75 years], **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge [65-74 years], **S**ex [Female] **sc**ore) schema and bleeding risk using the HAS-BLED (**H**ypertension, **A**bnormal Renal/Liver Function, **S**troke, **B**leeding History or Predisposition, **L**abile INR, **E**lderly [> 65 Years], **D**rugs/Alcohol Concomitantly) score (calculated from the data collection forms of each patient). In the case of stroke risk, there was only a 54% agreement between physician-estimated and $CHADS_2$-calculated stroke risk. In 13% of cases, the physician-estimated risk would have resulted in delivery of potentially unnecessary anticoagulation (estimated high risk but low calculated risk), and in 35% the physician-estimated risk would have led to undertreatment (estimated low risk but high calculated risk). More dramatic disparity was observed for bleeding risk in which agreement between the physician estimate and the empirically calculated score was only 31%. In this case, the physicians underestimated the risk of bleeding in 61% of patients and overestimated the risk in 8.0% of patients. However, despite apparent suboptimal stroke risk stratification and concerns about bleeding, the majority of patients were receiving OAC.

Unfortunately these findings are not isolated phenomena. The recently published **O**utcomes **R**egistry for **B**etter **I**nformed **T**reatment of **A**trial **F**ibrillation (ORBIT-AF) study

Received for publication June 16, 2015. Accepted June 21, 2015.

Corresponding author: Dr Jason G. Andrade, Montreal Heart Institute, 5000 Bélanger, Montreal, Québec H1T 1C8, Canada. Tel.: +1-514-376-3330 ×6279; fax: +1-514-593-2581.

E-mail: jason.guy.andrade@umontreal.ca

See page 279 for disclosure information.

http://dx.doi.org/10.1016/j.cjca.2015.06.025

observed a similar under- and overestimation of stroke risk, with disagreement in up to 80% of cases.[16] In this case, the difference was particularly marked for patients at high risk for stroke and bleeding, for whom physicians tended to underestimate risk in both instances. However, similar to the **F**acilitating **Re**view and **Ed**ucation to **O**pti**m**ize Stroke Prevention in **A**trial **F**ibrillation (FREEDOM AF) program, a significant majority of physician-estimated "low-risk" patients were receiving OAC (90% in Freedom AF program and 76% in ORBIT-AF). In the Freedom AF program, the use of OAC in this lower-risk group was disproportionately high, with 56% of patients with a CHA_2DS_2VASc of 0 receiving OAC therapy.

What messages should we take away from this study? First, we should view the results with some degree of caution. As alluded to earlier, the overall rate of OAC was significantly greater than would be expected, with community rates of OAC reported to be in the range of 50%-60%.[21] Although this may be a function of the inclusion criteria (enrolling primary care patients in whom OAC was felt to be warranted), it suggests that the results may not be generalizable. Second, despite the apparent familiarity of this group, there exist opportunities for future knowledge translation with respect to the management of AF and stroke prevention. The discordance between physician estimated risk and empirical risk suggests that the risk schemes are not understood or used appropriately, leading to inaccurate risk stratification with overestimation of stroke risk and overprescription of OAC therapy. Specifically, previous studies indicate that physicians selectively emphasize components of the risk prediction models, attributing greater weight to certain factors such as previous stroke and age in preference to others such as hypertension and diabetes. As a result, for the same empirical $CHADS_2$ score, a physician may subjectively categorize a patient as being at higher or lower risk. Third, the data from this series predate the release and uptake of non−vitamin K antagonist OAC (novel OAC) medications such as apixaban, dabigatran, and rivaroxaban. These novel OACs are currently advocated as the first-line option for OAC therapy in AF and are collectively prescribed more frequently than warfarin for stroke prevention in AF.[18,22] Given the different risk/benefit profiles of these newer medications, it is unknown whether the rate of OAC use would have differed with these agents. Future studies in this area would be enlightening. Finally, the annual rate of stroke to which the current Canadian Cardiovascular Society guidelines attribute a low risk of stroke,[22] and thus suggest that OAC is not justified, is $< 1.0\%$-1.5% and not the $< 3\%$ used in this study. As such, the use of a higher annual event rate would include a proportion of "high-risk" patients in the subjectively "low risk" category. That being said, when the low-risk group was re-examined using the CHA_2DS_2VASc, the use of OAC remained unexpectedly high (59% of CHA_2DS_2VASc of 0 and 76% of CHA_2DS_2VASc of 1 received OAC). It is important to recall that these patients represent a subgroup in which the use of OAC has been previously associated with apparent harm.[6]

This study by Angaran et al. highlights the discordance that exists between empirical risk assessment tools and subjective physician assessments, as well as between the assessment itself and subsequent rates of OAC. The study suggests that the decision to initiate OAC is complex and considers many factors beyond simple risk prediction tools. In other words, the assessment of risk involves an educated, informed, and balanced assessment of individualized risk with a weighting of consequences (permanent neurologic incapacity vs major bleeding events). Given this complexity, the need exists for future knowledge translation activities with respect to the management of AF and stroke prevention, as well as follow-up studies to ensure that these knowledge translation activities are effecting appropriate changes in practice.

Funding Sources

J.G.A. is supported by a Michael Smith Foundation Scholar Award.

Disclosures

The authors have no conflicts of interest to disclose.

References

1. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol 1998;82:2N-9N.

2. Wolf PA, Mitchell JB, Baker CS, Kannel WB, D'Agostino RB. Impact of atrial fibrillation on mortality, stroke, and medical costs. Arch Intern Med 1998;158:229-34.

3. Healey JS, Connolly SJ, Gold MR, et al. ASSERT Investigators. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med 2012;366:120-9.

4. Rietbrock S, Heeley E, Plumb J, van Staa T. Chronic atrial fibrillation: Incidence, prevalence, and prediction of stroke using the Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack (CHADS2) risk stratification scheme. Am Heart J 2008;156:57-64.

5. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007;146:857-67.

6. Singer DE, Chang Y, Fang MC, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. Ann Intern Med 2009;151:297-305.

7. Mohammed MA, Marshall T, Nirantharakumar K, Stevens A, Fitzmaurice D. Patterns of warfarin use in subgroups of patients with atrial fibrillation: a cross-sectional analysis of 430 general practices in the United Kingdom. PLoS One 2013;8:e61979.

8. Buckingham TA, Hatala R. Anticoagulants for atrial fibrillation: why is the treatment rate so low? Clin Cardiol 2002;25:447-54.

9. Gallagher AM, Rietbrock S, Plumb J, van Staa TP. Initiation and persistence of warfarin or aspirin in patients with chronic atrial fibrillation in general practice: do the appropriate patients receive stroke prophylaxis? J Thromb Haemost 2008;6:1500-6.

10. Kalra L, Yu G, Perez I, Lakhani A, Donaldson N. Prospective cohort study to determine if trial efficacy of anticoagulation for stroke prevention in atrial fibrillation translates into clinical effectiveness. BMJ 2000;320:1236-9.

11. Matchar DB, Samsa GP, Cohen SJ, Oddone EZ, Jurgelski AE. Improving the quality of anticoagulation of patients with atrial fibrillation in managed care organizations: results of the managing anticoagulation services trial. Am J Med 2002;113:42-51.

12. Gallagher AM, Setakis E, Plumb JM, Clemens A, van Staa TP. Risks of stroke and mortality associated with suboptimal anticoagulation in atrial fibrillation patients. Thromb Haemost 2011;106:968-77.

13. Winter Y, Wolfram C, Schaeg M, et al. Evaluation of costs and outcome in cardioembolic stroke or TIA. J Neurol 2009;256:954-63.

14. Gladstone DJ, Bui E, Fang J, et al. Potentially preventable strokes in high-risk patients with atrial fibrillation who are not adequately anticoagulated. Stroke 2009;40:235-40.

15. Petty GW, Brown RD Jr, Whisnant JP, et al. Ischemic stroke subtypes : a population-based study of functional outcome, survival, and recurrence. Stroke 2000;31:1062-8.

16. Steinberg BA, Kim S, Thomas L, et al. Lack of concordance between empirical scores and physician assessments of stroke and bleeding risk in atrial fibrillation: results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry. Circulation 2014;129:2005-12.

17. O'Brien EC, Holmes DN, Ansell JE, et al. Physician practices regarding contraindications to oral anticoagulation in atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry. Am Heart J 2014;167:601-609.e1.

18. Cairns JA. Which oral anticoagulant for which atrial fibrillation patient: recent clinical trials and evidence-based choices. Can J Cardiol 2013;29:1165-72.

19. Cullen MW, Kim S, Piccini JP Sr, et al. ORBIT-AF Investigators. Risks and benefits of anticoagulation in atrial fibrillation: insights from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry. Circ Cardiovasc Qual Outcomes 2013;6:461-9.

20. Angaran P, Dorian P, Tan MK, et al. The risk stratification and stroke prevention therapy care gap in Canadian atrial fibrillation patients. Can J Cardiol 2016;32:336-43.

21. Valentinis A, Ivers N, Bhatia S, et al. Atrial fibrillation anticoagulation care in a large urban family medicine practice. Can Fam Physician 2014;60:e173-179.

22. Verma A, Cairns JA, Mitchell LB, et al. Committee CCSAFG. 2014 focused update of the Canadian Cardiovascular Society Guidelines for the management of atrial fibrillation. Can J Cardiol 2014;30:1114-30.