

Atrial Fibrillation and Strokes: New Drugs and a New Attitude

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Approximately 2.3 million Americans have been diagnosed with atrial fibrillation (AF), and this number is projected to double by the year 2050.¹ The prevalence of this arrhythmia increases with age, from 0.1% in those <55 years of age to 9% in people >80 years of age.² Each year 60 000 strokes occur as a result of AF, and these events are more likely to be severely disabling or fatal. The literature suggests that restoring the hearts of these patients to sinus rhythm does appear to lower the risk of thromboembolic events.^{3,4} Many high-quality studies have demonstrated that adjusted-dose warfarin reduces the incidence of stroke by 62%, whereas patients taking aspirin have only a 22% reduction in stroke.⁵ Yet, despite this evidence of stroke reduction, only about half of AF patients are treated with anticoagulation.⁶

So, why are we, as caregivers, often reluctant to place asymptomatic patients with AF patients on antithrombotic agents such as warfarin? The principal problem is the difficulty of maintaining a patient on a therapeutic dosage. Too little anticoagulant is not effective in stroke prevention, and too much anticoagulant produces a high risk for hemorrhage. Achieving the ideal therapeutic level takes experience and can be labor intensive. This opens the door for both a new era in warfarin-monitoring programs, as well as new anticoagulants that have predictable dose responses.

Several issues related to this topic are worth emphasizing. First, should all patients with AF be treated prophylactically to decrease their chance of an embolic event? Certainly the data is convincing that this cardiac rhythm abnormality poses a substantial risk factor for stroke, and many of the patients with this disorder have other risk factors, including older age, diabetes,

hypertension, congestive heart failure, or prior cerebral-vascular accidents.⁷ However, some patients have no other apparent risk factors, or have clear contraindications for antithrombotic therapy. As a group, health-care providers probably undertreat AF. Based on published evidence, our instinct should be to treat almost all patients with an additional risk factor for stroke, unless there is a clear indication against this approach.

Second, do all patients treated for primary prophylaxis against stroke require anticoagulant therapy? Approximately one third of patients with AF do not have other stroke risk factors. In these patients, their <2% annual risk of stroke probably does not outweigh their 2% to 5% annual risk of severe or life-threatening hemorrhaging while receiving anticoagulants. Without extenuating circumstances, these low-risk patients should be treated with antiplatelet agents, such as aspirin. It is currently unknown whether the added benefit of double antiplatelet therapy, such as aspirin plus clopidogrel, outweighs the additional risk of bleeding.

Finally, what does the future hold for anticoagulant therapy in patients with AF? Anticoagulation clinics, home-monitoring devices, and computer algorithms provide easier, and probably safer, management of our patients taking warfarin. Additionally, new generations of anticoagulants, that have predictable dosing, are emerging from clinical trials. Ximelagatran is the first in its class of oral agents that reversibly inhibits thrombin. This drug does not require monitoring of international normalized ratios and has no currently known food or drug interactions. Idraparinux is a synthetic analog of the pentasaccharide sequence in heparin and low-molecular-weight heparin. Administered subcutaneously, it has a 130-hour half-

life, which allows it to be used once per week, and does not require monitoring. Today, the safety of these new agents is promising, and by reducing the need for monitoring, they may help overcome physicians' reluctance to use these drugs in clinical practice. On the other hand, we do not know the impact of reducing the frequency of contact with healthcare providers, which provides opportunities for patient education. This can only be answered with longer clinical trials.

In this supplement to *The American Journal of Managed Care*, 4 articles on AF provide readers with a comprehensive review of the epidemiology, management, pharmacoeconomics, and new therapies for the care of patients with serious arrhythmia.

The first paper, by Khalid Abusaada, MD, and colleagues, provides the epidemiologic background and treatment of AF. The authors discuss the critical aspects of the disease that physicians need to consider while evaluating a new patient with AF.

The second paper, by Alan S. Go, MD, addresses the concept of stratifying patients with stroke risk who also have AF. Citing well-controlled clinical trials and national, consensus-derived guidelines, Dr Go reviews the key studies that demonstrate the benefit of adjusted-dose warfarin in reducing the incidence of stroke in high-risk patients with AF.

The next paper, authored by Cheryl D. Bushnell, MD, MHS, and David B. Matchar, MD, discusses the pharmacoeconomic impact

of AF and stroke prevention. After highlighting the risk of stroke with AF, these authors discuss the cost-effectiveness of adjusted-dose warfarin therapy.

The final paper, written by Martin O'Donnell, MB, and Jeffrey I. Weitz, MD, provides readers with the latest pharmacologic drugs currently being studied for the prevention of stroke in patients with AF. Novel therapies and approaches are also discussed.

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