



Foreword: contemporary issues in the management and treatment of atrial fibrillation

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This supplement represents the first publication of Thrombosis Quorum (TQ), a recently established international consortium of multidisciplinary thrombosis-related specialists dedicated to raising the priority of thrombosis. TQ aims to address the unmet clinical needs in the prevention and treatment of thromboembolic conditions, and promote the optimum management of patients with or at risk of these disorders by providing a cross-disciplinary forum for information exchange and debate. This publication incorporates a collection of state-of-the-art articles written by the TQ Steering Group and co-authors, and in this instance, focuses on the management and treatment of patients with atrial fibrillation (AF).

AF is the strongest independent predictor for stroke, the leading cause of disability, and the second leading cause of death worldwide. As such, AF has become accepted as a common and rapidly growing clinical problem and disease entity, as highlighted in the first article of this series by Bernard Gersh and coworkers who describe AF as a 'growing epidemic' and 'an enormous public-health burden'. Although AF is primarily a disease of the elderly, the authors suggest that in most patients, the development of AF may be the consequence of a systemic condition of reduced vascular compliance, atherosclerosis, obesity and the metabolic syndrome, and inflammation. Thus, together with studies aimed at defining the structural and electrical phenotypes and molecular genetics of AF, ongoing research into some of the most clinically relevant areas of cardiovascular disease may provide additional insights into the cause and pathology of AF.

AF-related stroke is largely preventable by the implementation of oral anticoagulant therapy according to evidence-based treatment guidelines, as emphasized in the second article by Philip Bath and coworkers.

Anticoagulation with dose-adjusted vitamin K antagonists (VKAs), such as warfarin, (at the recommended international normalized ratio of 2.5; range 2.0–3.0) is the treatment of choice for preventing stroke and systemic cardioembolism. AF patients at low risk for stroke may benefit from aspirin. This paper provides a contemporary review of antithrombotic treatments for the primary and secondary prevention of stroke and its acute treatment in patients with AF.

The treatment theme is continued in the following article by Martin O'Donnell and coworkers who provide a clinical perspective into the potential role of emerging and innovative pharmacological and non-pharmacological therapies for stroke prevention in AF. These include dual antiplatelet therapy, novel anticoagulants such as oral direct thrombin inhibitors (e.g. ximelagatran) and Factor Xa inhibitors (e.g. idraparinux), the role of lowering blood pressure and lipids, local delivery of nitric oxide, catheter ablation techniques, and excision of the left atrial appendage.

At present, however, and although they have been in use for almost 60 years, the VKAs (e.g. warfarin, acenocoumarol, and phenindione) remain the only oral anticoagulants currently available. Indeed, current evidence-based guidelines, as reviewed by Joseph Emmerich and coworkers, recommend rate control with long-term anticoagulation for most patients with newly detected AF. However, despite the evidence that VKAs are highly effective at reducing the risk of stroke, only a small proportion of patients with AF whom best-practice guidelines identify as eligible for oral anticoagulant therapy actually receive it. VKAs have considerable pharmacological and practical drawbacks: they are difficult to administer because they have a narrow therapeutic window and their activity is influenced by dietary vitamin K intake and by a multitude of commonly used drugs. Hence, regular monitoring of coagulation and dose adjustment are required to maintain an effective

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level of anticoagulation and to avoid serious bleeding during VKA therapy.

Further, the VKAs are widely perceived to be associated with an unacceptable risk of intracranial haemorrhage. The fear of bleeding is a major consideration when implementing anticoagulation therapy, as the risk of bleeding may be higher than the risk of stroke for some patients, which may explain why some physicians do not perceive the guidelines to be fully justified in clinical practice. Sam Schulman and Rebecca Beyth review the epidemiology and risk factors for bleeding complications with VKAs in patients with AF and the applicability of bleeding rates obtained in clinical trials to clinical practice. Effective corrective treatment of excessive anticoagulation and bleeding episodes, which are crucial for the outcome and different modalities, are also discussed.

Finally, Paul Miller and coworkers summarize the key components of health economic evaluations of antithrombotic treatments for stroke prevention in patients with AF. Of the key components of economic analyses of antithrombotic therapies for stroke prevention, the avoidance of stroke is likely to have the greatest impact on costs and quality of life. Thus, health economic decision-making must balance these gains against the cost of the drug and the management

of VKA therapy. The authors suggest that the substantial socioeconomic burden of stroke can be reduced by ensuring that patients with AF receive appropriate anticoagulant therapy and that effective and/or improved antithrombotic treatment strategies are likely to reduce the burden of stroke, as well as bleeding complications.

In summary, therefore, this series of articles authored by eminent experts in the field of thrombosis, reflects an up-to-date review of antithrombotic therapy for the prevention of stroke in patients with AF. Considering the complexities surrounding prescribing oral anticoagulation in patients with AF, new strategies with a superior benefit:risk ratio to current treatment modalities are required in the armamentarium for the prevention of thromboembolic events in patients with AF.

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