Atrial fibrillation (AF) is the most common sustained arrhythmia in humans and affects 1–2% of the general population worldwide. It affects 3 and 6 million people in the United States and Europe, respectively. Its incidence rises with age and the lifetime risk of AF development in those older than 40 years has been estimated to be approximately 25%. On the other hand, AF also affects a significant proportion of younger patients, with a prevalence of 0.7% in those aged between 55 and 59 years. These data were derived from population-based studies conducted in Western countries and the epidemiology picture in the Asia–Pacific region, which constitutes more than 50% of the global population, is less well studied. It has been estimated that the age-standardized prevalence of AF is 0.65% in China, and ranges from 0.7% to 1.5% in other Asian countries, which is slightly lower than that of Western countries. It is also expected that these figures will increase 2.5–3-fold during the next 50 years. AF doubles the risk of death and increases the risk of stroke by 5-fold. Although it commonly coexists with other cardiovascular disorders, it also adversely affects the prognosis of those with coronary artery disease, heart failure, or even hypertension.

Management of AF is a complex issue. The last published guidelines for management of AF by the ACC/AHA/ESC were released in 2006. However, the adoption of those management guidelines into clinical practice was a real challenge and was limited by cultural, social and economic factors. Both patients and physicians may frequently ask the same question when facing AF: Is it better to be in sinus rhythm? The debate between rhythm and rate control has lasted for decades and lead to multiple randomized clinical trials testing the hypothesis that rhythm control is superior to rate control, as some cardiologists and electrophysiologists deeply believe, in achieving better clinical outcomes.

What has been consistently observed in these clinical trials is that both strategies are equivalent if cardiovascular events, such as death or stroke, are chosen as the primary endpoints in patients at risk of stroke and with or without heart failure, provided appropriate antithrombotic therapy is offered to eligible patients. In other words, proper anticoagulation, instead of deciding on a rate or rhythm control strategy, is probably the key to lower cardiovascular events in these patients. The clinical implications of these findings are now translated into and emphasized in the latest management guidelines for AF published by the European Society of Cardiology this year. The guidelines clearly state that the 2 strategies are not mutually exclusive. The focus of AF management nowadays should shift from a focus on the rate or rhythm control decision to a comprehensive treatment plan for an individual; that is, don’t just look at the ECG but the whole patient!

Evaluation of the thromboembolic risk in AF patients has become the top priority in the management algorithm, irrespective if at the acute stage or as a long-term objective. The most widely adopted assessment tool has been the CHADS score. It has been very useful in the primary care setting because it can be easily remembered by physicians and does not require any sophisticated investigations. Patients classified as high risk for thromboembolism (ie, CHADS score ≥2) should receive anticoagulation, whereas those at low or intermediate risk can receive either antiplatelet or oral anti-coagulation (OAC) therapy. However, in a recent analysis of these schemes for assessing stroke risk, a substantial proportion of patients (>60%) were classified as intermediate risk and then a difficult decision about the ideal thromboprophylaxis will be encountered. In addition, female patients with a borderline age (eg, 65–74 years) and no other risk factor are, in fact, not truly at low risk, even though the CHADS score is still zero. To address this issue, a new assessment tool has been introduced in the new guidelines, namely, the CHA2DS2-VASc score, which takes into account several important predictors of stroke in patients with non-valvular AF, such as age 65–74 years, female sex and coexisting vascular heart disease. It should not be considered as a brand new scheme, but rather a refined version. OAC is still recommended for those with CHADS score ≥2, but a detailed assessment with regards to the non-major but relevant risk factors is necessary for those with CHADS score 0 or 1. OAC is preferred for those with CHA2DS2-VASc score of 1, but no antithrombotic therapy is recommended for CHA2DS2-VASc score of 0. The new guidelines also stress the importance of bleeding risk assessment with the HAS-BLED scheme. Caution should be taken when prescribing OAC to those with a HAS-BLED score ≥3.

Can we simply apply this new scheme to the whole world, including Asia-Pacific region? The answer is uncertain. There are major differences in stroke types among white and
non-white ethnic groups. For example, hemorrhagic stroke is more prevalent in Asians, whereas stroke attributable to AF is more likely in whites than in non-whites. In a recent retrospective analysis, a significantly lower rate of stroke with warfarin therapy among non-whites with AF was not observed. Moreover, the acceptance of warfarin among Asians is also very low. In a nationwide study, less than 23% of Taiwanese with AF and high thromboembolic risk received warfarin. The role of the novel oral direct thrombin inhibitor, which was recently approved by the Food and Drug Administration (FDA) for stroke prevention in AF, in improving compliance by obviating the need for strict dietary requirements and frequent blood monitoring when compared with vitamin-K-dependent OAC, is still not certain and has not been clearly addressed in the new guidelines. Safety issues, including the lack of an antidote, management of hemorrhage, optimal dosage for an individual and long-term side-effects, with this new drug remain unanswered, but it seems to be a promising alternative to warfarin, based on the data from the RELY study. The exact number of Asian participants in RELY was unclear, and further studies with this new drug or other upcoming oral factor Xa inhibitors in this region of the world are deemed necessary because the stroke pattern, potential benefit and the associated bleeding risk is not entirely certain.

The role of another new drug, dronedarone, is much more clearly defined in the new guidelines. It has been approved as a first line therapy in AF patients with or without structural heart disease. In addition, it is the first antiarrhythmic agent approved by the FDA with the indication of reducing the risk of cardiovascular hospitalization among patients with non-permanent AF, as demonstrated by the ATHENA study. The most interesting finding from ATHENA is, perhaps, that in the post hoc analysis the benefit of the new drug was not limited to only those who converted to sinus rhythm, which may further support the notion that the rate or rhythm strategy debate is probably not the key to favorable cardiovascular outcomes in selected AF patients. However, the new drug should not be considered as a true substitute for amiodarone, particularly in patients with severe heart failure (New York Heart Association class III or IV), as it was associated with worsening of heart failure in the ANDROMEDA study. Although its efficacy in maintaining sinus rhythm might be lower than that of amiodarone, the favorable side-effect profile will certainly make dronedarone the drug of choice in those with left ventricular hypertrophy, coronary artery disease and mild heart failure, as stated in the new guidelines. Data are lacking, however, about the efficacy of this new drug to prevent AF recurrence when comparing it with flecainide or propafenone in those with no evidence of structural heart disease. Post-marketing surveillance about the safety of any new drug is absolutely necessary to avoid or allow early detection of unforeseen risk.

Apart from the effect on mortality and morbidity, AF also exerts deleterious effect on quality of life, which sometimes may be recognized only after restoration of sinus rhythm. Catheter ablation for AF was first stated in the 2006 guidelines as a second-line therapy in those with drug-resistant AF. In a meta-analysis, a relative risk reduction of 65% for AF recurrence was noted in patients randomized to catheter ablation when compared with those continuing with antiarrhythmic drugs, and improvement in quality of life was clearly observed after ablation. In the latest guidelines, catheter ablation can be considered as an initial therapy in symptomatic patients with paroxysmal AF and minimal or no heart disease. This recommendation deserves special attention. The procedure itself is technically demanding and operator experience does affect the treatment outcome and, even more importantly, procedural safety. The associated mortality is approximately 0.1% and serious complications, such as stroke and cardiac perforation, can be up to 1–2%. Recurrence of AF is not uncommon after a single procedure and up to 20–30% of patients with paroxysmal AF may require second or even multiple procedures to achieve maintenance of sinus rhythm. The escalated recommendation should be restricted to high-volume centers with extensive experience in performing the procedures, and certainly an objective competency assessment is required before adopting this as the first-line therapy. The proper role of catheter ablation for AF will better be defined after the CABANA trial (NCT 00578617).

Prevention of AF has been proposed as a research strategy in future studies. In the latest guidelines, “upstream” therapy for AF prevention has been emphasized and there is some evidence to suggest that early rhythm control for new-onset AF may be of value in preventing progression of the disease. It is reasonable to use angiotensin-converting enzyme inhibitors or equivalent to prevent AF in patients with a low ejection fraction or hypertension, as stated in the guidelines as a class IIa recommendation. What has not been addressed in the new guidelines is the management of AF in patients with implantable devices. Pacemakers, implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy (CRT) would undoubtedly enhance the detection of asymptomatic AF, which also carries prognostic implications. On the other hand, the occurrence of AF may render CRT less effective and also lead to an increased risk of inappropriate shock in ICD recipients. Choice of pacing mode or site may also have an effect on the prevention of AF recurrence in patients with a pacing indication as well. A clear guideline that sums up all the available evidence is essential, particularly with the increasing number of devices being implanted in recent years.

How should we deal with the new guidelines for AF management? There is always a significant gap between management guidelines and real-world clinical practice. The decision to adopt the guidelines should be individualized and perhaps may vary markedly in different parts of the world. Despite the fact that the Asia-Pacific region constitutes more than half of the world’s population and 80% of the cardiovascular disease burden is noted in developing countries, most of the participants in clinical trials are still restricted to either the United States or Europe. Globalization of clinical trial recruitment for AF management is urgently needed and the results from the ATHENA and RELY studies were encouraging in this respect. Lastly, we have to thank the members of the task force for summarizing the up-to-date clinical evidence into this enlightening guideline and for redirecting us away from the narrow-minded trap of the rate or rhythm strategy debate for AF management.

References
FUNG JWH et al.
