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Review

Atrial fibrillation management in Asia: From the Asian expert forum on atrial fibrillation

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ABSTRACT

Atrial fibrillation (AF), the most common sustained cardiac arrhythmia, is associated with increased morbidity and mortality. AF has a slightly lower incidence and prevalence in Asian populations than in Western populations, but the associated relative risk of stroke and mortality is similar. Patients with AF in Asia have similar disease profiles and $CHADS_2$ score distributions compared to those in the West, with the exception of a slightly higher prevalence of valvular heart diseases in Asia. Acute ventricular rate control should be the initial consideration in patients with AF and rapid ventricular rate. Anti-arrhythmic drugs have only a modest long-term effect on maintenance of sinus rhythm, and clinical trials in both the West and the East show that chronic rhythm control is not superior to chronic rate control in terms of cardiovascular outcomes, most likely because the benefit of anti-arrhythmic drugs in these trials was often offset by proarrhythmic effects. ECG-driven trials for AF should be replaced by outcome-driven ones. ATHENA is the largest outcome trial to confirm the superiority of a new anti-arrhythmic drug in improving cardiovascular outcomes. The choice of anti-arrhythmic drugs for AF should be based on both safety and efficacy in improving cardiovascular outcomes. For long-term rate control, a lenient strategy with a ventricular rate of less than 110 bpm may be adequate, but more strict rate control may be required if patients continue to complain of symptoms. Catheter ablation should be reserved for patients who remain symptomatic despite optimal medical therapy.

1. Introduction

1.1. Definition and detection of atrial fibrillation

1.1.1. Defining atrial fibrillation

Atrial fibrillation (AF) is a cardiac arrhythmia with the following characteristics [1]:

1. The surface electrocardiogram (ECG) shows irregular RR intervals (i.e. RR intervals that do not follow a repetitive pattern).
2. The surface ECG shows no distinct P waves. (Some apparently regular atrial electrical activity may be seen in some ECG leads, most often in lead V1.)
3. The atrial cycle length (i.e. the interval between two atrial activations) is usually variable and less than 300 beats per minute (bpm).

The ventricular response depends on the electrophysiological properties of the atroventricular (AV) node and other conducting tissues, vagal and sympathetic tone, the presence or absence of accessory pathways, and the action of drugs. When AV block or ventricular or AV junctional tachycardia is present, cardiac cycles may be regular. In patients with pacemakers, diagnosis of AF may require pacemaker inhibition in order to expose fibrillatory activity. Irregular, sustained, wide-QRS-complex tachycardia suggests either AF conduction over an accessory pathway or AF with bundle branch block. Atrial flutter is usually readily distinguished from AF. Extremely rapid rates (i.e. greater than 200 bpm) suggest an accessory pathway or ventricular tachycardia [2].

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1.2. Types of atrial fibrillation

There are five types of AF, which vary in the presentation and duration of the arrhythmia [1].

1. *First diagnosed AF* is what every patient who presents with AF for the first time is considered to have, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms.
2. *Paroxysmal AF* self-terminates, usually within 48 h. Although AF paroxysms may continue for up to 7 days, the 48-hour time point is clinically important because after that point, the likelihood of spontaneous conversion is low and anticoagulation must be considered.
3. *Persistent AF* is present when an AF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion.
4. *Long-standing persistent AF* is AF that lasted for *at least* 1 year before a rhythm control strategy was adopted.
5. *Permanent AF* is said to exist when the presence of the arrhythmia is accepted by the patient (and physician). By definition, rhythm control interventions are not pursued in patients with permanent AF. Should a rhythm control strategy be adopted, the arrhythmia is re-designated as "long-standing persistent AF".

1.3. Detection of atrial fibrillation

Detection during the arrhythmia episode can be achieved with a 12-lead ECG, by Holter monitoring, by telemetry recording, or with an event recorder. Patients at risk for AF are encouraged to feel their pulse when they experience palpitations. If the pulse feels rapid and irregular, they should have the irregularity confirmed either with a 12-lead ECG, a Holter or an external event recorder.

Patients with known AF should have at least a 12-lead ECG performed at each clinic visit, the objective being to evaluate the efficacy of treatment strategies. For patients being treated with rhythm management, the ECG serves to confirm treatment efficacy and monitor the QT duration for proarrhythmia effects of the antiarrhythmic agents. For patients being treated with a rate control strategy, a 24-hour Holter can be used to confirm adequate rate control.

2. Epidemiology of atrial fibrillation

2.1. Incidence and prevalence of atrial fibrillation

AF is the most common sustained tachyarrhythmia in clinical practice. Between 1980 and 2000, the incidence of AF in the United States increased from 3.04 per 1000 person-years to 3.68 per 1000 person-years [3]. The incidence of AF is lower in Asian populations. In a community-based prospective cohort of 3560 participants in Taiwan, the incidence of AF was 1.68 per 1000 person-years for men and 0.76 per 1000 person-years for women [4].

AF becomes more prevalent with age, affecting less than 0.5% of patients aged 40–50 years, but between 5 and 15% of patients aged 80 years [1]. The lifetime risk of developing AF is 1 in 4 for men aged 40 years and older [5]. Although the prevalence is higher in men, the overall number of men and women with AF is about the same, given women's greater longevity [6].

AF is estimated to affect 1% of the overall population [6] but there is good reason to believe that its prevalence may be considerably higher. Lack of awareness of the condition among the public may prevent patients from seeking medical attention. Even if patients do have symptoms, diagnosis may be thwarted by the limited availability of 12-lead ECGs, which are needed to make a definitive diagnosis of AF, and the paroxysmal nature of the condition in many patients. For these reasons, the true prevalence of AF is thought to be as high as 2% [7,8].

Some data indicate that the prevalence of AF in Asian populations is roughly 70% that of Caucasian populations: 1.6% in Japan [9], 0.7% in Korea [10], 1.5% in Singapore [11], 0.7% in China [12], and 1.1% in Taiwan [4]. A recent report estimated that 8 million patients in China have AF [13]. As the population ages and the prevalence of hypertension, metabolic syndrome, and diabetes rises [14,15] the prevalence rate of AF in Asia is expected to increase [16,17].

2.2. Co-morbidities and Other Conditions Associated with Atrial Fibrillation

It was once thought that, unlike their counterparts in clinical trials, AF patients seen in daily clinical practice are free from complex co-morbid diseases. However, recent evidence has called this into question. In surveys such as RECORD AF and RealiseAF, AF patients treated in routine clinical practice had similar comorbidities as those in clinical trials [18,19].

Patients with AF in the Asia Pacific region have disease profiles similar to those of patients in the rest of the world. Although valvular heart disease is more common in the Asia Pacific region than in the West, rates of valvular heart disease in the RealiseAF registry (which included 10,523 AF patients worldwide) were not vastly different: 38.8% of the 742 patients from Taiwan had valvular heart diseases versus 26.7% of patients in the total cohort [19]. Rates of hypertension (which, in most surveys, cohorts, and clinical trials, ranks as the most common co-morbid disease in patients with AF; see Fig. 1) were also comparable: in the RealiseAF registry, 72% of the total population and 73% of the Taiwanese population had hypertension. Taiwanese patients also had rates of heart failure, coronary artery disease, and diabetes that were comparable to the total population (46%, 32%, and 21%, respectively, in the total cohort, and 41%, 35% and 27%, respectively, in the Taiwan subset; see Figs. 2–4). Interestingly, chronic obstructive pulmonary disease was found in just 10% of the total RealiseAF population but in 17% of the Taiwan subset.

Other reports from Asian countries have noted similar high prevalences of co-morbid diseases [13,20]. This is reflected in a mean $CHADS_2$ score of 2.2 in the Taiwan subset of the RealiseAF survey and 1.9 in the total population. These data suggest that AF patients are more complex than was once thought, both in the Asia Pacific region and in the rest of the world. In fact, AF patients with no co-morbid cardiovascular disease (patients with "lone" AF) are becoming uncommon (Fig. 5). In the RealiseAF survey, just 5% in the total population and 3% in the Taiwanese population had lone AF.

Identifying co-morbid conditions, such as hypertension, heart failure, and diabetes, is essential in the care of patients with AF. The patient's prognosis, their risk of stroke, the risk of hemorrhage with the use of anticoagulation therapy, and the choice of antiarrhythmic drugs can all be affected by the presence of co-morbid conditions.

2.3. Prognosis of atrial fibrillation

Reports from the Western world indicated that patients with AF have a 2-fold higher risk of mortality, 3-fold higher risk of hospitalization, and 5-fold higher risk of stroke compared to matched controls [21–23]. This holds true in the Asia Pacific region. The relative risk of mortality for patients with AF was found to be 1.88 in Japan [24] and 2.23 in Taiwan [4]. The relative risk of stroke was found to be 2.78 in China [12], 3.60 in Singapore [11], 3.7 in Japanese men [25], and 3.87 in Taiwan [4].

The annual risk of ischemic stroke in patients with nonvalvular AF is 5%, which is 2 to 7 times higher than that of the general population [2]. If transient ischemic attacks and clinically silent strokes detected on brain imaging are also considered, the rate of brain ischemia accompanying nonvalvular AF may be greater than 7% [26]. Things