



Management of atrial fibrillation in Chinese patients

Ma Changsheng^{a,*}, Qi Wenhong^b

^a Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China

^b Department of Cardiology, Ruijin Hospital, Shanghai Jiaotong University, Shanghai 200025, China

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Summary Atrial fibrillation (AF) has been labeled as “epidemic” only in recent years. A population-based study in China revealed that 0.8% of Chinese are currently afflicted by AF with an absolute number of over 10 million. The latest population census revealed that older people (>60 years) account for 11% of the general population and they are expected to surpass 400 million by 2045. The prevalence of AF is driven up with the expansion of the elderly population, and the estimated number of AF patients in China is projected to surpass 25 million by 2045. AF has long been deemed a non-fatal disease, as reflected by an underemphasis on stroke prevention and rate control in China. Limitations of treatment with antiarrhythmic drugs stimulated the development of catheter ablation therapy. Chinese physicians started to treat AF by catheter ablation in 1998, and recently, 3-D mapping system guided ablation has gained in popularity. According to the China AF Ablation Registry, 5626 patients have received AF ablation up to 2006. From the latest experience, ablation renders a cumulative success rate of 70–80%. However, the long-term efficacy of this treating modality in the Chinese remains to be defined. With improvement in education and knowledge of AF disease, medication-based management, including anticoagulation and rate control, is also enhanced.

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AF has been labeled as “epidemic” only in recent years. According to the Framingham Heart Study, AF affects 1.0% of the general population [1]. A population-based study in China revealed that 0.8% of Chinese are currently afflicted by AF,

with an absolute number over 10 million [2]. The epidemiology of AF has undergone significant changes during the past decades, as reported by a recent community-based study. The prevalence of AF doubled in 2000 compared with 1980; therefore following this trend, the prevalence of AF will likely be tripled by 2050 [3]. AF is strongly associated with age [4], and its prevalence is increased by the expansion of the elderly in the population

* Corresponding author. Tel.: +86 10 64456412; fax: +86 10 64456078.

E-mail address: chshma@vip.sina.com (C. Ma).

[2,5] (Table 1). Based on the Chinese Population Census, the elderly (>60 years old) currently account for 11% of the general population with an absolute number of 144 million, and this figure will keep climbing and is expected to surpass 400 million by 2045 (Fig. 1). Even assuming no further increase in the incidence of AF, the estimated number of AF patients in China is about to surpass 25 million.

In the Framingham study, age, diabetes, hypertension, myocardial infarction, heart failure, and valvular disease were significantly associated with the risk of developing AF [1]. A study in China revealed the same predisposing factors for AF [2]. In the 1960s and 1970s, the leading risk factor for AF was hypertension among males and rheumatic fever among females. However, with a significant improvement in the living conditions in China, rheumatic heart disease has been on a steep decline during the past 2 decades, while hypertension, with its very high prevalence in Chinese, has emerged as the single most important risk factor for AF after age adjustment [2]. This was corroborated by a recent study among hospitalized patients, which found aging, hypertension, coronary artery disease, and heart failure as the four most common conditions associated with AF among both male and female patients (Fig. 2), and rheumatic heart disease is no longer a disease commonly encountered in clinical settings [5].

AF therapy has experienced significant changes during the past decade. The initial decision on AF management involves rate control, rhythm control, and prevention of thromboembolism. To understand how Chinese physicians manage patients with AF in clinical practice, a retrospective study by Qi et al. [5] involving 41 major hospitals was conducted throughout the country from 1991 to 2001. Analysis included 9297 patients hospitalized for AF (7.9% of total cardiology admission). Permanent AF accounted for 49.5% of all enrolled patients, of which paroxysmal and persistent AF were 33.7% and 16.7%, respectively. Rhythm control (56.4%) was mainly used for patients with paroxysmal AF, while rate control was preferred for the majority (82.8%) of patients with chronic AF. Cardioversion had been attempted in less than 50% of patients with persistent AF, but only 31.1% of these patients remained in stable sinus rhythm thereafter. This study also demonstrated how these therapeutic strategies were carried out. The most common agent chosen for rhythm control was Amiodarone, followed by Propafenone and Sotalol. Digitalis (digoxin) was the primary choice when rate control was considered, while beta blockers and calcium channel blockers were second line choices. In those

enrolled patients, 64.5% received antithrombotic therapy, but long-term prevention with anticoagulation was documented in only 6.6% of patients.

One of the deleterious consequences of AF is ischemic stroke. A study of 80,000 permanent residents in Beijing found a prevalence of stroke of 1.0% in the general population (unpublished study by Dr. Zhao Dong from our institution), which is consistent with several review studies [6]. In a previous study, which included 520 patients with non-valvular AF, and an age range from 40 to 102 years, after a mean of 6.45 ± 4.03 years follow up, the annual incidence of stroke was 5.3%, which was significantly higher than that in the general population [7] (Fig. 3). The prevalence of stroke was even higher in patients hospitalized for AF, reaching 17.5% or 24.81% as demonstrated by 2 recent hospital-based studies [5,8].

While AF has long been deemed a non-fatal disease, its hazards are not fully appreciated. This was mirrored by the low use of warfarin for stroke prevention. In the hospital-based study in Chinese patients described earlier, warfarin was used in only 6.6% of all enrolled patients [5]. In practice, warfarin was used in less than 3% of Chinese patients with AF and for those taking warfarin, less than half had their INR (International Normalized Ratio) routinely monitored [2]. Because those studies described only the epidemiologic profile, whether the low use of warfarin is due to socioeconomic reasons or low CHADS₂ (Cardiac Failure, Hypertension, Age, Diabetes, Stroke [Doubled]) scores remains to be clarified. We conducted a survey among Chinese physicians during the Fourth China Atrial Fibrillation Symposium (4th CAFS) in 2006 to explore the medical reasons for a low use of warfarin, and we found that approximately one out of every two colleagues is unwilling to prescribe warfarin to AF patients older than 70 years for fear of bleeding even in the presence of other risk factors for stroke. When the dosage is properly titrated, warfarin provides protection against thromboembolic events. Even for elderly patients (>75 years), the Birmingham Atrial Fibrillation Treatment of the Aged Study (BAFTA) supported the use of warfarin [9]. However, a recent study by Hylek et al. [10] found age ≥ 80 (13.08% versus 4.75%) and INR >4.0 were associated with increased bleeding risk. Similar findings were also observed by Poli et al. [11], and they found a trend to a progressive increase in the bleeding risk with the increase of the CHADS₂ score in elderly people. Both studies were not designed to address whether bleeding risk outweighed benefits. Therefore, anticoagulation therapy among elderly people remains a challenge warranting further investigations.

Warfarin has been widely accepted as the cornerstone treatment for patient with AF. Even in non-selected individuals with AF, one Chinese study found warfarin worked to decrease the risk of ischemic stroke by 62% when compared with aspirin [12]. The recommended INR intensity in AF guidelines was mainly based on clinical trials from western studies. To obtain the optimal anticoagulation intensity for Chinese patients, a retrospective study was conducted in 435 patients from 10 medical centers and 6 community hospitals. Medical records were reviewed in all patients. Investigators found that an INR <1.5 was associated with increased thromboembolic events, while INR >3.0 was the sole independent risk factor for bleeding events. They suggested an optimal intensity of INR between 1.5 and 3.0 for Chinese patients [13]. A recent study by Shen et al. [14] was designed to study racial differences in the risk for intracranial hemorrhage among patients with AF taking warfarin. They found Nonwhites (Blacks, Hispanics, and Asians) with AF were at greater risk for warfarin-related intracranial hemorrhage. A recent Japanese study also supported the hypothesis that Asians are more vulnerable to bleeding due to warfarin. They also found the incidence of major

bleeding and intracranial hemorrhages among Japanese NVAF patients receiving low-dose warfarin was 2.38% and 0.60% per patient-year, respectively, which is higher than that in western patients [15]. Although we have very limited data on Chinese, the maximal tolerated dosage of warfarin is likely to be lower for Chinese patients.

AAD (antiarrhythmic drugs) have long been held as a mainstay for managing AF in China. As our survey revealed during the 4th CAFS, more than half of Chinese physicians consider AAD as effective options for maintaining sinus rhythm, and AAD tend to be prescribed as the initial therapy for >65% of AF patients. The potential deleterious effects of AAD may be underestimated. Indeed, AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management), RACE (the RATE Control versus Electrical cardioversion for persistent atrial fibrillation), and STAF (the Strategies of Treatment of Atrial Fibrillation) failed to show any difference between rate and rhythm control. At least, antiarrhythmic drugs were not found to be superior to rate control agents with regards to survival in patients with AF.

Limitations of AAD prompted the development of catheter ablation therapy. Different from AAD therapy, catheter ablation offers the chance of a lasting cure. Chinese physicians started to treat AF by focal ablation in the region of the pulmonary valve (PV) in 1998 [16]. However, they were frustrated with the initial explorations because of very limited efficacy and significant complications from this procedure. Shortly thereafter, focal ablation retreated from clinical practice, and was replaced

Table 1 Age-adjusted incidence of AF in Chinese

Age	Male (%)	Female (%)	Total (%)
30–39	0	0	0
40–49	0.3	0.2	0.2
50–59	0.5	0.6	0.5
60–69	1.4	1.1	1.3
70–79	3.6	2.6	3.1
80–89	7.5	7.4	7.5
Total	0.9	0.7	0.8

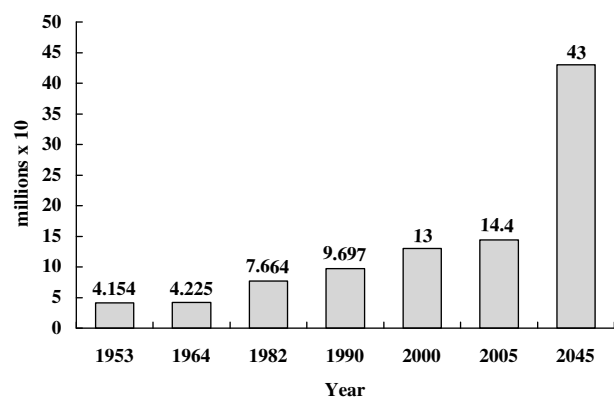


Figure 1 Expansion of the elderly (>60 years) in the population of China Ministry of Civil Affairs of the People’s Republic of China: <http://www.mca.gov.cn>.

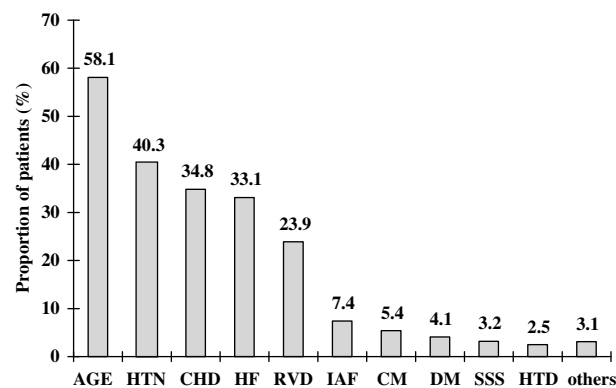


Figure 2 Diseases associated with AF among Chinese patients HTN: hypertension; CHD: coronary heart disease; HF: heart failure; RVD: rheumatic valvular disease; IAF: idiopathic atrial fibrillation; CM: cardiomyopathy; DM: diabetes mellitus; SSS: sick sinus syndrome; HTD: hyperthyroidism. (Wenhong Qi. Retrospective investigation of hospitalized patients with atrial fibrillation in mainland China [5].

by segmental PV ablation. Recently, a 3-D mapping system guided approach has gained in popularity, and clinical efficacy has markedly increased with reduced radiation exposure and complications. Until June 2007, 80 labs across the country have been equipped with 3-D mapping systems, most of them about to be operative for AF ablation. According to the China AF Ablation Registry, 5626 patients received AF ablation until 2006; 2430 were ablated solely in 2006. The mean age of those registered patients is 54.8 years. Paroxysmal AF, chronic AF, and permanent AF accounts for 85.67%, 11.51% and 2.82% of all registered patients, respectively. Of those patients, 45.93% had at least one type of structural heart disease, and a mean left ventricular ejection fraction of 59%. The average success rate varies with the ablation techniques applied during different years. From the latest experience, the cumulative success rate is approaching 70–80% [17,18]. However, most of the published results were from non randomized studies, based on symptomatic, short-term follow up. Whether ablation is superior to antiarrhythmic agents, or sinus rhythm can be maintained after ablation, or maintenance of sinus rhythm can be translated into a reduction in thromboembolic events including death needs to be determined. To address these issues, a prospective, multi-center case-control study has been initiated. Its aim is to answer whether catheter ablation should be considered as frontline therapy for Chinese patients.

AF continues to be a difficult condition to treat. With the expansion of the elderly in the population of China, AF will emerge as a predominant disease in cardiology. To meet the challenges, the Chinese Heart Rhythm Society (CHRS) has worked with the Chinese Society of Pacing and Electrophysiology

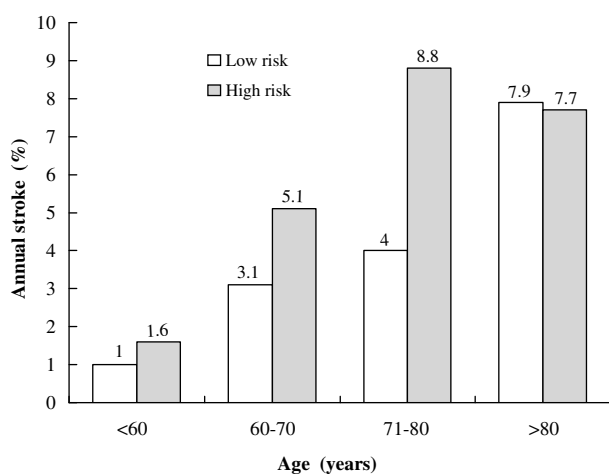


Figure 3 Annual incidence of stroke among Chinese AF patients.

(CSPE) to develop and update Guidelines for Management of Atrial Fibrillation after a thorough assessment of evidence and clinical practice applied in China and abroad. CHRS has joined hands with other academic societies in China to develop programs for professional education among physicians. The benefits of warfarin for stroke prophylaxis in AF patients are increasingly recognized, and its use among patients with AF has been steadily increasing. Recent surveys suggest the use of warfarin has plateaued at 50–60% of eligible patients with AF in big cities such as Beijing and Shanghai. Rate control is increasingly being adopted as a basic treatment modality, especially for patients with persistent AF. Catheter ablation, on the other hand, has the potential to evolve into a promising choice for curing AF.

Conflict of interest statement

None.

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