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Risk factors for new-onset atrial fibrillation: A focus on Asian populations

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ABSTRACT

The incidence of new-onset atrial fibrillation (NOAF) is increasing both in the Asian populations and Western countries. Several demographic and clinical risk factors were independently associated with NOAF, including ageing, male sex, obesity, obstructive sleep apnea syndrome, hypertension, coronary artery disease, renal dysfunction and heart failure. However, some differences in the incidence of NOAF, the prevalence of some risk factors and lifestyle or environmental conditions may exist between Asian and Western countries. Early recognition and holistic management of risk factors in an integrated manner may help reduce the burden of NOAF and its complications. While some risk scores have been developed to predict the risk of NOAF, thus far none are currently recommended or adequately validated to be used as a screening tool especially in the Asian population.
The present semi-systematic review article aims to provide a comprehensive overview on the risk factors associated to NOAF, focusing on those explored in the Asian populations.

1. Introduction

Atrial fibrillation (AF) is the most common supraventricular arrhythmia in the general population and is associated with increased risk of ischemic stroke/systemic embolism, heart failure (HF), myocardial infarction and mortality [1].

The prevalence [2] and incidence of new-onset AF (NOAF) is increasing worldwide, with an estimated rate of 9.03 per 1000 patient-years [3].

In general, the Asian populations have a lower risk of developing NOAF with a hazard ratio (HR) of 0.78 (95% Confidence Interval [CI], 0.77–0.79) [3] compared with non-Asian population. This finding was recently confirmed by a metanalysis showing an incidence rate of 5.38 (95%CI, 4.53–6.24) per 1000 patient-years of NOAF in Asian countries [4].

The most common risk factors for NOAF are rheumatic heart disease (RHD), cardiomyopathy, hyperthyroidism, chronic obstructive pulmonary disease (COPD), hypertension, coronary artery disease (CAD), HF, diabetes, renal dysfunction, obstructive sleep apnoea syndrome (OSAS), ageing, male sex, obesity, excessive alcohol drinking, and tobacco consumption. In addition, some laboratory variables such as growth differential factor 15, troponin, C-reactive protein (CRP), interleukin-2, interleukin-6, epicardium adipose thickness and left atrium (LA) diameter have been linked to NOAF. However, some difference between the Asian (Table 1) and non-Asian populations (Supplementary Table 1) have been reported.

The present semi-systematic review article (Supplementary data for search strategy) aims to provide a comprehensive overview on the risk factors associated to NOAF, focusing on those explored in the Asian populations. In addition, we provide an overview of clinical scores developed to predict NOAF.

2. Rheumatic heart disease (RHD)

The presence of RHD has been firmly associated with an increased risk for NOAF. A recent consensus document from the European Heart Association with an endorsement from other international societies proposed that a new classification replacing the classic definition of "valvular AF" which is obsolete and should no longer be used [5] (Supplementary data).

In Asia, one epidemiological study including 13 cohorts with 29,079 Chinese patients, showed that RHD was the most potent risk factor for NOAF (Odds Ratio [OR]:97.1, 95%CI 58.0–162.7) [6]. Another large cohort study (n = 471,446) in South-Western China has demonstrated that RHD was a significant risk factor for NOAF (Table 1) [7]. The prevalence of RHD in Asia is still considerable, although the global age-standardized mortality due to RHD has decreased by 47.8% from 1990 to 2015 [8]. The most recent prevalence of RHD in different regions of

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Table 1
Studies investigating risk factors for NOAF among the Asian populations.

Risk factors	Study	Country	HR (95%CI)
Rheumatic heart disease	Yunnan AF Study [7]	China	67.08 (43.40–103.68)
	Mainland China [6]	China	97.12 (58.02–162.71)
	Kim et al. [80]	South Korea	1.97 (1.06–4.14)
Cardiomyopathy	Yunnan AF Study [7]	China	15.08 (8.00–28.43)
Hyperthyroidism	Yunnan AF Study [7]	China	5.03 (2.08–12.16)
COPD	Yunnan AF Study [7]	China	2.47 (1.62–3.74)
Ageing	Yunnan AF Study [7]	China	1.07 (1.06–1.07)
	NPMS [34]	Japan	2.35 (2.03–2.72)
	NHIS Study [36]	South Korea	3.23 (2.67–3.91)[a]
Male sex	NHIS Study [36]	South Korea	1.30 (1.20–1.42)
	Urban Han Study [81]	China	2.08 (1.32–3.23)
	The Suita Study [26]	Japan	2.08 (1.64–2.63)
	NPMS [34]	Japan	2.28 (1.77–2.92)
Overweight & Obesity	National Sample [41]	South Korea	1.52 (1.30–1.78)[b]
	The Suita Study [26]	Japan	1.65 (1.29–2.11)[c]
Coronary artery disease	NHIS Study [36]	South Korea	1.64 (1.50–1.79)
	The Suita Study [26]	Japan	1.94 (1.18–3.18)
	Urban Han Study [81]	China	1.98 (1.32–2.97)
	Yunnan AF Study [7]	China	3.90 (3.30–4.62)
Heart failure	NHIS Study [36]	South Korea	1.52 (1.37–1.69)
	Yunnan AF Study [7]	China	8.85 (6.36–12.32)
Hypertension	Urban Han Study [81]	China	1.64 (1.12–2.40)
	NHIS Study [36]	South Korea	1.65 (1.52–1.80)
	Yunnan AF Study [7]	China	1.72 (1.48–2.01)
	The Suita Study [26]	Japan	1.75 (1.33–2.29)
Diabetes mellitus	Yunnan AF Study [7]	China	1.82 (1.25–2.63)
Renal impairment	The ESRD Study [82]	Taiwan	1.46 (1.32–1.61)[d]
Excessive alcohol drinking	The Suita Study [26]	Japan	1.96 (1.42–2.69)
	The CIRCS Study [73]	Japan	2.61 (1.55–4.39)
Current smoking	The Suita Study [26]	Japan	1.52 (1.09–2.13)

COPD: chronic obstructive pulmonary disease; the Hazard ratios (HRs) were all presented as multivariable-adjusted HR; NPMS: Niigata Preventive Medicine Study; CIRCS: Circulatory Risk in Communities Study; NHIS: National Health Insurance Service.
[a] For ≥80 vs. 50–59.
[b] For obesity.
[c] For overweight.
[d] For hemodialysis.

Asia ranged from 2.6 to 12.3 per 100,000 patient-years [8]. The countries with the most substantial estimated numbers of cases of RHD were India (13.17 million), China (7.07 million), Pakistan (2.25 million), Indonesia (1.18 million), together accounting for nearly 70% of cases [8]. Therefore, RHD still contributes significantly to the risk of NOAF in Asia.

3. Cardiomyopathy

Patients with cardiac structural abnormalities have been shown to be at a higher risk of NOAF. The most frequent condition is presented by hypertrophic cardiomyopathy. Among different populations, the prevalence of AF in hypertrophic cardiomyopathy ranged from 12% to 28% [9]. Also, in a large systemic review analysis of hypertrophic cardiomyopathy including 33 studies with 7381 patients, the mean prevalence of AF was 22.45% [10]. Although hypertrophic cardiomyopathy significantly increases the risk of NOAF, the prevalence in Asia seems to be low. In an electrocardiogram-based screening program in a young male South-East Asian population (n = 18,476), the prevalence of hypertrophic cardiomyopathy was 0.005%, which is much lower compared with the prevalence in the Western population (0.2%) [11,12].

In addition, dilated cardiomyopathy (DCM) is also a significant risk factor for NOAF. In a large Chinese cohort study, DCM was a strong predictor of NOAF with HR at 15.08 (95%CI, 8.00–28.43) [7]. Furthermore, the presence of DCM conferred a high lifetime risk of AF at 65% for men and 72% for women [7]. In the population over 20 years, the prevalence of DCM was 0.06% in the Southwest China [7]. While, the actual prevalence could be higher in general population, because DCM may also have more impacts in younger individuals [13].

4. Hyperthyroidism

The rate of NOAF is increased by 12% in patients with high-normal euthyroidism, by 31% in subclinical hyperthyroidism, and by 42% in overt hyperthyroidism [14].

In a cohort study including 471,446 Asian participants, of whom nearly 1000 suffering from hyperthyroidism, the HR for NOAF was

Table 2
Predictive scores for new-onset AF.

Score	Database/Cohort	Number of subjects	C index (95%CI)	Variables
FHS score [38]	FHS	4764	0.78 (0.76–0.80)	Age, sex, significant murmur, heart failure, systolic blood pressure, hypertension treatment, body mass index, PR interval
CHARGE-AF score [25]	ARIC, CHS, FHS	18,556	0.77 (0.75–0.78)	Age, race, height, weight, systolic/diastolic blood pressure, current smoking, use of antihypertensive medication, diabetes, history of myocardial infarction and heart failure
ARIC score [24]	ARIC	14,546	0.78 (N/A)	Age, race, height, smoking status, systolic blood pressure, hypertension medication usage, pericardial murmur, left ventricular hypertrophy, left atrial enlargement, diabetes, coronary heart disease, heart failure

ARIC, Atherosclerosis Risk in Communities Study; CHS, the Cardiovascular Health Study; FHS, the Framingham Heart Study; NHIRD, National Health Insurance Research Database.