Clinical risk scores for the prediction of incident atrial fibrillation: a modernized review

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Atrial fibrillation (AF) is considered the most common sustained arrhythmia. Major cardiovascular risk factors that have been identified to initiate and perpetuate AF include age, sex, arterial hypertension, heart failure, valvular heart disease and diabetes mellitus. In the literature, several studies aimed to formulate easily – applied and accurate risk stratification scores, based on antecedent cardiovascular events, comorbidities and biomarkers for the prediction of new-onset AF. The present narrative review addresses the most universally accepted and efficient clinical scores, with an extended applicability in different populations and ages, particularly scores derived from the Framingham Heart Study, the Atherosclerosis Risk in Communities, the Malmo Diet and Cancer Study, as well as the CHARGE-AF, the CHADS₂, CHA₂DS₂-VASc, HATCH and CH₂EST scores. Identification of incident AF can be challenging, thus dictating for utilization of validated clinical instruments in everyday clinical practice.

Key words: atrial fibrillation/diagnosis, cardiac arrhythmias/atrial fibrillation, cardiovascular diseases/epidemiology, ethnic groups, prognosis, risk assessment, risk factors.

What is new? What is important?

The clinical assessment of cardiovascular risk through easily applicable risk scores can accurately predict incident atrial fibrillation.

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice. Major risk factors include age, gender, arterial hypertension, diabetes mellitus, artery disease, heart failure, pulmonary disease, as well as structural heart disease [1]. Lately, a steady increase in the prevalence [2] and incidence rates of AF has been observed. Although the actual data regarding the overall AF incidence is inconsistent, sustaining significant differences between inpatient and outpatient settings, the largest dynamic range involving the incidence rates over time was documented in individuals aged 85 years or older [3]. AF is a significant risk factor for serious adverse cardiovascular events, such as myocardial infarction, heart failure [4] and ischemic stroke, with approximately one-third of all strokes globally accredited to AF [5]. In the Framingham Study, the annual risk of stroke

attributable to AF was 1.5% among patients aged 50–59 years and could reach up to 23.5% in patients over 80 years of age [6]. Arrhythmic-caused strokes are often more severe than non-arrhythmic-related strokes, with the risk of AF-related stroke mortality increasing from 1.5% in those aged 50–59 years to 24% in those aged 80–89 years [6].

Hence, developing risk scores to predict an individual's absolute risk of developing this arrhythmia, with a high clinical applicability and specificity, will substantially aid the diagnosis of atrial fibrillation. Moreover, clinicians will be able to further assess clinical and non-clinical biomarkers and lastly guide them towards a more comprehensive and targeted treatment.

This narrative review summarizes current evidence of using relevant clinical scoring systems for the prediction of new-onset atrial fibrillation. The authors evaluated original investigations published in

PubMed from 1995 to 2020, using keywords such as clinical scores, scoring systems, prediction and atrial fibrillation. We sought to evaluate the efficacy and accuracy of risk predictive systems in healthy

individuals, without previously diagnosed arrhythmias, stroke, catheter ablation or cardiac surgery, of different populations – Asians, Caucasians, African Americans and ages older than 18 years.

Figure 1. Included studies of the narrative review.

To our knowledge, a standardized integrative instrument of multiple risk factors able to accurately establish an individual's lifetime risk to develop AF is unavailable. However, recent studies have developed and examined several potential AF risk scores, for everyday use in the clinical practice. Their development originated from community-based studies, in which the primary focus was identification of cardiovascular risk factors. A summarizing table of the clinical scores, their study population characteristics and parameters investigated can be found at the end of the article (Table 1).

Scoring systems stemming from the Framingham Heart Study

Firstly, the **Framingham Heart Study (FHS)**, which assessed a 10-year risk prediction model with clinical and electrocardiographic parameters, identified a 10% of study participants with incident atrial fibrillation, after a 10-year follow-up [7]. The incorporation of echocardiographic parameters may improve performance slightly, as observed in secondary analyses. The risk score is reasonably accurate for stratification of individuals into risk categories, with similar accuracy across both sexes, young adults and elderly populations. However, this score was applied in white population, while its utility to predict the

10-year risk of developing AF in non-whites was uncertain. Luckily, a secondary analysis validating the score in whites and African Americans, concluded that the risk of incident AF in community, could be assessed reliably [7]. A major limitation of the study was the exemption of thyroid status and physical activity, thus declining risk prediction ability in a subset of patient groups [6,7].

Scoring systems stemming from the Atherosclerosis Risk in Communities Study

Secondly, the **Atherosclerosis Risk in Communities Study (ARIC)**, in a prospective, biracial (whites and blacks) community-based cohort, developed an additional risk score model, in which commonly identified risk factors, were assimilated to develop a 10-year risk score of new-onset AF, showing a moderately good discrimination under the Cox regression model [8]. Interestingly, the study found the incidence of AF to be greater in whites than in blacks. Nevertheless, most risk factors predicted AF by race in a similar manner [9], while the Framingham study performed better in predicting AF in whites, than blacks. Furthermore, an interaction with race and left ventricular hypertrophy (LVH), as well as interactions of diabetes and coronary heart disease (CHD) with age were also found during the study [8,9].

Table 1
Summary of included clinical scores for the prediction of new-onset atrial fibrillation

CLINICAL SCORE	STUDY POPULATION	VARIABLES
FHS	<ul style="list-style-type: none"> • 4,764 individuals • Aged 45–95 years • White race • 10 year-risk score assessment 	<ul style="list-style-type: none"> • Age • Sex • Body mass index • Systolic blood pressure • Pulse pressure • Hypertension medication • PR interval duration • ECG left ventricular hypertrophy • Heart failure • Clinically significant heart murmur
ARIC	<ul style="list-style-type: none"> • 15,792 individuals • Aged 45–64 years • Biracial study (whites, blacks) • 10-year risk score assessment 	<ul style="list-style-type: none"> • Age • Race • Height • Smoking • Systolic blood pressure • Hypertension treatment • Diabetes • Coronary heart disease • Heart failure • Left atrial enlargement • Cardiac murmur • ECG left ventricular hypertrophy • Prolonged P wave duration
CHARGE-AF	<ul style="list-style-type: none"> • 18,556 individuals • Aged 46–94 years • Biracial (whites, blacks) • 5-year predictive model 	<ul style="list-style-type: none"> • Age • Race • Anthropometric data • Systolic blood pressure • Diastolic blood pressure • Smoking status • Hypertension medication • Diabetes • Past history of myocardial infarction • Past history of heart failure • PR interval duration
MDCS	<ul style="list-style-type: none"> • 30,447 individuals • Age 44–73 years • White race 	<ul style="list-style-type: none"> • Age • Sex • Systolic blood pressure • Diastolic blood pressure • Antihypertensive treatment • Body mass index • Low-density lipoprotein • High-density lipoprotein • Current smoking • History of diabetes mellitus • History of myocardial infarction • History of heart failure
Suita	<ul style="list-style-type: none"> • 6,898 individuals • Aged between 30–79 years • Asian race • 10-year risk prediction model 	<ul style="list-style-type: none"> • Age • Gender • Systolic hypertension • Weight • Drinking status • Coronary artery disease • Smoking status

Table 1 (continued)

		<ul style="list-style-type: none"> • Lipoprotein-cholesterol level • History of arrhythmia • Presence of cardiac murmur
CHADS ₂	<ul style="list-style-type: none"> • Cross-studied in different databases 	<ul style="list-style-type: none"> • Congestive heart failure • Hypertension • Age • Diabetes • Stroke/Transient Ischemic Attack
CHA ₂ DS ₂ -VASc	<ul style="list-style-type: none"> • Cross-studied in different databases 	<ul style="list-style-type: none"> • Congestive heart failure • Hypertension • Age • Diabetes • Stroke/Transient Ischemic Attack • Vascular disease • Sex category
HATCH	<ul style="list-style-type: none"> • 670,804 individuals • Older than 20 years of age • Asian race • 10-year prediction capability 	<ul style="list-style-type: none"> • Hypertension • Age more than 75 years • Transient Ischemic Attack or stroke • Chronic obstructive pulmonary disease • Heart failure
C2HEST	<ul style="list-style-type: none"> • 471,446 individuals • Aged 31–63 years • Asian race • 11-years predictivity 	<ul style="list-style-type: none"> • Coronary Artery Disease/ Chronic Obstructive Pulmonary Disease • Hypertension • Age more than 75 years • Systolic heart failure • Thyroid disease (hyperthyroidism)

Scoring systems stemming from the CHARGE-AF and other studies

Moreover, the **CHARGE-AF** score, was developed from a pooled diverse population from 3 large cohorts in the United States, including the Atherosclerosis Risk in Communities study, the Cardiovascular Health Study, and the Framingham Heart Study, with a 5-year risk prediction [2]. Incorporating parameters were readily available in clinical practice, with statistical analysis exhibiting a good discrimination [10]. The electrocardiographic parameters were found to offer no additional predictive ability, as compared to other variables examined. The study validated the derived models in participants from the Age, Gene and Environment-Reykjavik study and the Rotterdam Study, where it was shown that discrimination was acceptable and calibration adequate [10]. Over 26,000 participants were evaluated, with characteristics of age over 45 years and less than 94 years, as well as African Americans and white populations, thus

increasing the generalizability over previously established scores [10].

Important mentioning to the **Malmö Diet and Cancer Study** (MDCS), a prospective cohort study, with a risk model composition of age, sex, hypertension, history of diabetes mellitus and related cardiovascular disease, as well as laboratory biomarkers and individual habits. The model performed with reasonable accuracy in middle-age individuals without disease. Additional biomarkers did not significantly improve the ability to predict 5-year risk of AF with the exception of natriuretic peptides [11]. In a related publication from the same registry, heart failure and myocardial infarction were considered the strongest risk factors for the occurrence of atrial fibrillation [12].

A primary score, **CHADS₂** was synthesized to evaluate the risk of thromboembolic risk in patients with established AF. Nowadays, using the more recently developed **CHA₂DS₂-VASc** scoring system, by including additional stroke risk factors (vascular diseases and female gender), was suggested to guide clinicians towards a more

effective antithrombotic therapy for AF patients. However, recent reports have implied that the aforementioned risk scores also are capable of predicting incident AF, mainly due to the assessment of risk factors shared in atrial fibrillation and stroke [13]

Previous studies have focused on white and black individuals, excluding significant populations such as Asians. For this reason, recent studies sought to determine risk factor models predicting AF in participants from Korea, Taiwan and China [14,15]. Starting with the evaluation of the CHADS2 score in 702,502 Chinese individuals in Taiwan, aged more than 18 years, with no prior history of cardiac arrhythmias or rheumatic heart disease, it was found very useful in the prediction of AF, identifying an incidence of 1.5 per 1,000 patients [15]. Later on, the **HATCH** score was evaluated as a prognostic tool for new-onset AF in Asian subjects, even though it was developed primarily as a score predicting the permutation of paroxysmal AF to persistent by the Euro Heart Survey [16]. The study had a follow up of 9 years and reported an incidence of 1.4% of new-onset AF from 670804 patients [17]. Overall, it performed very well in risk estimation and stratification of Asian patients for new-onset AF and furthermore proved an extended use in estimating the individual risk of incidental AF for patients with different comorbidities, as opposed to risk models like ARIC and FHS. The **Suita** study from Japan [17] evaluated 6,898 participants between 30–79 years old, without a previously diagnosed cardiac arrhythmia and after evaluating traditional risk factors, the authors were able to identify patients with a 10-year risk of incident AF. However, the clinical score has a certain degree of complexity, while an external validation study of other Japanese cohorts is necessary to validate Suita's findings. Finally, a study involving 471,446 subjects from the Chinese Yunnan Insurance Database and 451,199 subjects from the Korean National Health Insurance Service, aimed to investigate risk factors for incident AF in Asian subjects. This study indicated the superiority of the **C2HEST** score in comparison to CHADS2 and CHA2DS2-VASc in predicting incident AF among these populations [14]. The C2HEST score was developed as a simple clinical tool, incorporating readily variables used in everyday

clinical practice [15]. It was later concluded that the C2HEST score was superior to CHADS2 and CHA2DS2-VASc scores in both cohort studies examined in predicting new-onset AF.

Critical assessment, limitations and future research

This narrative review summarizes the existing scoring systems for the prediction of incident AF, in an effort to spark evidence-based dialogue on current medical practice, providing grasps for the future. The efficacy of the existing scoring system seemingly varies among different populations. This variation may depend on racial hereditary traits or behavioral risk factors associated with particular populations residing in the United States, in Northern European countries, in Asia and beyond. Indeed, the Framingham study predictive model appears reliable for white Americans, while the ARIC study has shown similar predictive efficacy in both white and African Americans. At the same time, the C2HEST and HATCH scoring systems appear superior for the prediction of AF in Asian populations. Available evidence suggests that the CHA2DS2-VASc scoring system is not only suitable for optimizing antithrombotic treatment but also capable of predicting incident AF [18]. Certainly, the repeatability of these results in different communities and populations ought to be assessed, once relevant evidence becomes available. Finally, yet importantly, a follow-up systematic review or metaanalysis would describe the impact of each scoring system in greater depth.

CONCLUSION

There are several scoring systems with validated efficacy in predicting new-onset atrial fibrillation in different populations. The most significant parameters taken into consideration are age, sex, arterial hypertension, diabetes mellitus and heart disease. The Framingham study has elucidated the potential benefit from incorporating echocardiographic indices in the existing scoring systems. Despite their differences, all the reviewed studies, including the CHARGE-AF, the Malmo Diet and Cancer Study and

Atherosclerosis Risk in Communities study yielded the significance of the aforementioned factors, whose modifiable components can be addressed in a preventive and outpatient practice context. Incorporating this evidence in everyday

clinical practice can significantly increase the detection of early episodes of the arrhythmia, hence decreasing atrial fibrillation burden, initiating early anticoagulant therapy and preventing adverse thromboembolic events.

Fibrilația atrială (AF) este una dintre cele mai frecvente aritmii. Factorii de risc importanți cunoscuți a fi implicați în inițierea și persistența AF sunt vârsta, genul, hipertensiunea arterială, insuficiența cardiacă, diabetul zaharat și boala valvulară. În literatură sunt descrise mai multe scoruri ce au ca scop stratificarea riscului pentru dezvoltarea AF. Articolul de față prezintă succint cele mai importante scoruri cu aplicabilitate crescută, precum cele din studiul Framingham, CHARGE-AF, CHADS₂, CHA₂DS₂-VASc, HATCH și scorul CH₂EST. Identificarea AF incidente reprezintă o provocare și sunt astfel necesare instrumente clinice validate în practica curentă.

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