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MINI-REVIEW ARTICLE

CHARGE-AF: A Useful Score For Atrial Fibrillation Prediction?

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Abstract: Atrial fibrillation (AF) is the commonest arrhythmia in clinical practice and is associated with increased morbidity and mortality. Various predictive scores for new-onset AF have been proposed, but so far, none have been widely used in clinical practice. CHARGE-AF score was developed from a pooled diverse population from three large cohorts (Atherosclerosis Risk in Communities study, Cardiovascular Health Study and Framingham Heart Study). A simple 5-year predictive model includes the variables of age, race, height, weight, systolic and diastolic blood pressure, current smoking, use of antihypertensive medication, diabetes mellitus, history of myocardial infarction and heart failure. Recent studies report that the CHARGE-AF score has good discrimination for incident AF and seems to be a promising prediction model for this arrhythmia. New screening tools (smartphone apps, smartwatches) are rapidly developing for AF detection. Therefore, the wide application of the CHARGE-AF score in clinical practice and the upcoming usage of mobile health technologies and smartwatches may result in better AF prediction and adequate stroke prevention, especially in high-risk patients.

Keywords: Atrial fibrillation, CHARGE-AF score, cardiovascular, myocardial infarction, FHS-AF, prediction.

1. INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice and is associated with increased morbidity and mortality, thus portending significant burdens to patients, societal health, and the health economy [1, 2]. AF-related outcomes include stroke, heart failure (HF), cognitive decline and vascular dementia, decreased quality of life, frequent hospitalizations and death [1]. Increasing age is a prominent AF risk factor, but the increasing burden of other comorbidities, including hypertension, diabetes mellitus, heart failure, coronary artery disease, chronic kidney disease, obesity, and obstructive sleep apnea, is also important [2]. The establishment of prevention strategies and prognosis optimization is crucial for identifying high-risk individuals and the latest ESC guidelines suggest AF screening in patients after an ischemic stroke [1]. Various predictive scores for new-onset AF have been proposed, but none have been widely used in clinical practice (Table **1**) [3-13]. We present the recent knowledge regarding CHARGE-AF as a predictive score for AF.

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2. CURRENT EVIDENCE REGARDING CHARGE-AF RISK SCORE

Alonso *et al*. derived pooled data from three large community-based cohorts in the United States ([Atherosclerosis Risk in Communities study (ARIC), Cardiovascular Health Study (CHS) and Framingham Heart Study (FHS)] and developed CHARGE-AF, a simple 5-year risk score for AF prediction [3]. Overall, 26000 white and African Americans, aged between 45 and 94, were evaluated. A number of sociodemographic variables and cardiovascular risk factors were consistently associated with age- and sex-adjusted AF incidence across cohorts. The researchers observed a higher risk of incident AF in men, older individuals, those with higher height, weight, and blood pressure, treated hypertension, current smokers, diabetes mellitus, and a previous history of heart failure or myocardial infarction. Therefore, the CHARGE-AF score included variables such as age, race, height, weight, systolic and diastolic blood pressure, current smoking, use of antihypertensive medication, diabetes mellitus, and history of myocardial infarction and heart failure. The score reportedly showed good discrimination (C-statistic, 0.765; 95% CI, 0.748 to 0.781, pooled for ARIC, FHS and CHS studies) [3]. Further validation of the score was performed in two additional cohorts in Europe (AGES and the Rotterdam Study [RS]), showing acceptable discrimination [3]. Noteworthy, the CHARGE-AF score is simple and includes variables easily obtained in clinical settings [3-13].

A recent meta-analysis provided an overview of prediction models for incident AF risk that are applicable in and have been derived, validated, and/or augmented in community cohorts [14]. Noteworthy, only three models (CHARGE-AF, FHS, CHA2DS2-VASc) were proved to have significant overall discrimination for AF incidence at any follow-up duration and with any calibration despite high heterogeneity. Among these three models, CHARGE-AF and FHS-AF 10-year models were derived specifically for incident AF risk prediction (overall C-statistic 0.71 and 0.70, respectively). Notably, only CHARGE-AF showed significant overall discrimination with a uniform prediction window. These results favor CHARGE-AF as the most suitable prediction model for incident AF [14]. Table **2** illustrates the score points of various risk scores used for AF - prediction.

Table 1. Predictive scores for new-onset atrial fibrillation.

Study (Ref)	Cases / Number of Pts	Age (Years)	Follow-up, Years	Database/Type of Study	Variables/ Key Findings
CHARGE-AF score [3] (5-year risk)	1.771/18.556	46-94yrs	5yrs	ARIC, CHS, FHS/ Prospective Cohort Study	C index of 0.77 (0.75-0.78)/ age, ethnicity, height, weight, SBP/DBP, current smoking, HT treatment, DM, HF, myocardial infarction,
FHS score [4] (10-year risk)	457/4.764	60.9 (45-95)yrs	10yrs	FHS/ Cohort Study	C index of 0.78 (0.76-0.80)/ Age sex, significant murmur, HF, SBP, HT treatment, body mass index, PR interval
ARIC score [5] (10-year risk)	616/14.546	45-64yrs	10yrs	ARIC/ Prospective Cohort	C index of 0.78/ Age, ethnicity, height, smoking, SBP, HT therapy, pericardial murmur, left ventricular hypertrophy, left atrium enlargement, DM, HF, CAD
C2HEST score [6] (1-year risk model)	14.095/ 240.459	N/A	7.9±11.5mths	French nationwide study/ Retrospective cohort study	C index of 0.734 (0.732-0.736)/ CAD or COPD, HT, elderly, systolic HF, thyroid disease
C2HEST score [7]	921/471.446	47 ± 16yrs	11(4.1 ± 3.5)yrs	Chinese Yunnan Insurance Database/ Cohort Study	C index of 0.75 (0.73-0.77)/ CAD or COPD, HT, elderly, systolic HF, thyroid disease
WHS score [8] (10-year risk model)	616/19.940	52.9 (49-59) yrs	14.5yrs	Women's Health Study/ Prospective Cohort study	C index of 0.72 (0.68-0.75)/ Age, weight, height, SBP, alcohol use, smoking
MHS score [9] (10-year risk model)	2.791/145.182	63yrs	10yrs	Maccabi Healthcare services/ Prospective Cohort Study	C index of 0.75 (0.74-0.76)/ Age, Sex, Body mass index, myocardial infarction, PAD, HT therapy, SBP, COPD, autoimmune/inflammatory disease, age to HF
JMC score [10] (7-year risk model)	349/65.984	52yrs	5.5yrs	Retrospective cohort study	C index of 0.77/ Age, waist circumference, DBP, alcohol consumption, heart rate, cardiac murmur
Shandong score [11]	134/33.186	56.69 ± 9.85 years (45-85) years	2.6 years	Shandong multi-center health check-up longitudinal study/ Prospective cohort study	C index of 0.77/ Age, sex, CAD, HT
AI-ECG model output [12]	1.936	75.8 (70.4-81.8) years	7.4 years (4.7-10.9)	Mayo Clinic Study of Aging/ Prospective Cohort Study	C index of 0.69 (0.66-0.72)/ AI-ECG algorithm
EHR-AF [13] (5-year risk)	14.334/ 412.085	45-95 years	5 years	Partners HealthCare System Research Patient Data Registry	C index of 0.777 (0.771-0783)/ male sex, age, race, smoking, height, weight, DBP, HT, hyperlipidemia, HF, CAD, valvular disease, previous stroke/TIA, PAD, chronic kidney disease, and hypothyroidism

Abbreviations: Pts, Patients: SBP, Systolic Blood Pressure: DBP, Diastolic Blood Pressure: HT, Hypertension: DM, Diabetes Mellitus: HF, Heart Failure: CAD, Coronary Artery Disease: COPD, Chronic Obstructive Pulmonary Disease: PAD, Peripheral Artery Disease: TIA, Transient Ischemic Attack: Mths, Months: Yrs, Years

Table 2. Score points of various risk scores used for AF prediction.

Risk Model	Charge-AF	FHS-Score	ARIC Score	C2HEST Score	WHS Score	MHS Score	JMC Score	Shandong Score	EHR-AF
Prediction of AF incidence (years)	5	10	10	11	10	10	7		5
Variables	-								
Age	√	√	√	√	√	√	√	√	√
Sex	-	√	-	-	-	√	-	√	√
Race	√	-	√	-	-	-	-	-	√
Body measure-ments	√	√	√	√	√	√	√	-	√
Blood pressure	√	-	√	-	-	-	-	-	-
Heart Rate	-	-	-	-	-	-	√	-	-
History of Heart Failure	√	√	√	√	-	√	-	-	√
Hypertension	√	√	√	√	√	√	√	√	√
Diabetes Mellitus	√	-	√	-	-	√	-	-	-
Stroke	-	-	-	-	-	-	-	-	√
Coronary Artery Disease	√	-	√	√	-	-	-	√	√
Vascular Disease	-	-	-	-		√		-	√
Alcohol use	-	-	-	-	√	-	√	-	
Smoking	√		√	-	√	-	-	-	√
ECG parameters	-	√	√	-	-	-	-	-	-
COPD	-	-	-	√	-	√	-	-	-
Autoimmune/ Connective Tissue/ Inflammatory Disease	-	-	-	-	-	√	-	-	-
Significant Mur-mur	-	√	√	-	-	-	√	-	-
Serum Lipids	-	-	-	-	-	-	-	-	-
Glomerual Filtra-tion Rate	-	-	-	-	-	-	-	-	√
Urine Albumin Secretion	-	-	-	-	-	-	-	-	-
Thyroid Disease	-	-	-	√				-	√
Dyslipidemia	-	-	-	-	-	-	-	-	√
Valvular Disease	-	-	-	-	-	-	-	-	√

Similar findings were reported by another systematic review that compared the efficacy of risk models to predict AF [15]. The researchers used established risk prediction models and evaluated their predictive performance utilizing data from 2.5M individuals who attended vascular screening departments in the USA and the UK, as well as the subgroup of 1.2M patients with CHA2DS2-VASc ≥2 [15]. Out of 14 risk prediction models identified, only 6 had AUROC curves of 0.70 or above, and calibration plots showed very good concordance between the predicted and observed risks of AF [15]. CHARGE-AF and Maccabi Healthcare Services (MHS) risk scores were reported to have the highest observed prevalence in the highest decile of predicted risk and showed an observed prevalence of AF of 1.6% with a number needed to screen of 63. Using single time point ECG, these models can reduce the number of patients needed to screen to detect one case of AF. This is promising because the above-mentioned models may be used for more selective opportunistic or systematic screening [15].

Alonso *et al*. evaluated 6663 male and female individuals between 45 to 84 years without AF at baseline enrolled in a Multi-Ethnic Study of Atherosclerosis (MESA) [16]. They used a simple CHARGE-AF model and a biomarker-enriched CHARGE-AF model that considers levels of NT-proBNP and C-reactive protein. The reported c-statistic was 0.779 for the CHARGE-AF simple model and 0.825 for the biomarker-enriched model [16]. Bundy *et al*. reinforced these findings, evaluating risk prediction models of AF from MESA. Among 3,534 participants (mean age, 61.3 years; 48.0% male), the researchers investigated possible improvements for the prediction of AF risk within 5 years when adding novel candidate variables that were identified by machine learning methods to the CHARGE-AF enriched model, which includes height, age, weight, race/ethnicity, blood pressure, diabetes mellitus, current smoking, NT-proBNP and antihypertensive medication [17]. Compared with the CHARGE-AF enriched model (c-statistic of 0.804), variables identified by machine learning, including biomarkers, ECG parameters, subclinical cardiovascular variables and cardiac magnetic resonance imaging variables, did not significantly improve prediction. A 23-item score that was derived by machine learning methods demonstrated a c-statistic of 0.806, whereas another model that included age, weight, current smoking, age, coronary artery calcium score weight, NT-proBNP, and cardiac troponin-T achieved a c-statistic of 0.802 [16]. Therefore, simple models of CHARGE-AF seem to remain the gold standard for predicting AF.

An interesting study that included 1936 participants with a median age of 75.8 years and a median CHARGE-AF score of 14.0 investigated the utility of artificial intelligence-enabled electrocardiography (AI-ECG) as a predictor of AF and assessed its performance compared to CHARGE-AF [12]. Participants with AI-ECG AF model output of >0.5 at the first visit showed a 21.5% cumulative incidence of AF at 2 years compared to 52.2% at 10 years. When the AI-ECG AF model and CHARGE-AF score were included in the same model, they independently predicted future AF without a statistically significant interaction (P=0.54). AI-ECG AF demonstrated a C-statistic of 0.69 compared to 0.69 for CHARGE-AF, while combined CHARGE-AF score and AI-ECG showed a C-statistic of 0.72 [17].

Even though African-Americans and Hispanics have an increased number of traditional AF risk factors, they show reduced incidence of AF compared with non-Hispanic whites. This is characterized as a "racial paradox" [18]. Shulman *et al*. evaluated the Framingham Heart Study (FHS) and CHARGE-AF risk models in an underserved urban population and compared their performance among African-Americans, Hispanics and non-Hispanic whites [19]. For the CHARGE-AF model, in non-Hispanic whites, the AUC was 0.673, for African-Americans 0.706 and for Hispanics 0.711 [19]. This seems quite important because non-Hispanic whites are characterized by increased AF incidence and by different risk factors and suggests that other factors in this cohort that predict AF were probably present and were not accounted for in these traditional models. Despite that, this study also showed that CHARGE-AF has good discrimination in all racial and ethnic groups [19].

Two revolutionary studies were published recently to determine whether AF risk could be estimated accurately with routinely ascertained features obtained from electronic health records (EHRs) [13, 20]. Humle *et al*. identified 412,085 individuals aged between 45 and 95 without prevalent AF. The researchers derived and validated a prediction model for 5-year AF risk using split-sample validation and compared it with other assessment methods of AF incidence [13]. This model demonstrated good discrimination (C-statistic 0.777, 95%CI 0.771-0.783) and calibration (0.99, 95%CI 0.96-1.01) in the validation sample. Model discrimination and calibration were also favorable to CHARGE-AF with a c-statistic of 0.753 [95%CI 0.747-0.759]; calibration slope 0.72, 95%CI 0.71-0.74) [15]. In the other study, Khurshid *et al*. included 4,508,180 individuals with complete AF risk data, 2 or more office visits within two years and no prevalent AF in the analysis (age 62.5, 56.3% female). EHR-AF demonstrated favorable AF discrimination (c-index 0.808 [95%CI 0.807-0.809]) [20]. Notably, CHARGE-AF score had similar discrimination for incident AF (0.806 [0.805-0.807]) compared to EHR-AF score, but C_2HEST (0.683 [95% CI, 0.682-0.684]) and CHA2DS2-VASc (0.720 [95% CI, 0.719-0.722]) scores were less favorable [20] (Fig. **1**).

Regarding the above-mentioned studies, the CHARGE-AF score appears to be a useful risk score for primary AF screening. Further research could assess the importance of implementing AF screening models, aided by software that automatically extracts data from EHRs, regarding patients' clinical variables and risk categories and suggests parameters that should be induced for better AF risk stratification.

3. MOBILE HEALTH TECHNOLOGIES FOR AF DETECTION

Mobile health technologies are rapidly evolving to detect AF [21]. The teleCheck-AF approach supports integrated care through teleconsultation and improves AF diagnosis and management. It incorporates three main parameters: i) structured teleconsultation, ii) app-based on-demand heart rate and rhythm monitoring infrastructure, and iii) comprehensive AF management [22]. Kardia Mobile Cardiac Monitor (KMCM) utilizes AF detection algorithms and a handheld cardiac rhythm recorder to detect AF [22]. KMCM automat-

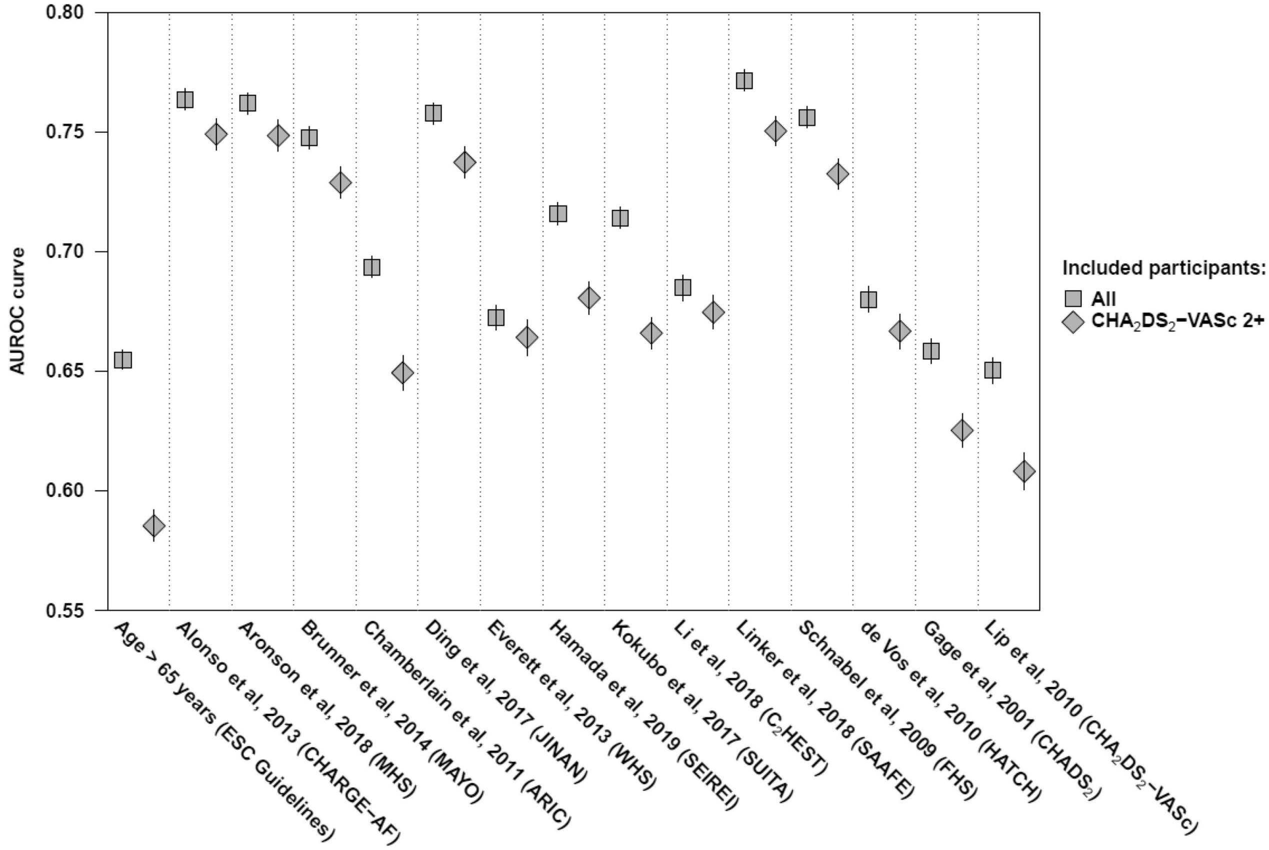

Fig. (1). Discriminative performance. Squares represent the AUROC curves in the analysis of all 2.5M participants and diamonds in 1.2M participants with CHA2DS2-VASc of two or more. The vertical bars represent the 95% CIs. The AUROC curves are based on the regression equation in 12 prediction models [15]. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

ed algorithm interpretation was reported to have 94.1% specificity and 96.6% sensitivity for the detection of AF when compared with ECGs that were interpreted by physicians [22]. Recently, Apple promoted the self-diagnosis of AF via a novel Apple watch feature that enables users to record a rhythm strip, thus facilitating health promotion and preventative efforts [23]. Moreover, creating easy-to-interpret ECG app data summaries with the help of AI in the EHR might be one of the solutions to deal with the abundance of data. These findings show the way for the routine use of this novel technology in everyday clinical practice in patients with increased predictive scores for new-onset AF. Once AF is detected, stroke and thromboembolism prevention will be feasible due to appropriate anticoagulation. Considering this, CHARGE- AF usage per new screening tools for AF detection (smartphone apps, smartwatches) will provide more efficient stroke and thromboembolism prevention.

CONCLUSION

CHARGE-AF seems to be a promising risk score for AF screening in terms of performance and applicability. It contains variables easily extracted from EHRs and requires only easily obtainable body measurements (height, weight, and blood pressure) at a meager cost. Its wide application in clinical practice and new screening tools for AF detection may result in better AF prediction and adequate stroke prevention therapy, especially in high-risk patients.

LIST OF ABBREVIATIONS

AF = Atrial Fibrillation

HF = Heart Failure

ARIC = Atherosclerosis Risk in Communities study

CHS = Cardiovascular Health Study

FHS = Framingham Heart Study

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

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