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SHORT REPORT
Arrhythmias and electrophysiology

Changes in the CHA_2DS_2-VAS_C score as a predictor of incident atrial fibrillation in older Chinese individuals: the AF-CATCH study

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Aims Incidence of atrial fibrillation is highly associated with age and cardiovascular co-morbidities. Given this relationship, we hypothesized that the dynamic changes resulting in an increase in the CHA_2DS_2-VAS_C score over time would improve the efficiency of predicting incident atrial fibrillation on repeated screening after a negative test.

Methods and results We investigated in an analysis of the AF-CATCH trial [quarterly vs. annual electrocardiogram (ECG) screening for atrial fibrillation in older Chinese individuals] data, the association between the changes in the CHA_2DS_2-VAS_C score from baseline to end-of-study visit and the risk of incident atrial fibrillation. Participants without a history of atrial fibrillation and with a sinus rhythm at baseline were randomized to the annual (usual) or quarterly 30 s (intensive) single-lead ECG screening groups. During a median follow-up of 2.1 years in 6806 participants, the incidence rate of atrial fibrillation increased from 4.2 per 1000 person-years in participants with a change in the CHA_2DS_2-VAS_C score of 0 to 6.4 and 25.8 per 1000 person-years in participants with a change in the CHA_2DS_2-VAS_C score of 1 and ≥2, respectively. A change in the CHA_2DS_2-VAS_C score of ≥2 was associated with a significantly elevated risk of incident atrial fibrillation.

Conclusions Patients with substantial changes in the CHA_2DS_2-VAS_C score were more likely to develop incident atrial fibrillation, and regular re-assessments of cardiovascular risk factors in the elderly are probably worthwhile to improve the detection of atrial fibrillation.

Registration URL: http://www.clinicaltrials.gov; Unique identifier: NCT02990741.

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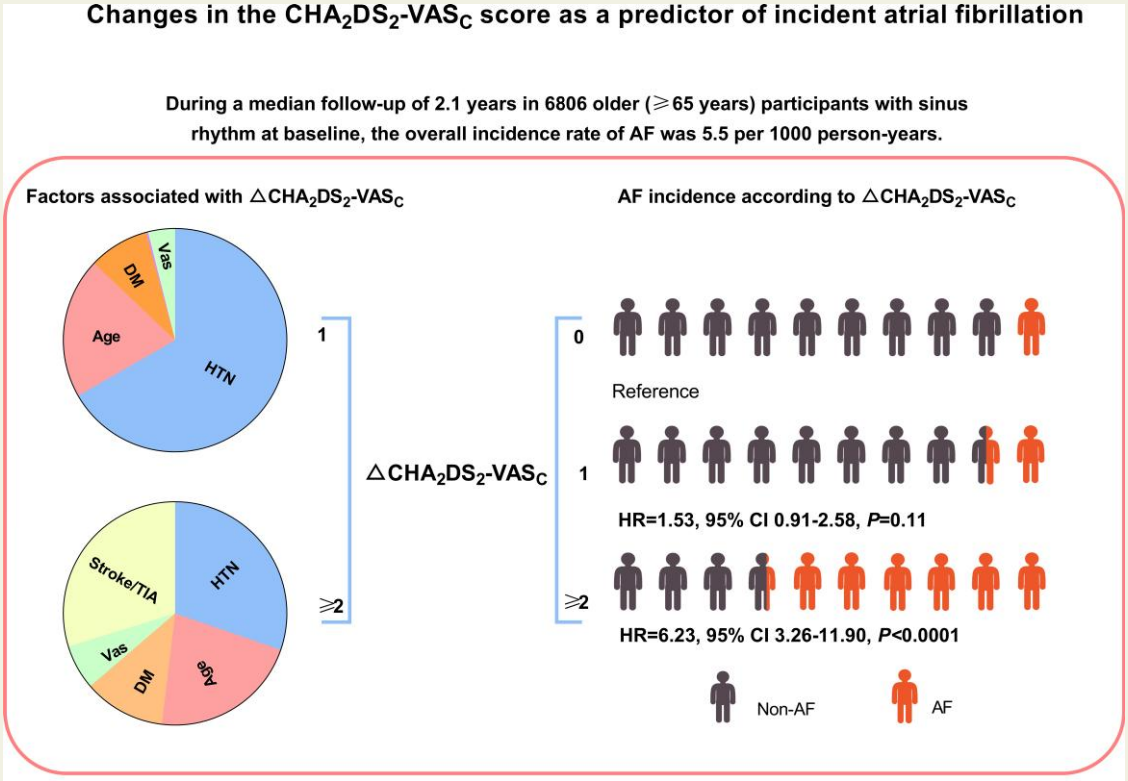
Graphical Abstract



△CHA_2DS_2-VAS_C, the change in the CHA_2DS_2-VAS_C score from baseline to end-of-study visit; AF, atrial fibrillation; HTN, hypertension; DM, diabetes mellitus, TIA, transient ischemic attack; Vas, vascular disease; HR, hazard ratio; CI, confidence interval.

Keywords Incident atrial fibrillation • Screening • CHA_2DS_2-VAS_C score • Hypertension • Risk factor

Introduction

Atrial fibrillation is the most frequent cardiac arrhythmia in the elderly. Incidence of atrial fibrillation is highly associated with age and cardiovascular co-morbidities as well, such as hypertension, diabetes mellitus, stroke or transient ischaemic attack (TIA), congestive heart failure, ischaemic heart disease, and valvular heart disease.[1] Given this relationship with both age and cardiovascular co-morbidities, which are part of the CHA_2DS_2-VAS_C score, we hypothesized that the dynamic changes resulting in an increase in the CHA_2DS_2-VAS_C score over time would improve the efficiency of predicting incident atrial fibrillation on repeated screening after a negative test. CHA_2DS_2-VAS_C score is a recommended tool to guide decisions on the use of oral anticoagulants to prevent stroke in atrial fibrillation.[2] However, it may change over time, in response to the dynamic changes of the afore-mentioned cardiovascular risk factors, and such dynamic changes have been shown to be related to stroke outcomes.[3] Opportunistic screening in patients contacting the health system and ≥65 years of age has been recommended in many atrial fibrillation guidelines.[4] In those who do not show atrial fibrillation on the initial screening, it has been shown that a similar proportion will show atrial fibrillation on the subsequent screen.[5] In an analysis of the AF-CATCH trial [quarterly vs. annual electrocardiogram (ECG) screening for atrial fibrillation in older Chinese individuals] data,[6] we investigated the association between the changes in the CHA_2DS_2-VAS_C score from baseline to end-of-study visit and the risk of incident atrial fibrillation, to determine whether atrial fibrillation detection might be enriched in those study participants who had an increased CHA_2DS_2-VAS_C score.

Methods

In the AF-CATCH study, participants without a history of atrial fibrillation and with sinus rhythm at baseline were randomized to the annual (usual) or quarterly 30 s (intensive) single-lead ECG screening groups. The primary outcome was the detection rate of new-onset atrial fibrillation. The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine. Written informed consent was obtained from all study participants at baseline screening clinic visits. For database management and statistical analysis, we used SAS software (Version 9.4; SAS

Table 1 Baseline characteristics

Characteristic	△CHA_2DS_2-VAS_C = 0 (*n* = 4827)	△CHA_2DS_2-VAS_C = 1 (*n* = 1752)	△CHA_2DS_2-VAS_C ≥2 (*n* = 227)	*P* ANOVA
Age, years	71.5 ± 6.4	71.4 ± 5.5	73.0 ± 5.2	0.001
65–74 years	3552 (73.6)	1430 (81.6)	187 (82.4)	<0.0001
≥75 years	1275 (26.4)	322 (18.4)	40 (17.6)	<0.0001
Congestive heart failure	28 (0.6%)	6 (0.3%)	0	0.38
Hypertension	3290 (68.2)	438 (25.0)	66 (29.1)	<0.0001
Diabetes mellitus	1109 (23.0)	263 (15.0)	35 (15.4)	<0.0001
Previous stroke, TIA, or thromboembolism	341 (7.1)	82 (4.7)	10 (4.4)	0.001
Vascular disease	355 (7.4)	97 (5.5)	18 (7.9)	0.03
Women	2741 (56.6)	970 (55.2)	113 (49.6)	0.08
Baseline CHA_2DS_2-VAS_C score	3 (2–4)	2 (2–3)	2 (1–3)	<0.0001
Body mass index, kg/m^2	24.7 ± 3.4	24.2 ± 3.4	24.2 ± 3.1	<0.0001
Systolic blood pressure, mmHg	138.6 ± 18.6	135.1 ± 19.1	136.4 ± 18.2	<0.0001
Diastolic blood pressure, mmHg	74.6 ± 9.5	73.6 ± 9.5	73.3 ± 9.2	0.0002
Pulse rate, beats per min	73.5 ± 11.1	73.2 ± 10.7	73.8 ± 9.9	0.56
Current smoking	674 (14.2)	249 (14.3)	36 (16.1)	0.68
Alcohol intake	590 (12.4)	222 (12.8)	33 (14.9)	0.48
Blood biochemistry				
Fasting plasma glucose concentration, mmol/L	5.68 (5.17–6.40)	5.76 (5.20–6.60)	5.70 (5.30–6.64)	0.06
Serum triglycerides concentration, mmol/L	4.99 (4.32–5.63)	5.05 (4.35–5.75)	5.20 (4.32–5.89)	0.20
Total cholesterol concentration, mmol/L	1.43 (1.05–2.00)	1.43 (1.03–2.07)	1.47 (1.09–2.05)	0.03
LDL cholesterol concentration, mmol/L	3.00 (2.44–3.58)	3.06 (2.47–3.68)	3.14 (2.42–3.89)	0.02
HDL cholesterol concentration, mmol/L	1.50 (1.29–1.80)	1.55 (1.32–1.83)	1.54 (1.29–1.81)	0.04
Serum creatinine concentration, mmol/L	69 (59–81)	68 (59–79)	69 (59–81)	0.45
Serum uric acid concentration, mmol/L	330 (279–390)	324 (274–383)	328 (280–379)	0.02

Values are mean ± standard deviation, median (interquartile range), or count (percentage) as appropriate. TIA, transient ischaemic stroke. Alcohol intake was defined as a per week volume of alcohol consumption of ≥5 g. Current smoking was defined as the present regular use of cigarettes (>1 per day) at the time of the study.

Institute, Cary, NC, USA). The log-rank test was used to compare the cumulative incidence of atrial fibrillation between various groups with the Kaplan–Meier survival function to show the time to incidence of atrial fibrillation. Because the systemic screening during follow-up was on annually or quarterly basis, we performed Cox regression in adjusted analyses to compute hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between the changes in the CHA_2DS_2-VAS_C score and atrial fibrillation, while accounting for the covariables including the randomization group of the trial. For all analyses, a two-sided *P*-value <0.05 was considered statistically significant.

Results

During a median follow-up of 2.1 years in 6806 participants [2982 (43.8%) men, mean age ± standard deviation of 71.4 ± 6.2 years, and mean CHA_2DS_2-VAS_C score of 2.8 ± 1.2, *Table 1*], the CHA_2DS_2-VAS_C score remained unchanged in 4827 individuals and increased by 1 and ≥2 in 1752 and 227 individuals, respectively. The corresponding number of incident cases of atrial fibrillation was 39, 22, and 12, respectively, corresponding to an atrial fibrillation detection rate of 0.8%, 1.3%, and 5.3%, respectively. The incidence rate of atrial fibrillation increased from 4.2 per 1000 person-years in participants with a change in the CHA_2DS_2-VAS_C score of 0 to 6.4 and 25.8 per 1000 person-years in participants with a change in the CHA_2DS_2-VAS_C score of 1 and ≥2, respectively. After adjustment for baseline CHA_2DS_2-VAS_C score, body mass index, current smoking and alcohol intake, fasting plasma glucose and serum total cholesterol, creatinine and uric acid, the HRs for the incidence of atrial fibrillation in participants with a change in CHA_2DS_2-VAS_C score of 1 and ≥2 vs. those with a change in CHA_2DS_2-VAS_C score of 0 was 1.53 (95% CI 0.91–2.58, *P* = 0.11) and 6.23 (95% CI 3.26–11.90, *P* < 0.0001, Figure *1*), respectively.

Discussion

Our study showed a significant association between changes of CHA_2DS_2-VAS_C score and the incidence of atrial fibrillation in older individuals. A change in the CHA_2DS_2-VAS_C score of ≥2 was associated with a significantly elevated risk of incident atrial fibrillation. CHA_2DS_2-VAS_C score has been found useful in predicting stroke risk of new-onset atrial fibrillation and the risk of new-onset atrial fibrillation.[7] Some of the cardiovascular risk factors that constitute the CHA_2DS_2-VAS_C score change over time, especially in the elderly population. Indeed, in our study, in addition to advancing age (21% of the increments of the score), the prevalence of hypertension also increased from 55.7 to 75.0% during follow-up (59% of the increments of the score, *Figure 2*). In participants with an increase of

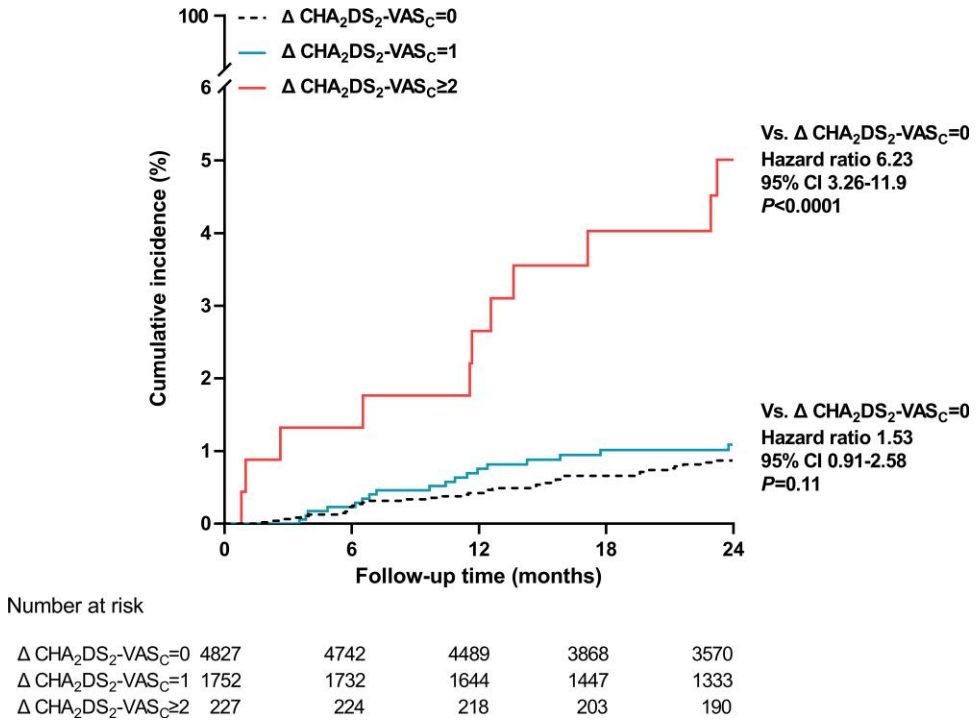


Figure 1 Cumulative incidence of atrial fibrillation according to dynamic CHA_2DS_2-VAS_C score.

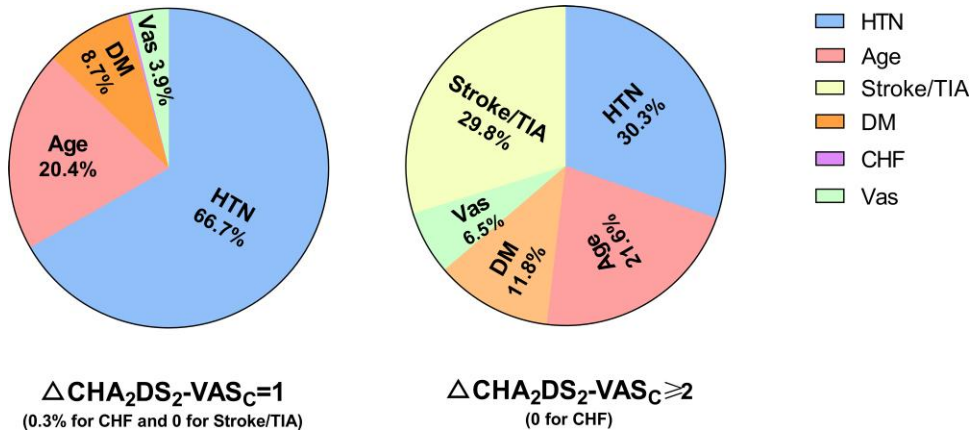


Figure 2 Contribution in the percentage of various components to the changes of the CHA_2DS_2-VAS_C score of 1 and ≥2, respectively. △CHA_2DS_2-VAS_C, the change in the CHA_2DS_2-VAS_C score from baseline to end-of-study visit. HTN, hypertension; DM, diabetes mellitus; TIA, transient ischaemic attack; CHF, congestive heart failure; Vas, vascular disease.

CHA_2DS_2-VAS_C score of 1, the contribution in percentage was 66.7, 20.4, 8.7, and 3.9% for hypertension, age, diabetes mellitus, and vascular disease, respectively, while in participants with an increase of CHA_2DS_2-VAS_C score of ≥2, it was 30.3, 29.8, 21.6, 11.8, and 6.5% for hypertension, stroke/TIA/thromboembolism, age, diabetes mellitus, and vascular disease, respectively. Atrial fibrillation increases disproportionally in older adults, rendering age one of the best predictors of atrial fibrillation.[8] Risk factors are dynamic and given the elderly population with multiple co-morbidities, the CHA_2DS_2-VAS_C score needs to be re-evaluated at each clinical review. With the increasing availability of big data and artificial intelligence technology, regular re-assessments of cardiovascular risk factors are increasingly feasible. For those who have changes in the CHA_2DS_2-VAS_C score of ≥2 over time, particularly associated with the development of hypertension, are more likely to develop atrial fibrillation, hence more frequent repeats of single-timepoint

screening or continuous monitoring (e.g. prolonged Holter monitoring or a wearable-patch[9]) might be worthwhile to detect atrial fibrillation.

Our study had a number of limitations. The number of incident cases of atrial fibrillation was relatively small. In addition, our analysis was based on the data from a randomized, controlled trial that had limited cardiac evaluations. We did not perform echocardiography. The possibility of unmeasured confounders cannot be entirely excluded.

In conclusion, our study in an elderly Chinese population showed a significantly increased risk of incident atrial fibrillation in participants with a change in CHA_2DS_2-VAS_C score of ≥2 over 2 years. Our findings suggest that patients with substantial changes in the CHA_2DS_2-VAS_C score are more likely to develop incident atrial fibrillation, and regular re-assessments of cardiovascular risk factors in the elderly are worthwhile to improve detection of atrial fibrillation. Further research is needed to address this important research question.

Lead author biography

Wei Zhang is a PhD student in Cardiovascular Medicine at Shanghai Jiao Tong University, China. He received his B.S. degree in Medicine at Chongqing Medical University, Chongqing, China, in 2017 and the M.S. degree in Medicine at Shanghai Jiao Tong University, School of Medicine, Shanghai, China, in 2020. His research covers a wide area of cardiovascular health, but to some extent focuses on hypertension, diabetes mellitus, and atrial fibrillation.

Data availability

Data cannot be shared publicly because of ethical restrictions. Data are available from Ruijin Hospital Ethics Committee (contact via wyfkjc@163.com) for researchers who meet the criteria for access to confidential data.

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Conflict of interest: Dr J.-G.W. reports receiving lecture and consulting fees from Novartis, Omron, Servier, and Viatris.

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