Changes in the CHA₂DS₂-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 CHA₂DS₂-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 CHA₂DS₂-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 in decreased from 4.2 per 1000 person-years in participants with a change in the CHA₂DS₂-VAS c score of 0 to 6.4 and 25.8 per 1000 person-years in participants with a change in the CHA₂DS₂-VAS c score of 1 and ≥2, respectively. A change in the CHA₂DS₂-VAS c score of ≥2 was associated with a significantly elevated risk of incident atrial fibrillation.

Conclusions
Patients with substantial changes in the CHA₂DS₂-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**

Changes in the CHA$_2$DS$_2$-VAS$_C$ score as a predictor of incident atrial fibrillation

During a median follow-up of 2.1 years in 6606 older (≥ 65 years) participants with sinus rhythm at baseline, the overall incidence rate of AF was 5.5 per 1000 person-years.

Factors associated with $\Delta$CHA$_2$DS$_2$-VAS$_C$

1. Age
2. HTN
3. Stroke/TIA
4. DM
5. CHF
6. Valve

$\Delta$CHA$_2$DS$_2$-VAS$_C$ score on the change in the CHA$_2$DS$_2$-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.

AF incidence according to $\Delta$CHA$_2$DS$_2$-VAS$_C$

- Reference
- HR=1.53, 95% CI 0.91-2.58, P=0.11
- $\geq$2
  - HR=6.23, 95% CI 3.26-11.90, P<0.0001

**Keywords**

Incident atrial fibrillation • Screening • CHA$_2$DS$_2$-VAS$_C$ score • Hypertension • Risk factor

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**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. Given this relationship with both age and cardiovascular co-morbidities, which are part of the CHA$_2$DS$_2$-VAS$_C$ score, we hypothesized that the dynamic changes resulting in an increase in the CHA$_2$DS$_2$-VAS$_C$ score over time would improve the efficiency of predicting incident atrial fibrillation on repeated screening after a negative test. CHA$_2$DS$_2$-VAS$_C$ score is a recommended tool to guide decisions on the use of oral anticoagulants to prevent stroke in atrial fibrillation. 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. Opportunistic screening in patients contacting the health system and ≥65 years of age has been recommended in many atrial fibrillation guidelines. 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. In an analysis of the AF-CATCH trial [quarterly vs. annual electrocardiogram (ECG) screening for atrial fibrillation in older Chinese individuals] data, we investigated the association between the changes in the CHA$_2$DS$_2$-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$_2$DS$_2$-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 Institute, Cary, NC).
Table 1  Baseline characteristics

| Characteristic                        | △CHA2DS2-VASC = 0 (n = 4827) | △CHA2DS2-VASC = 1 (n = 1752) | △CHA2DS2-VASC ≥ 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 CHA2DS2-VASC score          | 3 (2–4)                      | 2 (2–3)                       | 2 (1–3)                       | <0.0001 |
| Body mass index, kg/m²               | 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    |
| 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.

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 CHA2DS2-VASC score of 2.8 ± 1.2. Table 1], the CHA2DS2-VASC 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 CHA2DS2-VASC score of 0 to 6.4 and 25.8 per 1000 person-years in participants with a change in the CHA2DS2-VASC score of 1 and ≥2, respectively. After adjustment for baseline CHA2DS2-VASC 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 CHA2DS2-VASC score of 1 and ≥2 vs. those with a change in CHA2DS2-VASC 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 CHA2DS2-VASC score and the incidence of atrial fibrillation in older individuals. A change in the CHA2DS2-VASC score of ≥2 was associated with a significantly elevated risk of incident atrial fibrillation. CHA2DS2-VASC score has been found useful in predicting stroke risk of new-onset atrial fibrillation and the risk of new-onset atrial fibrillation. Some of the cardiovascular risk factors that constitute the CHA2DS2-VASC 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...
CHA2DS2-VASC 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 CHA2DS2-VASC 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.

Risk factors are dynamic and given the elderly population with multiple co-morbidities, the CHA2DS2-VASC 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 CHA2DS2-VASC 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

Figure 1 Cumulative incidence of atrial fibrillation according to dynamic CHA2DS2-VASC score.

Figure 2 Contribution in the percentage of various components to the changes of the CHA2DS2-VASC score of 1 and ≥2, respectively. △CHA2DS2-VASC, the change in the CHA2DS2-VASC score from baseline to end-of-study visit. HTN, hypertension; DM, diabetes mellitus; TIA, transient ischaemic attack; CHF, congestive heart failure; Vas, vascular disease.
screening or continuous monitoring (e.g. prolonged Holter monitoring or a wearable-patch\(^3\)) 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\(_2\)DS\(_2\)-VAS\(_c\) score of \(\geq 2\) over 2 years. Our findings suggest that patients with substantial changes in the CHA\(_2\)DS\(_2\)-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.

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### Conflict of interests

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

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