

Postoperative atrial fibrillation: Prediction of subsequent recurrences with clinical risk modeling and artificial intelligence electrocardiography



Alanna M. Chamberlain, PhD,^{*,†} Nicholas P. Bergeron, MD,[‡] Abdullah K. Al-Abcha, MD,^{*} Susan A. Weston, MS,[†] Ruoxiang Jiang, BS,[†] Zach I. Attia, PhD,^{*} Paul A. Friedman, MD, FHRS,^{*} Bernard J. Gersh, MB, ChB, DPhil, FHRS,^{*} Peter A. Noseworthy, MD, MBA, FHRS,^{*} Konstantinos C. Siontis, MD, FHRS^{*}

From the ^{*}Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, [†]Department of Quantitative Health Sciences, Mayo Clinic, Rochester, Minnesota, and [‡]Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota.

Introduction

Postoperative atrial fibrillation (POAF) after noncardiac surgery comprises approximately 13% of all new atrial fibrillation (AF) diagnoses in the community and has been associated with increased risk of subsequent stroke and transient ischemic attack compared to patients without a history of AF.^{1–3} However, the management of POAF after noncardiac surgery, including the indications and approaches to ambulatory rhythm monitoring and oral anticoagulation (OAC) for stroke prophylaxis, remains uncertain. Recent data have also demonstrated that AF tends to recur in about one-third of patients with POAF within the first year of the index POAF episode.⁴ Patients at risk for recurrent AF during follow-up are most likely to benefit from OAC. However, there are currently no established approaches to predicting subsequent AF after the initial POAF episode in patients undergoing noncardiac surgery.

The CHARGE-AF (Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation) risk model was developed to predict incident AF based on clinical information using community-based cohorts from the United States and Europe.⁵ Furthermore, a recently developed artificial intelligence–enhanced electrocardiography (AI-ECG) model using deep-learning convolutional neural network methodology has been shown to predict subclinical AF from the standard 12-lead ECG.⁶ However, the performance of CHARGE-AF or the AI-ECG model in predicting subsequent AF after initial POAF episode has not been established.

The purpose of this study was to assess whether among patients with POAF associated with noncardiac surgery, a clinical risk score designed to predict AF (CHARGE-AF) and an AI-ECG model designed to identify the signature of AF on the sinus rhythm ECG would be able to classify risk for subsequent AF. Additionally, it was hypothesized that a combined approach of AI-ECG with the CHARGE-AF model would be able to determine those most at risk compared to either independent scoring system.

Methods

The cohort originated from a Rochester Epidemiology Project study of 452 patients with POAF <30 days after noncardiac surgery (2000–2013). Approximately one-quarter of patients underwent orthopedic surgeries, and another quarter underwent gastrointestinal surgeries, followed by thoracic/pulmonary (excluding large vessel) in 21%, urogenital in 6.9%, neurosurgical in 6.4%, and other in 16.7%.¹ In the current analysis, 340 patients with POAF who had at least 1 standard, digitally stored, 10-second, 12-lead ECG in sinus rhythm within 30 days before the surgery date, who survived ≥30 days after the surgery, and who granted Minnesota research authorization for use of their medical records for research were included. The previously developed AI-ECG model for AF prediction was applied to each patient's sinus rhythm ECG closest to the surgical date.⁶ In addition, each individual's CHARGE-AF score predicting the 5-year risk of AF was calculated. Variables included age, race, height, weight, systolic and diastolic blood pressures, current smoker, antihypertensive medications, diabetes, history of myocardial infarction and history of heart failure. Thirty-two subjects had missing data for at least 1 of the variables and were excluded from the analyses, resulting in a cohort of 308 patients. Patients were followed from the date of POAF until subsequent AF (manually validated based on ECG documentation at least 30 days after the

KEYWORDS Artificial intelligence; CHARGE-AF score; Electrocardiography; Postoperative atrial fibrillation; Predictive modeling (Cardiovascular Digital Health Journal 2024;5:111–114)

Address reprint requests and correspondence: Dr Konstantinos Siontis, Department of Cardiovascular Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905. E-mail address: siontis.konstantinos@mayo.edu.

KEY FINDINGS

- Patients with postoperative atrial fibrillation (POAF) after noncardiac surgery are at risk for recurrent subsequent atrial fibrillation (AF). However, uncertainty exists regarding the optimal utilization of anticoagulation and rhythm monitoring strategies in patients with POAF.
- In this analysis, the top tertiles of both the CHARGE-AF (Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation) score and an AF artificial intelligence–enhanced electrocardiography (AI-ECG) model, a deep-learning model previously developed to predict subclinical AF from the standard 12-lead ECG, were associated with higher incidences of subsequent AF compared to the other tertiles.
- However, both scoring systems, each alone and combined, demonstrated only modest discriminating value for prediction of subsequent AF after POAF.

occurrence of POAF), death, last follow-up, or December 31, 2018, whichever occurred first. Kaplan-Meier curves for time to subsequent AF were presented for tertiles of the CHARGE-AF and AI-ECG scores. *C*-statistics were calculated for predicting subsequent AF from Cox models with the AI-ECG score, the CHARGE-AF score, and both scores together as predictors. The research reported here adhered to the Helsinki Declaration (as revised in 2013).

Results

During a median [interquartile range] follow-up of 2.8 [0.7–5.7] years, 156 patients with POAF had subsequent AF at least 30 days after their POAF episode. The risk of subsequent AF differed by tertiles of CHARGE-AF score

(Figure 1A) and by tertiles of AI-ECG score (Figure 1B). Event rates for subsequent AF after POAF for tertiles of the CHARGE-AF score and AI-ECG score are given in Table 1. The rate of subsequent AF was 87.16 per 1000 person-years for tertile 1 of CHARGE-AF score and increased to 198.51 per 1000 person-years for tertile 3. For AI-ECG score, the corresponding rates were 90.93 and 226.00 per 1000 person-years for tertiles 1 and 3, respectively. The *C*-statistics for predicting subsequent AF were similar for the CHARGE-AF score (0.59) and the AI-ECG score (0.59) (Figure 2). With the combined AI-ECG+CHARGE-AF model, the *C*-statistic was 0.61. There was no difference between CHARGE-AF vs CHARGE-AF+AI-ECG ($P = .53$) or AI-ECG vs CHARGE-AF+AI-ECG ($P = .19$) models. Results for CHARGE-AF were not different when treating each of the score's components as a separate variable in the prognostic analysis.

Discussion

Uncertainties in POAF management after noncardiac surgery remain. Distinguishing POAF patients who are at greatest risk for recurrent AF from those having an isolated POAF episode triggered by perioperative stress is important in guiding management decisions such as OAC and intensity of rhythm monitoring. A tool to discriminate between isolated one-off POAF from POAF with a high likelihood of recurrence does not exist. In this analysis, the top tertiles of both the AI-ECG and CHARGE-AF scores were associated with higher incidences of subsequent AF compared to the other tertiles. However, AI-ECG did not improve the prediction of subsequent AF after POAF above and beyond the CHARGE-AF score. Both scoring systems alone and in combination showed, at best, modest discriminating value. This is in contrast to incident AF occurring in the community outside of the perioperative setting in which both CHARGE-AF and

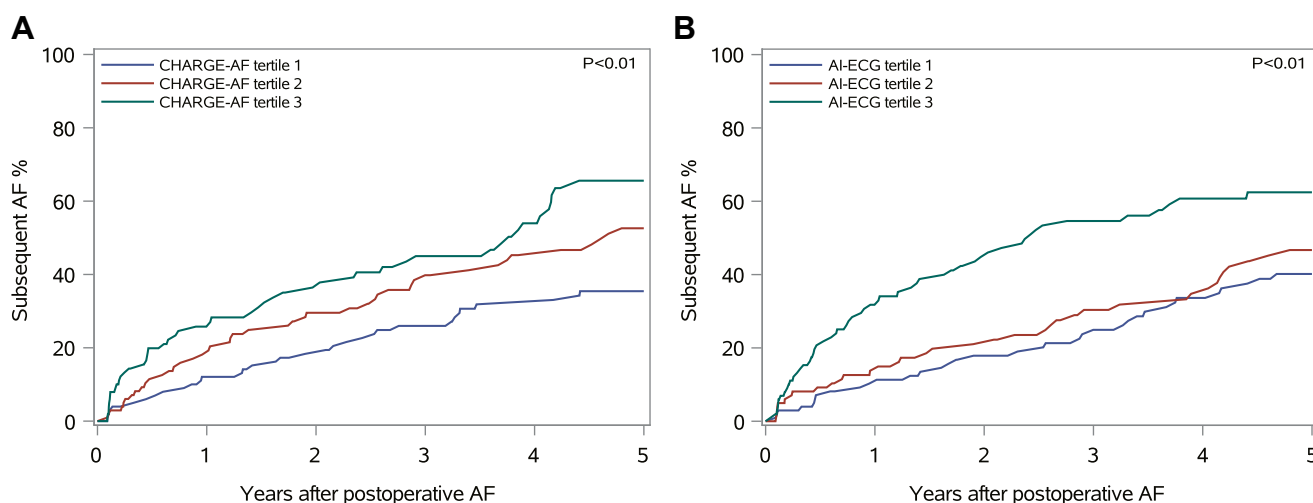


Figure 1 Time to subsequent atrial fibrillation by tertiles of CHARGE-AF score (A) and AI-ECG score (B) among patients with atrial fibrillation within 30 days after noncardiac surgery. AF = atrial fibrillation; AI-ECG = artificial intelligence–enhanced electrocardiography; CHARGE-AF = Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation.

Table 1 Event rates of subsequent AF by tertiles of CHARGE-AF score and AI-ECG score among patients with AF within 30 days after noncardiac surgery

	CHARGE-AF score			AI-ECG score		
	Tertile 1	Tertile 2	Tertile 3	Tertile 1	Tertile 2	Tertile 3
No. of patients	102	103	103	102	103	103
No. of deaths	48	72	93	57	80	76
No. of subsequent AF*	48	55	53	48	46	62
Follow-up (y) (median [interquartile range])	6.94 [4.19–11.62]	5.20 [2.21–7.93]	3.37 [1.00–5.36]	6.84 [3.45–11.01]	4.42 [1.42–7.35]	3.71 [1.64–6.62]
Rate per 1000 person-years (95% CI)	87.16 (64.26–115.56)	141.37 (106.5–184.01)	198.51 (148.7–259.66)	90.93 (67.04–120.56)	113.71 (83.25–151.67)	226 (173.27–289.72)
One-year probability of event (%) (95% CI)	12.07 (5.42–18.25)	18.15 (9.93–25.62)	25.77 (16.26–34.20)	10.26 (4.02–16.09)	13.77 (6.50–20.47)	31.77 (21.64–40.58)

AF = atrial fibrillation; AI-ECG = artificial intelligence-enhanced electrocardiography; CHARGE-AF = Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation; CI = confidence interval.
*AF > 30 days after index date (postoperative AF episode).

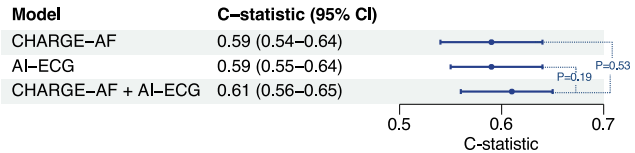


Figure 2 C-statistics for prediction of subsequent atrial fibrillation among patients with atrial fibrillation within 30 days after noncardiac surgery. CI = confidence interval; other abbreviation as in Figure 1.

AI-ECG have shown superior discrimination predictive performances.^{5–7}

In the paradigm of AI modeling, we previously demonstrated that the AI-ECG algorithm that was originally developed for prediction of AF in all-comers resulted in lower performance when tested for the prediction of POAF.⁸ Similarly, CHARGE-AF was developed in the outpatient setting and has not been previously validated in inpatients or for POAF specifically. These data highlight that the distinct pathophysiology of POAF may not be encapsulated in the parameters of otherwise well-performing models for AF prediction. Extrapolation of model performance to settings different from those in which a model was developed should be done with caution.

Furthermore, the results of this analysis suggest that a general AI-ECG model may not be well suited in every clinical scenario and that a dedicated scoring system (AI-ECG, clinical risk factor-based, or combined) is needed to identify those at highest risk of developing subsequent AF after POAF. Analysis of preoperative ECGs in sinus rhythm in conjunction with immediate postoperative ECGs in AF or sinus rhythm might further improve the performance of AI predictive modeling. Of note, AI-ECG may have the advantage of easy acquisition and repeatability as an objective measure of the dynamic AF risk at multiple time points before and/or after surgery. These practical issues of predictive modeling for POAF after noncardiac surgery require evaluation in prospective implementation studies.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. This study used the resources of the Rochester Epidemiology Project (REP) medical records-linkage system, which is supported by the National Institute on Aging (NIA; AG 058738), by the Mayo Clinic Research Committee, and by fees paid annually by REP users.

Disclosures

Drs Attia, Friedman, Noseworthy, and Siontis are inventors of AI-ECG algorithms. Mayo Clinic has licensed some of these algorithms to Anumana, Inc., with potential for commercialization. Dr Siontis has received research funding from Anumana, Inc., for work related to AI-ECG algorithms (via the institution). All other authors have no conflicts of interest to disclose.

Authorship

All authors attest they meet the current ICMJE criteria for authorship

References

1. Siontis KC, Gersh BJ, Weston SA, et al. Association of new-onset atrial fibrillation after noncardiac surgery with subsequent stroke and transient ischemic attack. *JAMA* 2020;324:871–878.
2. Siontis KC, Gersh BJ, Weston SA, et al. Associations of atrial fibrillation after noncardiac surgery with stroke, subsequent arrhythmia, and death: a cohort study. *Ann Intern Med* 2022;175:1065–1072.
3. Gialdini G, Nearing K, Bhavé PD, et al. Perioperative atrial fibrillation and the long-term risk of ischemic stroke. *JAMA* 2014;312:616–622.
4. McIntyre WF, Vadakken ME, Connolly SJ, et al. Atrial fibrillation recurrence in patients with transient new-onset atrial fibrillation detected during hospitalization for noncardiac surgery or medical illness: a matched cohort study. *Ann Intern Med* 2023;176:1299–1307.
5. Alonso A, Krijthe BP, Aspelund T, et al. Simple risk model predicts incidence of atrial fibrillation in a racially and geographically diverse population: the CHARGE-AF consortium. *J Am Heart Assoc* 2013;2:e000102.
6. Attia ZI, Noseworthy PA, Lopez-Jimenez F, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. *Lancet* 2019;394:861–867.
7. Noseworthy PA, Attia ZI, Behnken EM, et al. Artificial intelligence-guided screening for atrial fibrillation using electrocardiogram during sinus rhythm: a prospective non-randomised interventional trial. *Lancet* 2022;400:1206–1212.
8. Siontis KC, Noseworthy PA, Arghami A, et al. Use of artificial intelligence tools across different clinical settings: a cautionary tale. *Circ Cardiovasc Qual Outcomes* 2021;14:e008153.