American Journal of Hypertension, 2025, **XX**, 1–12
https://doi.org/10.1093/ajh/hpaf149
Advance access publication 9 August 2025
Original Article

Original Article

Factors Associated With New-Onset Atrial Fibrillation in Thai Adults with Hypertension

Varisa Limpijankit[1,*], Thinnakrit Sasiprapha, [2] Htun Teza, [3] Anuchate Pattanateepapon, [3] Sukanya Siriyotha, [3] Suparee Boonmanunt, [3] John Attia[4], and , Ammarin Thakkinstian[3]

[1]Chulalongkorn University International Medical Program, The Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[2]Division of Cardiology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
[3]Department of Clinical Epidemiology and Biostatistics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
[4]Centre for Clinical Epidemiology and Biostatistics, School of Medicine and Public Health, Faculty of Health and Medicine, University of Newcastle, and Hunter Medical Research Institute, New Lambton, NSW, Australia

[*]Corresponding author: Varisa Limpijankit (varisa.limpijankit@docchula.com).

BACKGROUND: Data on risk factors for new-onset atrial fibrillation (NOAF) in hypertensive Asian populations are limited. This study aimed to identify predictors of NOAF in Thai adults with hypertension (HTN).

METHODS: We conducted a retrospective cohort study of adults (≥18 years) newly diagnosed with HTN at Ramathibodi Hospital, Bangkok, from 2010 to 2023. Patients with prior AF or predisposing conditions (e.g., valvular disease and hyperthyroidism) were excluded. Baseline demographics, comorbidities, and medication use were analyzed as time-varying covariates using multivariable Cox models.

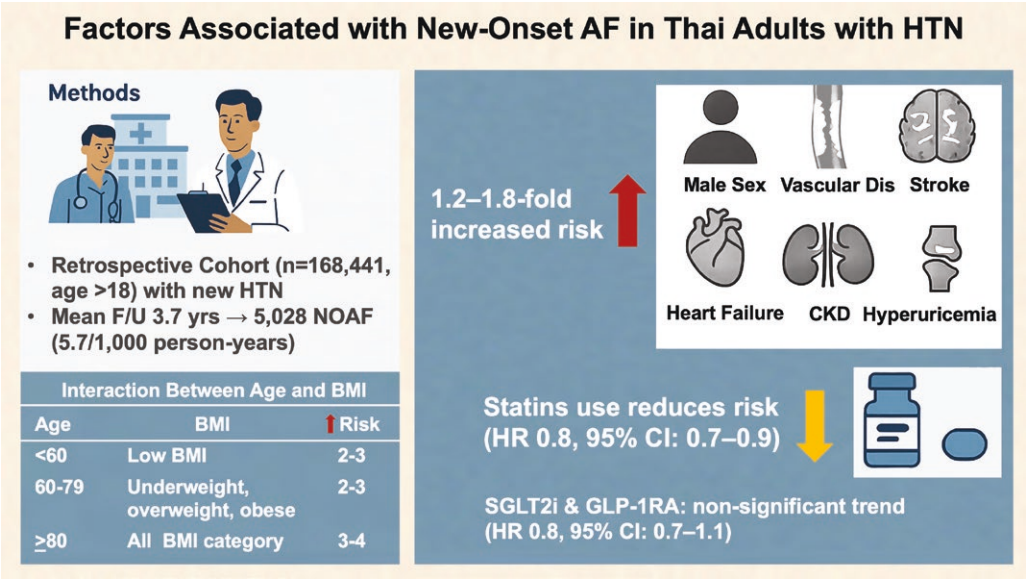
RESULTS: Of 293,798 hypertensive patients, 168,441 met the criteria. Over a median follow-up of 3.7 years, 5,028 developed NOAF (5.7 per 1,000 person-years). A significant interaction between age and body mass index (BMI) was observed. In patients <60 years, low BMI increased NOAF risk (HR: 2.3; 95% CI: 1.4–3.6), while overweight and obesity did not. In those ≥60–79 years, NOAF risk increased 2- to 3-fold in underweight, overweight, and obese individuals compared to normal BMI. In patients ≥80 years, the risk was 3- to 4-fold higher across all BMI categories. Male sex and comorbidities (vascular disease, stroke, heart failure, chronic kidney disease, and hyperuricemia) were associated with a 1.2–1.8-fold increased risk. Statin use reduced NOAF risk (HR: 0.8; 95% CI: 0.7–0.9), while SGLT2 inhibitors and GLP-1 receptor agonists showed a non-significant protective trend (HR: 0.8; 95% CI: 0.7–1.1).

CONCLUSIONS: In Thai hypertensive patients, older age, male sex, abnormal BMI, and comorbidities predict NOAF, while statin use may be protective. Further prospective studies are needed to confirm these findings.

Keywords: blood pressure; cohort; hypertension; new-onset atrial fibrillation; risk factors; statins; Thailand.

Received 2 July 2025; **revised** 29 July 2025; **accepted** 4 August 2025.

Graphical Abstract



Systemic arterial hypertension (HTN) is one of the most prevalent chronic non-communicable diseases worldwide and a leading contributor to cardiovascular (CV) disease and all-cause mortality.[1,2] According to the World Health Organization, HTN affects approximately 22% of the global population and 26% of individuals in Southeast Asia.[3] In Thailand, the 2019 National Health Survey reported that 25% of adults are hypertensive,[4] a condition responsible for nearly two-thirds of all strokes and half of all coronary artery disease (CAD) events.[5]

HTN is a well-established risk factor for atrial fibrillation (AF),[6,7] implicated in up to 50% of AF cases.[8] Chronic, uncontrolled HTN promotes the development of AF through a multifaceted pathophysiological process that includes structural remodeling (e.g., left ventricular hypertrophy, atrial enlargement, and fibrosis), electrical disturbances, neurohormonal dysregulation, and heightened sympathetic activity.[9,10] Furthermore, systemic inflammation, oxidative stress, and endothelial dysfunction—frequently observed in hypertensive patients—further facilitate the formation of an arrhythmogenic substrate that disrupts atrial function and promotes both the initiation and persistence of AF.[11–13] Notably, HTN increases the risk of developing AF by 1.8-fold and accelerates progression to permanent AF by 1.5-fold.[9]

The coexistence of HTN and AF significantly increases the risk of stroke, heart failure, and mortality,[10–14] highlighting the importance of early identification of individuals at high risk for new-onset AF (NOAF). Proactive interventions, including lifestyle modification and guideline-directed medical therapy for HTN, have the potential to delay or prevent AF onset and its associated complications.[15,16]

Although several AF risk prediction models have been developed, they are predominantly based on community cohorts from Western populations.[17–19] Only one—developed in the ESCARVAL (Estudio CARdiometabolico VALenciano)-RISK study—has been validated specifically for hypertensive individuals, identifying age, sex, obesity, and heart failure as key predictors of NOAF.[20] To improve risk stratification in Asian populations, the C_2HEST score was initially developed and validated in an Asian population and has since been applied in diverse ethnic populations, including non-Asian cohorts.[21] Incorporating CAD, chronic obstructive pulmonary disease, HTN, elderly age (≥75), systolic heart failure, and thyroid disease, the score demonstrated good predictive performance and outperformed the CHA2DS2-VASc scores in predicting incident AF.

AF is a complex, multifactorial condition influenced by aging, genetic predisposition, lifestyle factors, comorbidities, and concurrent treatment. However, the specific risk factors contributing to NOAF among hypertensive individuals in Asian populations remain poorly understood.[22] To address this gap, we conducted a large retrospective cohort study of Thai adults with HTN to identify factors associated with the development of NOAF, including demographic characteristics, comorbid conditions, and medication use.

METHODS

Study design and population

This retrospective cohort study utilized data from the Clinical Epidemiology and Biostatistics (CEB) HTN Data Warehouse at Ramathibodi Hospital, Mahidol University (Bangkok, Thailand). Data acquisition involved systematic extraction and linkage of records from the Ramathibodi Hospital Database, encompassing the period from January 1, 2010, to December 31, 2023. This dataset included comprehensive electronic medical records (EMRs) captured over the same interval. The study protocol was reviewed and approved by the Human Research Ethics Committee of Ramathibodi Hospital (COA.MURA 2024/681).

The Data Warehouse was constructed using three identification groups (Supplementary Figure 1): (i) patients identified solely on ICD-10 diagnosis codes for HTN (I10–I15); (ii) patients with both HTN diagnosis codes and prescriptions for antihypertensive medications, including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta-blockers(BBs),calciumchannelblockers(CCBs),diuretics,oralpha-blockers; (3) "inferred" HTN cases, defined as patients prescribed antihypertensive medications in the absence of a documented HTN diagnosis, provided there was no alternative indication for these medications (e.g., heart failure, cardiac arrhythmia, cirrhosis, benign prostatic hyperplasia).

Patients were included in the study if they met the following criteria: (i) age 18 years or older; (ii) newly diagnosed with uncomplicated HTN; and (iii) no prior diagnosis of AF, as confirmed by ICD-10 codes, ECG or Holter monitoring data, EMR review, and absence of prescriptions for oral anticoagulants (OACs). Patients were excluded if they had any predisposing conditions for AF, such as valvular heart disease or hyperthyroidism. To ensure proper follow-up, patients were required to have at least one follow-up visit occurring 30 days or more after the initial diagnosis, either in an outpatient clinic or during hospitalization.

To accurately identify newly diagnosed HTN cases, a 5-year washout period from 2005 to 2009 was applied, during which all available hospital records were reviewed. Only patients with no prior evidence of an HTN diagnosis or antihypertensive medication use during this period—and who received a new diagnosis from 2010 onward—were included in the final cohort.

Data collection

Demographic characteristics, body mass index (BMI), and comorbidities were collected at baseline and during follow-up using ICD-10 codes (Supplementary Table 1). Comorbidities included diabetes mellitus (DM), defined as fasting plasma glucose ≥126 mg/dL, HbA1c ≥6.5%, or the use of antidiabetic medications[23]; dyslipidemia, defined as total cholesterol ≥200 mg/dL, LDL-C ≥130 mg/dL, or the use of lipid-lowering therapy; and chronic kidney disease (CKD), defined by an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² on two separate occasions within 90 days. CV comorbidities included vascular diseases, such as CAD, peripheral artery disease, carotid or renal artery disease, and stroke.[24] Heart failure was defined by a left ventricular ejection fraction <40% or the use of guideline-directed medical therapy. Additional conditions included obstructive sleep apnea (OSA) and hyperuricemia, defined as serum uric acid >6 mg/dL in women or >7 mg/dL in men, or the use of urate-lowering medications. Where available, these data were cross-validated using additional sources within the CEB Warehouse.

Medication data were obtained from prescription records and pharmacy dispensing logs. These included antihypertensive agents, mineralocorticoid receptor antagonists (MRAs; e.g., spironolactone), antidiabetic medications (e.g., metformin, sulfonylureas, sodium-glucose cotransporter-2 inhibitors (SGLT2i), glucagon-like peptide-1 receptor agonists (GLP-1RA), insulin), statins, antiarrhythmic agents (e.g., amiodarone, digoxin, verapamil, and diltiazem), antiplatelets, and OACs. All medications were categorized by generic name and therapeutic class. Variables were treated as time-varying covariates up to the occurrence of NOAF.

The time-varying covariates included clinically relevant factors known to influence AF risk and that could change over the course of follow-up, based on data from both outpatient visits and hospitalizations. Specifically, the following variables were updated at each clinical encounter prior to AF onset or censoring: BMI, the occurrence of new comorbidities (e.g., DM, vascular disease, stroke, heart failure, dyslipidemia, CKD, and hyperuricemia), and adjustments to relevant medications (e.g., antihypertensives, antidiabetics, and statins).

Outcome and follow-up

The primary outcome was NOAF identified in both inpatient and outpatient settings, using data from the CEB-AF warehouse. Identification was based on ICD-10 codes, ECG/Holter monitoring reports, and prescriptions for OACs (Supplementary Figure 2). Records were matched using a hashed hospital ID and a date within 90 days. NOAF was confirmed if AF was documented by ECG or Holter monitoring, regardless of ICD coding, or if an ICD-coded AF diagnosis was accompanied by OAC use. For cases identified solely by ICD codes without OAC prescriptions, manual chart review was conducted. Patients were followed from the date of HTN diagnosis to the earliest of occurrence of NOAF diagnosis, death, or December 31, 2023. Time-to-event was calculated accordingly.

Statistical analysis

Continuous variables were reported as means ± standard deviations (SDs), and categorical variables as counts and percentages. Cox proportional hazards models with time-varying covariates were used to evaluate associations with NOAF. Covariates with $P < 0.20$ in univariate analysis were entered into a multivariate model, with final selection based on likelihood ratio tests. Interaction terms were assessed as appropriate. To address survival bias, a competing risk analysis using the Fine and Gray subdistribution hazard model was performed, treating all-cause death as a competing event. Sub-hazard ratios (SHRs) and 95% confidence intervals (CIs) were reported. In addition, a sensitivity analysis was conducted to assess the impact of BP control status—categorized as poor versus well-controlled—on the final model. Analyses were conducted using RStudio and STATA 18, with two-sided *P*-values <0.05 considered statistically significant.

RESULTS

Baseline characteristics

Of the 293,798 patients initially identified with HTN, 168,441 met the inclusion criteria and were included in the final analysis (Figure 1). Baseline characteristics were available for 63,045 patients and are summarized in Table 1. The cohort was predominantly female (58.7%), with a mean age of 59.5 ± 14.6 years. Nearly half (48.1%) were aged 60–79 years, and 8.2% were aged ≥80 years. Based on Asian BMI classifications, 36.8% were overweight (BMI > 23 kg/m²), and 33.4% were obese (BMI > 27 kg/m²). The prevalence of comorbidities at baseline included type 2 DM (20.4%), dyslipidemia (4.5%), CKD (13.2%), vascular disease (15.0%), heart failure (0.2%), stroke (4.2%), and hyperuricemia (13.1%).

At diagnosis, 61.3% of patients were prescribed antihypertensive medications—37.0% received monotherapy and 24.3% received combination therapy—while 38.7% were managed with lifestyle modification alone. MRAs were prescribed in 1.8% of cases. One-third of patients were treated with statins, and all diabetic patients were on antidiabetic medications, with only 1.2% receiving SGLT2 inhibitors or GLP-1 receptor agonists. Antithrombotic agents were prescribed in 18.4% (13.7% received antiplatelets and 4.7% oral anticoagulants), while 2.2% were on antiarrhythmic medications.

During follow-up, data were available for 99,408 patients. Compared to baseline, there was an increase in the prevalence of older age, overweight/obesity, and comorbidities including vascular disease (15.0% to 25.3%), stroke (4.2% to 5.9%), heart failure (0.2% to 1.0%), OSA (4.0% to 6.7%), and type 2 DM (19.1% to 27.2%). Use of statins and antidiabetic drugs increased, while the use of MRAs, antihypertensive agents, antithrombotic drugs, and antiarrhythmic medications remained relatively stable.

Incidence and predictors of NOAF

During a median follow-up of 3.7 years (range: 2.2–8.0), 5,028 of 168,441 patients (3.0%) developed NOAF, corresponding to an

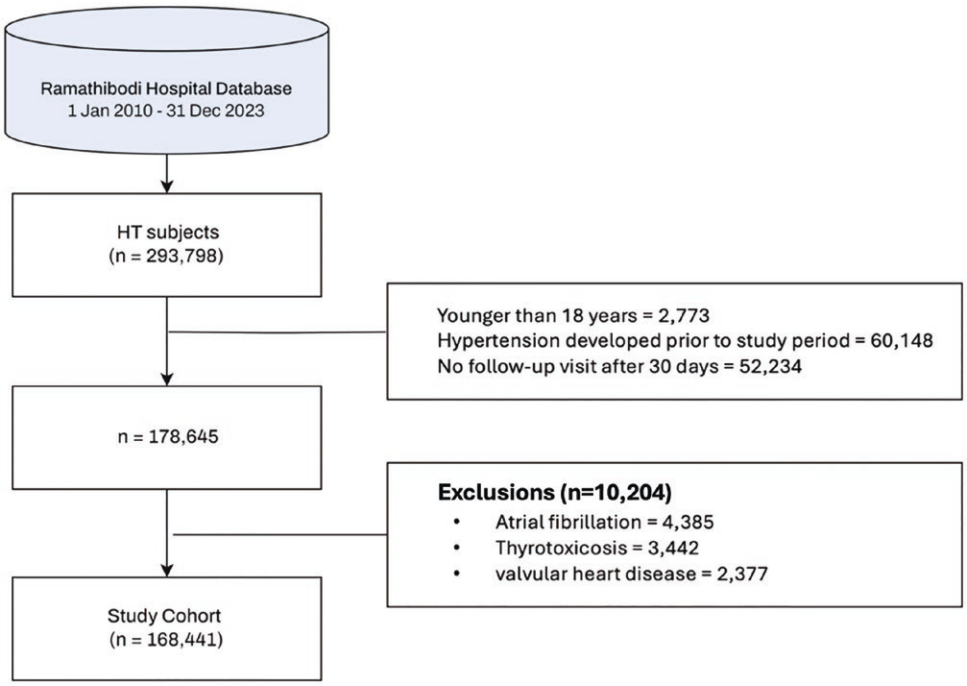


Figure 1. Study flowchart.

Table 1. Distribution of baseline and time-varying data.

Features	Baseline data (*n* = 168,441)	Time-varying data (*N* = 564,644)
Age, yrs, (mean ± SD)	59.5 ± 14.6	61.8 ± 14.2
<60 (%)	43.7	37.4
60–79 (%)	48.1	52.4
≥80, (%)	8.2	10.2
Female, (%)	58.7	58.7
Male, (%)	41.3	41.3
BMI, kg/m^2, (mean ± SD)	25.6 ± 4.8	26.2 ± 4.9
<18.5, (%)	4.1	3.2
18.5–22.9, (%)	25.7	22.4
23.0–26.9, (%)	36.8	36.3
≥27, (%)	33.4	38.2
Comorbidities		
Vascular disease, (%)	15.0	26.3
Stroke, (%)	4.2	5.9
Heart failure, (%)	0.2	1.0
Dyslipidemia, (%)	4.5	8.4
CKD, (%)	13.2	13.2
OSA, (%)	4.0	6.7
Hyperuricemia, (%)	13.1	13.4
Medications		
Antihypertensive (%)		
None	38.7	46.0
Monotherapy	37.0	30.3
Combination therapy	24.3	23.7
Type 2 DM (%)		
No	79.6	72.9
Yes, with other medications	19.2	24.9
Yes, with SGLT2i or GLP-1 agonist	1.2	2.3
MRAs, (%)	1.8	1.8
Statins, (%)	36.9	42.8
Antiarrhythmic agents, (%)	2.2	1.7
Anticoagulants, (%)	4.7	3.3
Antiplatelets, (%)	13.7	13.4

n = Number of patients; *N* = Number of observations.
Abbreviation: BMI, body mass index; CKD, chronic kidney disease; DM, diabetes mellitus; GLP, glucagon-like peptide; MRAs, mineralocorticoid receptor antagonists; OSA, obstructive sleep apnea; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

incidence rate of 5.7 per 1,000 person-years. Univariate analysis of time-varying covariates (n = 99,408) identified age as the most significant predictor (Table 2). Compared to patients under 60, those aged 60–79 had a hazard ratio (HR) of 2.4 (95% CI: 2.2–2.7), and those aged ≥80 had an HR of 6.4 (5.6–7.3). Male sex was associated with increased risk (HR 1.4 (1.3–1.5)). Notably, low BMI (<18.5 kg/m²) was associated with higher NOAF risk (HR 1.5 (1.2–1.8)), while overweight and obesity were associated with slightly lower risk (HRs ~0.9) compared to normal BMI.

Several comorbidities were associated with significantly increased NOAF risk, including vascular disease (HR 2.5 (2.3–2.7)), stroke (HR 1.9 (1.7–2.2)), heart failure (HR 5.2 (4.3–6.4)), OSA (HR 3.2 (2.9–3.5)), and hyperuricemia (HR 1.9 (1.7–2.1)).

Regarding treatment, combination antihypertensive therapy was more strongly associated with NOAF (HR 3.3 (3.0–3.6)) than

Table 2. Univariate analysis of time-varying covariates.

Factors	No AF (N = 163,415)	AF (N = 5,026)	Total time-at-risk	Incidence rate per 1,000 person-years	Hazard ratios
Age, yrs, (mean ± SD)	59.5 ± 14.6	68.3 ± 13.3			
<60	72,554	1,086	426806.6	2.5 (2.4, 2.7)	1
60–79	78,175	2,840	391592.4	7.2 (7.0, 7.5)	2.4 (2.2–2.7)
≥80	12,686	1,100	55825.8	19.7 (18.6, 20.9)	6.4 (5.6–7.3)
Female	96,392	2,410	524658.8	4.6 (4.4, 4.8)	1
Male	67,023	2,616	349566.1	7.5 (7.2, 7.8)	1.4 (1.3–1.5)
BMI, kg/m², (mean ± SD)	25.6 ± 4.8	24.6 ± 4.6			
<18.5	4,535	208	19050.31	10.92 (9.48, 12.51)	1.5 (1.2–1.8)
18.5–22.9	28,875	907	117698.22	7.71 (7.21, 8.22)	1
23.0–26.9	41,476	1,105	164563.62	6.71 (6.32, 7.12)	0.9 (0.8–1.0)
≥27	3,7844	793	146723.04	5.40 (5.04, 5.79)	0.9 (0.8–1.0)
Comorbidities					
Vascular disease, (%)					
No	139,512	3,641	772553.2	4.7 (4.6, 4.9)	1
Yes	23,903	1,385	101671.7	13.6 (12.9, 14.4)	2.5 (2.3–2.7)
Stroke, (%)					
No	156,775	4,629	846923.2	5.5 (5.3, 5.6)	1
Yes	6,640	397	27301.7	14.5 (13.1, 16.0)	1.9 (1.7–2.2)
Heart failure, (%)					
No	163,157	4,988	873594.2	5.7 (5.5, 5.9)	1
Yes	258	38	630.7	60.2 (42.6, 82.7)	5.2 (4.3–6.4)
CKD, (%)					
No	151,964	4,179	832365.7	5.0 (4.9, 5.2)	1
Yes	11,451	847	41859.2	20.2 (18.9, 21.6)	1.0 (0.8–1.1)
OSA, (%)					
No	156,742	4,891	850108.6	5.7 (5.6, 5.9)	1
Yes	6,673	135	24116.3	5.6 (4.7, 6.6)	3.2 (2.9–3.5)
Hyperuricemia, (%)					
No	142,401	3,947	776919.7	5.1 (4.9, 5.2)	1
Yes	21,014	1,079	97305.2	11.1 (10.4, 11.8)	1.9 (1.7–2.1)
Medications					
Antihypertensive, (%)					
None	64,126	1,127	445885.0	2.5 (2.4, 2.7)	1
Monotherapy	60,768	1,633	277052.9	5.9 (5.6, 6.2)	1.8 (1.6–2.0)
Combination therapy	38,521	2,266	151287.0	15.0 (14.4, 15.6)	3.3 (3.0–3.6)
Type 2 DM, (%)					
No	130,374	3,791	727897.7	5.2 (5.0, 5.4)	1
Yes, with other medications	31,036	1,169	141272.0	8.3 (7.8, 8.8)	1.2 (1.1–1.3)
Yes, with SGLT2i or GLP-1 agonist	2,005	66	5055.2	13.1 (10.1, 16.6)	1.4 (1.1–1.7)
MRAs, (%)					
No	160,824	4,633	862888.2	5.4 (5.2, 5.5)	1
Yes	2,591	393	11336.7	34.7 (31.3, 38.3)	3.6 (3.0–4.3)
Statins, (%)					
No	103,768	2,493	613140.7	4.1 (3.9, 4.2)	1
Yes	59,647	2,533	261084.2	9.7 (9.3, 10.1)	1.5 (1.4–1.6)
Antiarrhythmic agents, (%)					
No	160,671	4,010	860013.8	4.67 (4.53, 4.82)	1
Yes	2,744	1,006	14211.12	70.79 (66.48, 75.30)	6.5 (5.6–7.6)
Anticoagulants, (%)					
No	157,038	3,422	841556.74	4.07 (3.93, 4.20)	1
Yes	6,377	1,604	32668.17	49.10 (46.73, 51.56)	9.8 (8.8–10.8)
Antiplatelets, (%)					
No	141,988	3,347	763054.29	4.39 (4.24, 4.54)	1
Yes	21,427	1,679	111170.63	15.10 (14.39, 15.84)	2.3 (2.1–2.6)

Abbreviations as in Table 1.

monotherapy (HR 1.8 (1.6–2.0)) when compared to no treatment. Additional medications associated with increased NOAF risk included MRAs (HR 3.6 (3.0–4.3)), general antidiabetic medications (HR 1.2 (1.1–1.3)), and combined antidiabetic therapy with SGLT2i or GLP-1RA (HR 1.4 (1.1–1.7)). Statin use was also associated with increased risk (HR 1.5 (1.4–1.6)). Use of antithrombotic and antiarrhythmic agents was likewise linked to higher NOAF risk.

Multivariate analysis and interaction effects

Multivariate Cox regression (Table 3, Figure 2) identified 11 independent predictors of NOAF: older age, male sex, abnormal BMI, vascular disease, heart failure, CKD, stroke, hyperuricemia, type 2 DM, use of antihypertensive therapy, and statin use. An interaction between age and BMI was significant (likelihood ratio test: $\chi^2 = 17.1$, df = 6, $P = 0.009$) (Supplementary Table 2). Obese patients had a lower mean age (60.4 ± 13.3 years), while those with low BMI were older (64.1 ± 18.9 years) than patients with normal BMI (62.5 ± 15.5 years). The proportion of patients under 60 years was highest among those with obesity (41.5%), whereas those over 80 were most represented in the underweight group (24.2%).

Among patients with normal BMI, the strongest predictor of NOAF was age, followed by vascular disease, heart failure, CKD, hyperuricemia, and stroke. In patients under 60 with normal BMI, low BMI was significantly associated with increased NOAF risk [HR 2.3 (1.4–3.6)], while overweight and obesity were not significantly associated (HRs 1.1 and 0.8, respectively). In patients aged ≥60, the risk of NOAF increased approximately 2- to 3-fold in those who were underweight, overweight, or obese (vs. normal BMI), and by 3- to 4-fold in patients aged ≥80 across all BMI categories.

Comorbidities such as vascular disease, heart failure, CKD, hyperuricemia, and stroke remained strong predictors (HRs 1.2–1.8). Antihypertensive monotherapy and combination therapy

Table 3. Factors associated with AF using time-varying data: a multivariate Cox proportional hazards model.

Features		Time-varying data
Age group, yrs	**BMI**	
<60	18.5–22.9	1
60–79	18.5–22.9	2.2 (1.7–2.9)
≥80	18.5–22.9	4.2 (3.2–5.5)
Age group, yrs	BMI, kg/m^2	
<60	<18.5	2.3 (1.4–3.6)
<60	18.5–22.9	1
<60	23–26.9	1.1 (0.8–1.4)
<60	≥27	0.8 (0.6–1.1)
Age	BMI	
60–79	<18.5	3.2 (2.2–4.6)
60–79	23–26.9	1.7 (1.4–2.2)
60–79	≥27	2.0 (1.6–2.6)
≥80	<18.5	4.3 (2.8–6.5)
≥80	23–26.9	3.9 (3.0–5.1)
≥80	≥27	3.6 (2.8–4.8)
Female		1
Male		1.4 (1.2–1.5)
Comorbidities		
Vascular disease		
No		1
Yes		1.8 (1.6–1.9)
Stroke		
No		1
Yes		1.2 (1.0–1.4)
Heart failure		
No		1
Yes		1.7 (1.4–2.1)
CKD		
No		1
Yes		1.6 (1.5–1.8)
Hyperuricemia		
No		1
Yes		1.3 (1.1–1.4)
Medications		
Antihypertensive		
None		1
Monotherapy		1.7 (1.5–1.9)
Combination therapy		2.4 (2.1–2.7)
Type 2 DM		
No		1
Yes, with other medications		1.0 (0.9–1.1)
Yes, with SGLT2i or GLP-1 agonist		0.8 (0.7–1.1)
Statins		
No		1
Yes		0.8 (0.7–0.9)

n = Number of patients; *N* = Number of observations.
Abbreviations as in Table 1.

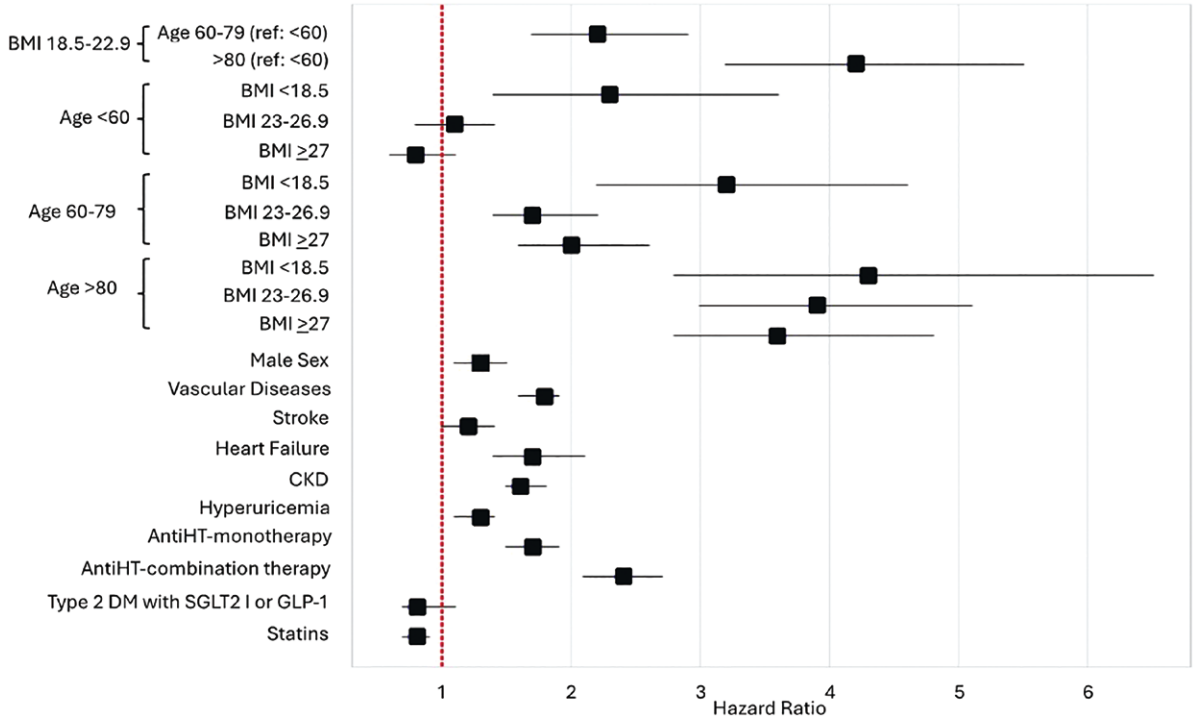


Figure 2. Forest plot of factors associated with AF in hypertension: a multivariable time-varying Cox model.

were associated with 1.7-fold and 2.4-fold increases in NOAF risk, respectively. In contrast, statin use was linked to a 20% reduction in risk (HR 0.8 (0.7–0.9)). Combined antidiabetic therapy including SGLT2i or GLP-1RA showed a non-significant protective trend (HR 0.8 (0.7–1.1)).

Sensitivity analysis

In the competing risk model (Supplementary Table 3), the overall death rate was 1.5 per 1,000 person-years. Subdistribution hazard ratios (SHRs) and 95% CIs were consistent with those obtained from the Cox model, confirming the robustness of our findings.

To evaluate the impact of BP control on the incidence of NOAF, patients were categorized as having poorly controlled BP (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg) or well-controlled BP (systolic BP < 140 mmHg and diastolic BP < 90 mmHg). As shown in Supplementary Table 4, the proportion of patients with poorly controlled BP increased over time. However, BP control status was not significantly associated with the risk of NOAF (HR: 1.01; 95% CI: 0.91–1.12; Supplementary Table 5). This suggests that BP control did not influence the risk of NOAF or alter the magnitude or direction of associations observed for other covariates in the final model (Table 3).

DISCUSSION

This large, real-world cohort study of 168,441 hypertensive patients in Thailand, with a median follow-up of 3.7 years, offers critical insights into the incidence and risk factors of NOAF. We identified eight factors associated with an increased risk of NOAF—some aligning with established literature, and others presenting novel or unexpected associations. These findings contribute valuable, population-specific data to the understanding of NOAF risk in Thai and Southeast Asian populations, providing a foundation for more tailored clinical management in these regions.

The incidence of NOAF in this cohort was 5.7 per 1,000 person-years, lower than global estimates ranging from 6.3 to 9.9 per 1,000 person-years.[17,25,26] This discrepancy may be due to differences in genetic background, healthcare access, lifestyle, HTN management practices, or the relatively short median follow-up period in our study compared to prior studies (3.7 vs. 7–10 years). A shorter follow-up may not fully capture the development of late-onset NOAF. Recent large-scale studies further support the need for region-specific risk assessment. Kim et al.[27] compared AF incidence and risk factors between White Europeans (UK Biobank) and Asians (Korean NHIS-HEALS) and found a higher AF incidence in Europeans, along with population-specific differences in risk factor strength. For example, BMI and smoking had a stronger association with AF risk in Europeans than in Asians. Similarly, Kang et al.[28] reported that East Asians experienced higher rates of ischemic, hemorrhagic, and AF-related stroke despite having lower BMI levels, suggesting a paradox potentially explained by differences in vascular biology, anticoagulation use, or healthcare infrastructure. These findings underscore the need for race- and region-specific risk stratification in AF. Despite a lower NOAF incidence in Asian populations, its strong association with adverse CV outcomes highlights the importance of long-term surveillance and early intervention. In hypertensive Asian patients, the high burden of AF-related stroke supports the use of tailored risk prediction and prevention strategies.

Consistent with previous studies,[17,20,22,29] older age and male sex were strong predictors of NOAF among hypertensive patients. In older individuals, atrial remodeling—characterized by fibrosis, loss of muscle mass, and disrupted cellular connectivity—creates a substrate conducive to AF. These structural changes, compounded by electrical remodeling and comorbidities more prevalent in men, explain much of the observed sex difference.[30,31] Future studies incorporating lifestyle factors, such as smoking and alcohol use, may help elucidate the biological and behavioral mechanisms driving these disparities. Clinically, our findings

support the need for early identification and intervention in older hypertensive men with multiple comorbidities to prevent NOAF and its sequelae.

Comorbid CV conditions, including vascular diseases, heart failure, and stroke, were also associated with an increased risk of NOAF. These conditions likely contribute to atrial dysfunction through mechanisms such as elevated left atrial pressure, altered hemodynamics, and structural remodeling. Notably, these factors are integral to the CHA_2DS_2-VASc score, which has been shown to correlate not only with stroke risk but also with incident AF.[32,33] Our results highlight the importance of holistic risk assessment and proactive management of comorbidities in hypertensive patients.

In line with previous studies,[34,35] CKD and hyperuricemia were independently associated with NOAF. CKD activates neurohormonal pathways (e.g., RAAS, sympathetic nervous system), induces oxidative stress, and promotes volume overload—each of which may facilitate AF development.[36] Hyperuricemia, often a consequence of CKD, exacerbates systemic inflammation and atrial fibrosis.[37] These findings underscore a potential role for uric acid-lowering agents as upstream therapies in AF prevention, especially in hypertensive patients with coexisting metabolic dysfunction.

Interestingly, patients on multiple antihypertensive medications showed a higher incidence of NOAF. While this may reflect more severe or treatment-resistant HTN, it could also be influenced by factors such as polypharmacy, medication interactions, autonomic dysregulation, or poor adherence. Some medications, like diuretics and alpha-blockers, may elevate AF risk via electrolyte imbalances or hypotensive episodes.[38,39] In contrast, ACEIs, ARBs, and BBs may offer protective effects through atrial remodeling and rate control.[40] Further investigation is warranted to determine the optimal antihypertensive regimens for AF prevention.

Whether well-controlled HTN can reduce the risk of NOAF remains a complex question. Our findings suggest that BP control status, as defined in this study, did not meaningfully influence AF risk. This contrasts with the findings from the Systolic Blood Pressure Intervention Trial (SPRINT),[41] which demonstrated that intensive BP control (target SBP < 120 mmHg) significantly reduced CV events, including AF, compared to standard BP targets. A key limitation of our study is the variability and limited reliability of office-based BP measurements in routine clinical practice. In particular, white coat HTN is frequently encountered in our setting, which may have contributed to misclassification and weakened the observed associations. Notably, the inclusion of BP control status did not materially alter the magnitude or direction of associations observed for other covariates in the final multivariable model. However, our findings should be interpreted in the context of prior evidence. In our study, the number of antihypertensive medications used remained relatively stable over time, suggesting limited titration or intensification of treatment. These findings underscore the importance of individualized HTN management, emphasizing not only achieving BP targets but also the optimization of drug selection and dosage adjustment to reduce AF risk, especially in older adults.

We also observed a significant protective association between statin use and NOAF. This aligns with previous reports linking statins to reduced incidence and recurrence of AF.[42,43] Beyond lipid-lowering, statins exert pleiotropic effects—anti-inflammatory, antifibrotic, and endothelial-stabilizing—that may mitigate atrial remodeling.[44] While promising, evidence remains inconclusive in non-ischemic populations.[45–47] Nevertheless, given their broader CV benefits, statins may be considered as part of a multifaceted AF prevention strategy in hypertensive patients, especially those with elevated atherosclerotic risk.[48]

Although the use of SGLT2i and GLP-1RA was associated with a trend toward reduced NOAF risk, the associations did not reach statistical significance. This may be due to limited sample size, as only 1.2% of patients were on these therapies. Mechanistically, both drug classes improve cardiovascular outcomes through anti-inflammatory, diuretic, and antifibrotic effects.[49–53] Meta-analyses of randomized controlled trials suggest a potential protective effect against AF,[54–56] but larger, well-powered studies are needed to evaluate their role in hypertensive populations.

A novel and clinically important finding was the age-specific relationship between BMI and NOAF. In individuals under 60, low BMI was associated with increased NOAF risk, whereas in those over 60, overweight and obesity were significant risk factors. This age-BMI interaction likely reflects differing mechanisms: in older adults, excess adiposity promotes atrial stretch, diastolic dysfunction, and systemic inflammation[29,57,58]; in younger individuals, underweight status may reflect frailty, malnutrition, or chronic illness, all of which can destabilize autonomic and cardiac electrical function. A large Korean cohort study of over 132,000 individuals reported a U-shaped association between BMI and AF risk, supporting our findings.[59]

Importantly, several studies across Asia have reported similar associations. A Taiwanese cohort study of over 64,000 patients with type 2 DM found that underweight individuals (BMI < 18.5) had the highest risk of AF, with a J-shaped relationship between BMI and AF incidence and a hazard ratio of 1.52, greater than that observed in obese individuals.[60] Similarly, a study from Guangzhou, China, reported that both underweight and obese patients experienced higher rates of AF recurrence following catheter ablation.[61] Collectively, these findings support a consistent U- or J-shaped association between BMI and AF across diverse Asian populations, underscoring underweight status as an independent and clinically significant risk factor for both incident and recurrent AF. These results emphasize the importance of age-specific BMI targets when assessing AF risk and reinforce the need to maintain a healthy BMI as part of AF prevention strategies.[62]

OSA, a known AF risk factor through mechanisms like intermittent hypoxia and sympathetic activation,[63,64] was not significantly associated with NOAF in our cohort. However, OSA is often underdiagnosed, particularly in resource-limited settings. Evidence shows that continuous positive airway pressure therapy reduces AF recurrence by up to 42%,[65] suggesting that improved screening and treatment of OSA may be an important, yet underutilized, component of AF prevention in hypertensive patients.

In summary, our study provides robust, region-specific evidence to inform NOAF prevention strategies in Asian hypertensive populations. It emphasizes the need for personalized, multifactorial approaches—optimizing BP control, managing comorbidities, maintaining a healthy weight, and judiciously using cardioprotective medications.

Study limitations

This study, the first large-scale investigation of NOAF risk factors in hypertensive Asian patients, has several limitations. First, as a retrospective cohort based in a tertiary care hospital, selection bias is possible; the patient population may not fully represent the broader Thai hypertensive population. Second, analyses were conducted using complete data from 99,408 of 168,441 patients, raising the potential for information bias due to missing

or inaccurate electronic health records. Third, despite adjusting for several key covariates, unmeasured confounding—particularly lifestyle factors such as diet, physical activity, smoking, and alcohol consumption—may have influenced the results. Fourth, while the findings are likely generalizable to similar healthcare settings in Thailand, extrapolation to other populations should be made cautiously, given regional variations in genetics, healthcare delivery, and social determinants of health. Lastly, the median follow-up duration of 3.7 years may have been insufficient to capture cases of late-onset NOAF, underscoring the need for extended follow-up in future studies.

CONCLUSIONS

In this large Thai cohort, older age, male sex, abnormal BMI (underweight or overweight/obese), and CV and metabolic comorbidities emerged as significant risk factors for NOAF among patients with HTN. Statin use was associated with a reduced risk, while the effects of SGLT2i and GLP-1RA require further investigation in larger and longer-term cohorts. These findings highlight the importance of individualized, comprehensive management strategies—including optimal BP control, weight management, and treatment of comorbidities—to prevent AF and improve CV outcomes. Prospective studies with longer follow-up are warranted to validate these findings and refine preventive strategies in this at-risk population.

Supplementary Data

Supplementary materials are available at *American Journal of Hypertension* (http://ajh.oxfordjournals.org).

Data Availability

The data supporting the findings of this study are not publicly available due to their sensitive nature. However, they can be obtained from the corresponding author upon reasonable request. The data are stored in a controlled-access repository at the Department of Clinical Epidemiology and Biostatistics (CEB), Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. Further information regarding the CEB Data Warehouse can be found at https://www.rama.mahidol.ac.th/ceb/CEBdatawarehouse/Overview.

Author Contributions

V.L. conceptualizations, methodology, data analysis, interpretation, and manuscript writing. T.S. methodology, study design, data acquisition, data analysis, interpretation, and manuscript revision. H.T. methodology, study design, data acquisition, data analysis, interpretation, and manuscript revision. A.P. methodology, data acquisition. S.S. methodology, and data acquisition. S.B. methodology, data acquisition. A.T. methodology, data analysis, interpretation, and manuscript revision. All authors read and approved the final manuscript.

Acknowledgments

The study team thanks Dr Arthur Brown for reviewing the manuscript and providing valuable comments, and the CEB Data Warehouse Working Group for their expert advice and support throughout this work.

Conflict of Interest

The authors declared no conflict of interest.

Funding

This work was supported by the National Research Council of Thailand (N42A640323).

REFERENCES

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol* 2020; 16:223–237. doi:10.1038/s41581-019-0244-2
2. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. *Circulation* 2016; 134:441–450. doi:10.1161/CIRCULATIONAHA.115.018912
3. World Health Organization. *Hypertension World Health Organization Newsroom*: World Health Organization (WHO) 2023. https://data.who.int/indicators/i/7DA4E68/608DE39?m49=764 (Updated 16 March 2023; Cited 29 March 2023).
4. Kunanon S, Chattranukulchai P, Chotruangnapa C, Kositanurit W, Methavigul K, Boonyasirinant T, Rawdaree P, Tejavanija S, Wataganara T, Satirapoj B, Roubsanthisuk W, Suwanwela NC, Sangwatanaroj S, Kunjara Na Ayudha R, Sitthisook S, Sukonthasarn A. 2019 Thai guidelines on the treatment of hypertension: executive summary. *J Med Assoc Thai* 2021; 104:1729–1738. doi:10.35755/jmedassocthai.2021.10.12199
5. World Health Organization. *Hypertension Care in Thailand: best practices and challenges, 2019*. World Health Organization Country Office for Thailand: Bangkok, 2019.
6. Aune D, Mahamat-Saleh Y, Kobeissi E, Feng T, Heath AK, Janszky I. Blood pressure, hypertension and the risk of atrial fibrillation: a systematic review and meta-analysis of cohort studies. *Eur J Epidemiol* 2023; 38:145–178. doi:10.1007/s10654-022-00914-0
7. Lee SR, Park CS, Choi EK, Ahn HJ, Han KD, Oh S, Lip GYH. Hypertension burden and the risk of new-onset atrial fibrillation: a nationwide population-based study. *Hypertension* 2021; 77:919–928. doi:10.1161/HYPERTENSIONAHA.120.16659
8. Healey JS, Connolly SJ. Atrial fibrillation: hypertension as a causative agent, risk factor for complications, and potential therapeutic target. *Am J Cardiol* 2003; 91:9G–14G. doi:10.1016/S0002-9149(03)00227-3
9. Ogunsua AA, Shaikh AY, Ahmed M, McManus DD. Atrial fibrillation and hypertension: mechanistic, epidemiologic, and treatment parallels. *Methodist DeBakey Cardiovasc J* 2015; 11:228–234. doi:10.14797/mdcj-11-4-228
10. Verdecchia P, Angeli F, Reboldi G. Hypertension and atrial fibrillation: doubts and certainties from basic and clinical studies. *Circ Res* 2018; 122:352–368. doi:10.1161/CIRCRESAHA.117.311402
11. Schulz E, Gori T, Münzel T. Oxidative stress and endothelial dysfunction in hypertension. *Hypertens Res* 2011; 34:665–673. doi:10.1038/hr.2011.39
12. Ihara K, Sasano T. Role of inflammation in the pathogenesis of atrial fibrillation. *Front Physiol* 2022; 13:862164. doi:10.3389/fphys.2022.862164
13. Maida CD, Vasto S, Di Raimondo D, Casuccio A, Vassallo V, Daidone M, Del Cuore A, Pacinella G, Cirrincione A, Simonetta I, Della Corte V, Rizzica S, Geraci G, Tuttolomondo A, Pinto A. Inflammatory activation and endothelial dysfunction markers

in patients with permanent atrial fibrillation: a cross-sectional study. *Aging (Milano)* 2020; 12:8423–8433. doi:10.18632/aging.103149
14. Aronow WS. Hypertension associated with atrial fibrillation. *Ann Transl Med* 2017; 5:457–457. doi:10.21037/atm.2017.10.33
15. Healey JS, Baranchuk A, Crystal E, Morillo CA, Garfinkle M, Yusuf S, Connolly SJ. Prevention of atrial fibrillation with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: a meta-analysis. *J Am Coll Cardiol* 2005; 45:1832–1839. doi:10.1016/j.jacc.2004.11.070
16. Larstorp ACK, Stokke IM, Kjeldsen SE, Hecht Olsen M, Okin PM, Devereux RB, Wachtell K. Antihypertensive therapy prevents new-onset atrial fibrillation in patients with isolated systolic hypertension: the LIFE study. *Blood Press* 2019; 28:317–326. doi:10.1080/08037051.2019.1633905
17. Schnabel RB, Sullivan LM, Levy D, Pencina MJ, Massaro JM, D'Agostino RB, Newton-Cheh C, Yamamoto JF, Magnani JW, Tadros TM, Kannel WB, Wang TJ, Ellinor PT, Wolf PA, Vasan RS, Benjamin EJ. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. *Lancet* 2009; 373:739–745. doi:10.1016/S0140-6736(09)60443-8
18. Chamberlain AM, Agarwal SK, Folsom AR, Soliman EZ, Chambless LE, Crow R, Ambrose M, Alonso A. A clinical risk score for atrial fibrillation in a biracial prospective cohort (from the Atherosclerosis Risk In Communities [ARIC] Study). *Am J Cardiol* 2011; 107:85–91. doi:10.1016/j.amjcard.2010.08.049
19. Alonso A, Krijthe BP, Aspelund T, Stepas KA, Pencina MJ, Moser CB, Sinner MF, Sotoodehnia N, Fontes JD, Janssens AC, Kronmal RA, Magnani JW, Witteman JC, Chamberlain AM, Lubitz SA, Schnabel RB, Agarwal SK, McManus DD, Ellinor PT, Larson MG, Burke GL, Launer LJ, Hofman A, Levy D, Gottdiener JS, Kääb S, Couper D, Harris TB, Soliman EZ, Stricker BH, Gudnason V, Heckbert SR, Benjamin EJ. 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. doi:10.1161/JAHA.112.000102
20. Orozco-Beltran D, Quesada JA, Bertomeu-Gonzalez V, Lobos-Bejarano JM, Navarro-Perez J, Gil-Guillen VF, Garcia Ortiz L, Lopez-Pineda A, Castellanos-Rodriguez A, Lopez-Domenech A, Cardona-Llorens AFJ, Carratala-Munuera C. A new risk score to assess atrial fibrillation risk in hypertensive patients (ESCARVAL-RISK Project). *Sci Rep* 2020; 10:4796. doi:10.1038/s41598-020-61437-w
21. Li YG, Pastori D, Farcomeni A, Yang PS, Jang E, Joung B, Wang YT, Guo YT, Lip GYH. A simple clinical risk score (C_2HEST) for predicting incident atrial fibrillation in Asian subjects: derivation in 471,446 Chinese subjects, with internal validation and external application in 451,199 Korean subjects. *Chest* 2019; 155:510–518. doi:10.1016/j.chest.2018.09.011
22. Krittayaphong R, Rangsin R, Thinkhamrop B, Hurst C, Rattanamongkolgul S, Sripaiboonkij N, Yindeengam A. Prevalence and associating factors of atrial fibrillation in patients with hypertension: a nation-wide study. *BMC Cardiovasc Disord* 2016; 16:57. doi:10.1186/s12872-016-0232-4
23. Looareesuwan P, Boonmanunt S, Siriyotha S, Lukkunaprasit T, Thammasudjarit R, Pattanaprateep O, Nimitphong H, Reutrakul S, Attia J, McKay G, Thakkinstian A. Retinopathy prediction in type 2 diabetes: time-varying Cox proportional hazards and machine learning models. *Inf Med Unlocked* 2023; 40:101285. doi:10.1016/j.imu.2023.101285
24. Lolak S, Attia J, McKay GJ, Thakkinstian A. Application of dragonnet and conformal inference for estimating individualized treatment effects for personalized stroke prevention: retrospective cohort study. *JMIR Cardio* 2025; 9:e50627. doi:10.2196/50627
25. Wilke T, Groth A, Mueller S, Pfannkuche M, Verheyen F, Linder R, Maywald U, Bauersachs R, Breithardt G. Incidence and prevalence of atrial fibrillation: an analysis based on 8.3 million patients. *Europace* 2013; 15:486–493. doi:10.1093/europace/eus333
26. Segan L, Canovas R, Nanayakkara S, Chieng D, Prabhu S, Voskoboinik A, Sugumar H, Ling L-H, Lee G, Morton J, LaGerche A, Kaye DM, Sanders P, Kalman JM, Kistler PM. New-onset atrial fibrillation prediction: the HARMS2-AF risk score. *Eur Heart J* 2023; 44:3443–3452. doi:10.1093/eurheartj/ehad375
27. Kim MH, Yang PS, Kim D, Jang E, Yu HT, Kim TH, Sung JH, Pak HN, Lee MH, Lip GYH, Joung B. Racial differences and similarities in atrial fibrillation epidemiology and risk factors in UK Biobank and Korean NHIS-HEALS cohort studies. *Heart Rhythm* 2025; 22:e277–e284. doi:10.1016/j.hrthm.2025.02.013
28. Kang DS, Yang PS, Kim D, Jang E, Yu HT, Kim TH, Sung JH, Pak HN, Lee MH, Lip GYH, Joung B. Racial differences in ischemic and hemorrhagic stroke: an ecological epidemiological study. *Thromb Haemost* 2024; 124:883–892. doi:10.1055/a-2278-8769
29. Heeringa J, van der Kuip DAM, Hofman A, Kors JA, van Herpen G, Stricker BHC, Stijnen T, Lip GYH, Witteman JCM. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J* 2006; 27:949–953. doi:10.1093/eurheartj/ehi825
30. Curtis AB, Rich MW. Atrial fibrillation in the elderly: mechanisms and management. *Heart Rhythm* 2007; 4:1577–1579. doi:10.1016/j.hrthm.2007.07.023
31. Westerman S, Wenger N. Gender differences in atrial fibrillation: a review of epidemiology, management, and outcomes. *Curr Cardiol Rev* 2019; 15:136–144. doi:10.2174/1573403X15666181205110624
32. Saliba W, Gronich N, Barnett-Griness O, Rennert G. Usefulness of CHADS2 and CHA2DS2-VASc Scores in the prediction of new-onset atrial fibrillation: a population-based study. *Am J Med* 2016; 129:843–849. doi:10.1016/j.amjmed.2016.02.029
33. Zhang W, Chen Y, Hu L-X, Xia J-H, Ye X-F, Cheng Y-B, Wang Y, Guo Q-H, Li Y, Lowres N, Freedman B, Wang JG; AF-CATCH Investigators and Coordinators. Changes in the CHA_2DS_2-VASC score as a predictor of incident atrial fibrillation in older Chinese individuals: the AF-CATCH study. *Eur Heart J Open* 2022; 2:1–5. doi:10.1093/ehjopen/oeac046
34. Horio T, Iwashima Y, Kamide K, Tokudome T, Yoshihara F, Nakamura S, Kawano Y. Chronic kidney disease as an independent risk factor for new-onset atrial fibrillation in hypertensive patients. *J Hypertens* 2010; 28:1738–1744. doi:10.1097/HJH.0b013e32833a7dfe
35. Gao Z, Shi H, Xu W, Guan Z, Su X, Guo N, Ma H. Hyperuricemia increases the risk of atrial fibrillation: a systematic review and meta-analysis. *Int J Endocrinol* 2022; 2022:8172639. doi:10.1155/2022/8172639
36. Voroneanu L, Ortiz A, Nistor I, Covic A. Atrial fibrillation in chronic kidney disease. *Eur J Intern Med* 2016; 33:3–13. doi:10.1016/j.ejim.2016.04.007
37. Deng Y, Liu F, Yang X, Xia Y. The key role of uric acid in oxidative stress, inflammation, fibrosis, apoptosis, and immunity in the pathogenesis of atrial fibrillation. *Front Cardiovasc Med* 2021; 8:641136. doi:10.3389/fcvm.2021.641136
38. Jong G-P, Chen H-Y, Li S-Y, Liou Y-S. Long-term effect of antihypertensive drugs on the risk of new-onset atrial fibrillation: a longitudinal cohort study. *Hypertens Res* 2014; 37:950–953. doi:10.1038/hr.2014.104

39. Haywood LJ, Ford CE, Crow RS, Davis BR, Massie BM, Einhorn PT, Williard A; ALLHAT Collaborative Research Group. Atrial fibrillation at baseline and during follow-up in ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial). *J Am Coll Cardiol* 2009; 54:2023–2031. doi:10.1016/j.jacc.2009.08.020
40. Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, Muiesan ML, Tsioufis K, Agabiti-Rosei E, Algharably EAE, Azizi M, Benetos A, Borghi C, Hitij JB, Cifkova R, Coca A, Cornelissen V, Cruickshank JK, Cunha PG, Danser AHJ, Pinho RM, Delles C, Dominiczak AF, Dorobantu M, Doumas M, Fernández-Alfonso MS, Halimi JM, Járai Z, Jelaković B, Jordan J, Kuznetsova T, Laurent S, Lovic D, Lurbe E, Mahfoud F, Manolis A, Miglinas M, Narkiewicz K, Niiranen T, Palatini P, Parati G, Pathak A, Persu A, Polonia J, Redon J, Sarafidis P, Schmieder R, Spronck B, Stabouli S, Stergiou G, Taddei S, Thomopoulos C, Tomaszewski M, Van de Borne P, Wanner C, Weber T, Williams B, Zhang ZY, Kjeldsen SE. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). *J Hypertens* 2023; 41:1874–2071. doi:10.1097/HJH.0000000000003480
41. Soliman EZ, Rahman AF, Zhang Z, Rodriguez CJ, Chang TI, Bates JT, Ghazi L, Blackshear JL, Chonchol M, Fine LJ, Ambrosius WT, Lewis CE. Effect of intensive blood pressure lowering on the risk of atrial fibrillation. *Hypertension* 2020; 75:1491–1496. doi:10.1161/HYPERTENSIONAHA.120.14766
42. Fang W, Li H, Zhang H, Jiang S. The role of statin therapy in the prevention of atrial fibrillation: a meta-analysis of randomized controlled trials. *Br J Clin Pharmacol* 2012; 74:744–756. doi:10.1111/j.1365-2125.2012.04258.x
43. Liu T, Li L, Korantzopoulos P, Liu E, Li G. Statin use and development of atrial fibrillation: a systematic review and meta-analysis of randomized clinical trials and observational studies. *Int J Cardiol* 2008; 126:160–170. doi:10.1016/j.ijcard.2007.07.137
44. Hadi HA, Mahmeed WA, Suwaidi JA, Ellahham S. Pleiotropic effects of statins in atrial fibrillation patients: the evidence. *Vasc Health Risk Manag* 2009; 5:533–551. doi:10.2147/VHRM.S4841
45. Alves-Cabratosa L, García-Gil M, Comas-Cufí M, Ponjoan A, Martí-Lluch R, Parramon D, Blanch J, Elosua-Bayes M, Ramos R. Statins and new-onset atrial fibrillation in a cohort of patients with hypertension. Analysis of electronic health records, 2006–2015. *PLoS One* 2017; 12:e0186972. doi:10.1371/journal.pone.0186972
46. Hung CY, Lin CH, Wang KY, Huang JL, Hsieh YC, Loh W, Lan TH, Chou P, Ting CT, Wu TJ. Dosage of statin, cardiovascular comorbidities, and risk of atrial fibrillation: a nationwide population-based cohort study. *Int J Cardiol* 2013; 168:1131–1136. doi:10.1016/j.ijcard.2012.11.087
47. Veronese G, Montomoli J, Schmidt M, Horváth-Puhó E, Sørensen HT. Statin use and risk of atrial fibrillation or flutter: a population-based case-control study. *Am J Ther* 2015; 22:186–194. doi:10.1097/MJT.0b013e31827ab488
48. Huang T, Yap L, Chen C, Lin H, Lin S, Li Y. Long-term statin use is associated with reduced rates of adverse events in patients with newly diagnosed atrial fibrillation. *J Am Heart Assoc* 2024; 13:e035827. doi:10.1161/JAHA.124.035827
49. Patel SM, Kang YM, Im K, Neuen BL, Anker SD, Bhatt DL, Butler J, Cherney DZI, Claggett BL, Fletcher RA, Herrington WG, Inzucchi SE, Jardine MJ, Mahaffey KW, McGuire DK, McMurray JJV, Neal B, Packer M, Perkovic V, Solomon SD, Staplin N, Vaduganathan M, Wanner C, Wheeler DC, Zannad F, Zhao Y, Heerspink HJL, Sabatine MS, Wiviott SD. Sodium-glucose cotransporter-2 inhibitors and major adverse cardiovascular outcomes: a SMART-C collaborative meta-analysis. *Circulation* 2024; 149:1789–1801. doi:10.1161/CIRCULATIONAHA.124.069568
50. He G, Yang G, Huang X, Luo D, Tang C, Zhang Z. SGLT2 inhibitors for prevention of primary and secondary cardiovascular outcomes: a meta-analysis of randomized controlled trials. *Heart Lung* 2023; 59:109–116. doi:10.1016/j.hrtlng.2023.02.009
51. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH; SELECT Trial Investigators. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med* 2023; 389:2221–2232. doi:10.1056/NEJMoa2307563
52. Wu J, Liu Y, Wei X, Zhang X, Ye Y, Li W, Su X. Antiarrhythmic effects and mechanisms of sodium-glucose cotransporter 2 inhibitors: a mini review. *Front Cardiovasc Med* 2022; 9:915455. doi:10.3389/fcvm.2022.915455
53. Bohne LJ, Jansen HJ, Dorey TW, Daniel IM, Jamieson KL, Belke DD, McRae MD, Rose RA. Glucagon-like peptide-1 protects against atrial fibrillation and atrial remodeling in type 2 diabetic mice. *JACC Basic Transl Sci* 2023; 8:922–936. doi:10.1016/j.jacbts.2023.01.005
54. Pandey AK, Okaj I, Kaur H, Belley-Cote EP, Wang J, Oraii A, Benz AP, Johnson LSB, Young J, Wong JA, Verma S, Conen D, Gerstein H, Healey JS, McIntyre WF. Sodium-glucose co-transporter inhibitors and atrial fibrillation: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2021; 10:e022222. doi:10.1161/JAHA.121.022222
55. Zhang H-D, Ding L, Mi L-J, Zhang A-K, Zhang K, Jiang Z-H, Yu F-Y, Yan X-X, Shen Y-J, Tang M. Sodium–glucose co-transporter-2 inhibitors for the prevention of atrial fibrillation: a systemic review and meta-analysis. *Eur J Prev Cardiol* 2024; 31:770–779. doi:10.1093/eurjpc/zwad356
56. Saglietto A, Falasconi G, Penela D, Francia P, Sau A, Ng FS, Dusi V, Castagno D, Gaita F, Berruezo A, De Ferrari GM, Anselmino M. Glucagon-like peptide-1 receptor agonist semaglutide reduces atrial fibrillation incidence: a systematic review and meta-analysis. *Eur J Clin Invest* 2024; 54:e14292. doi:10.1111/eci.14292
57. Lavie CJ, Pandey A, Lau DH, Alpert MA, Sanders P. Obesity and atrial fibrillation prevalence, pathogenesis, and prognosis: effects of weight loss and exercise. *J Am Coll Cardiol* 2017; 70:2022–2035. doi:10.1016/j.jacc.2017.09.002
58. Wong CX, Ganesan AN, Selvanayagam JB. Epicardial fat and atrial fibrillation: current evidence, potential mechanisms, clinical implications, and future directions. *Eur Heart J* 2017; 38:1294–1302. doi:10.1093/eurheartj/ehw045
59. Kang SH, Choi EK, Han KD, Lee SR, Lim WH, Cha MJ, Cho Y, Oh IY, Oh S. Underweight is a risk factor for atrial fibrillation: a nationwide population-based study. *Int J Cardiol* 2016; 215:449–456. doi:10.1016/j.ijcard.2016.04.036
60. Hsu JC, Yang YY, Chuang SL, Chung YW, Wang CH, Lin LY. Underweight is a major risk factor for atrial fibrillation in Asian people with type 2 diabetes mellitus. *Cardiovasc Diabetol* 2021; 20:226. doi:10.1186/s12933-021-01415-2
61. Deng H, Shantsila A, Guo P, Potpara TS, Zhan X, Fang X, Liao H, Liu Y, Wei W, Fu L, Wu S, Xue Y, Lip GYH. A U-shaped relationship of body mass index on atrial fibrillation recurrence post ablation: a report from the Guangzhou atrial fibrillation ablation registry. *EBioMedicine* 2018; 35:40–45. doi:10.1016/j.ebiom.2018.08.034

62. Pathak RK, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, Wong CX, Twomey D, Elliott AD, Kalman JM, Abhayaratna WP, Lau DH, Sanders P. Long-term effect of goal-directed weight management in an atrial fibrillation cohort: a long-term follow-up study (LEGACY). *J Am Coll Cardiol* 2015; 65:2159–2169. doi:10.1016/j.jacc.2015.03.002
63. Youssef I, Kamran H, Yacoub M, Patel N, Goulbourne C, Kumar S, Kane J, Hoffner H, Salifu M, McFarlane SI. Obstructive sleep apnea as a risk factor for atrial fibrillation: a meta-analysis. *J Sleep Disord Ther* 2018; 7:282. doi:10.4172/2167-0277.1000282
64. Linz D, McEvoy RD, Cowie MR, Somers VK, Nattel S, Lévy P, Kalman JM, Sanders P. Associations of obstructive sleep apnea with atrial fibrillation and continuous positive airway pressure treatment: a review. *JAMA Cardiol* 2018; 3:532–540. doi:10.1001/jamacardio.2018.0095
65. Shukla A, Aizer A, Holmes D, Fowler S, Park DS, Bernstein S, Bernstein N, Chinitz L. Effect of obstructive sleep apnea treatment on atrial fibrillation recurrence: a meta-analysis. *JACC Clin Electrophysiol* 2015; 1:41–51. doi:10.1016/j.jacep.2015.02.014