

# Original research

# New-onset atrial fibrillation after coronary surgery and stroke risk: a nationwide cohort study

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# ABSTRACT

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi. org/10.1136/heartjnl-2024-324573).

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Received 13 June 2024 Accepted 22 September 2024

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To cite: Taha A, Martinsson A, Nielsen SJ, et al. Heart Epub ahead of print: [please include Day Month Year]. doi:10.1136/ heartjnl-2024-324573

**Background** New-onset postoperative atrial fibrillation (POAF) after coronary artery bypass grafting (CABG) increases ischaemic stroke risk, yet factors influencing this risk remain unclear. We sought to identify factors associated with 1-year ischaemic stroke risk, compare the CHA<sub>2</sub>DS<sub>2</sub>-VASc (Congestive heart failure, Hypertension, Age  $\geq 75$  years. Diabetes, previous Stroke/transient ischaemic attack (TIA), Vascular disease, Age 65-74 years, Sex category) and ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) scores' predictive abilities for ischaemic stroke, and assess oral anticoagulation (OAC) dispensing at discharge in patients with POAF. Methods This nationwide cohort study used prospectively collected data from four mandatory Swedish national registries. All first-time isolated CABG patients who developed POAF during 2007-2020 were included. Multivariable logistic models were used to identify ischaemic

stroke predictors and C-statistics to assess the predictive abilities of the CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores in patients without OAC. OAC dispensing patterns were described based on stroke-associated factors.

Results In total, 10435 patients with POAF were identified. Out of those not receiving OAC (n=6903), 3.1% experienced an ischaemic stroke within 1 year. Advancing age (adjusted OR (aOR) 1.86 per 10-year increase, 95% CI 1.45 to 2.38), prior ischaemic stroke (aOR 18.56, 95% CI 10.05 to 34.28 at 60 years, aOR 5.95, 95% CI 3.78 to 9.37 at 80 years, interaction p<0.001), myocardial infarction (aOR 1.55, 95% CI 1.14 to 2.10) and heart failure (aOR 1.53, 95% CI 1.06 to 2.21) were independently associated with ischaemic stroke. The area under the receiver-operating characteristic curve was 0.72 (0.69-0.76) and 0.74 (0.70–0.78) for CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA, respectively (p=0.021). Altogether, 71.0% of patients with a stroke risk >2%/year, according to the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, were not discharged on OAC.

**Conclusions** Prior ischaemic stroke, advancing age, history of heart failure and myocardial infarction were associated with 1-year ischaemic stroke risk in patients with POAF after CABG. CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores predicted stroke risk with similar accuracy as in non-surgical atrial fibrillation cohorts. OAC dispense at discharge does not seem to reflect individual stroke risk.

# INTRODUCTION

Coronary artery bypass grafting (CABG) remains the most common cardiac surgical procedure, with

# WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ The occurrence of new-onset postoperative atrial fibrillation (POAF) following coronary artery bypass grafting (CABG) is linked to a moderate rise in the risk of ischaemic stroke.
- ⇒ However, the factors influencing this risk are not well understood, leading to a lack of specific recommendations for the use of oral anticoagulation (OAC) in patients with POAF after cardiac surgery.

# WHAT THIS STUDY ADDS

⇒ This study shows that prior ischaemic stroke, advanced age, history of heart failure and myocardial infarction are independently associated with a higher risk of ischaemic stroke within 1 year and that the CHA<sub>2</sub>DS<sub>2</sub>-VASc (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes, previous Stroke/transient ischaemic attack (TIA), Vascular disease, Age 65–74 years, Sex category) and ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) scores could be used to identify post-CABG POAF patients with high ischaemic stroke risk.

# HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These results emphasise the need for personalised anticoagulation strategies that align with individual stroke risks in post-CABG patients with POAF, aiming to enhance effective ischaemic stroke prevention.

more than 700 000 procedures conducted annually worldwide.<sup>1</sup> New-onset postoperative atrial fibrillation (POAF) occurs in approximately 30% of CABG patients.<sup>2</sup> <sup>3</sup> Current evidence suggests an association between POAF and a moderately increased long-term ischaemic stroke risk.<sup>4 5</sup> In patients with non-surgical atrial fibrillation (AF), oral anticoagulation (OAC) therapy is the first-line treatment for stroke prevention. However, in patients with POAF, evidence regarding the benefit of OAC is conflicting<sup>4</sup> <sup>6–9</sup> and its use varies considerably.<sup>10</sup> Additionally, international guidelines lack precise recommendations for the use of OAC in patients with POAF after cardiac surgery.<sup>11</sup>



Initiating OAC for stroke prevention in patients with POAF likely reflects their stroke risk, although studies on factors influencing that risk in this patient population are lacking. Additionally, the applicability of established AF stroke-risk stratification tools, like the CHA<sub>2</sub>DS<sub>2</sub>-VAS (Congestive heart failure, Hypertension, Age  $\geq$ 75 years, Diabetes, previous Stroke/transient ischaemic attack (TIA), Vascular disease, Age 65–74 years, Sex category)<sup>13</sup> or ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation)<sup>14</sup> scores in post-cardiac surgery POAF patients is not well-supported by evidence. It is also unclear if OAC currently captures patients with POAF at the highest risk of ischaemic stroke.

This study sought, first, to identify individual patient factors associated with ischaemic stroke during the first postoperative year in a nationwide cohort of patients with POAF after CABG. Second, we assessed and compared the predictive accuracy of CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores for ischaemic stroke. Finally, OAC dispenses at discharge in relation to factors associated with stroke risk were assessed.

# METHODS

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were adhered to in writing this manuscript.<sup>15</sup> The used data will be provided on reasonable request and following approval by the SWEDEHEART Registry, the Swedish National Board of Health and Welfare, and the Ethical Review Authority.

# Patients

This was a registry-based cohort study including all patients undergoing first-time isolated CABG in Sweden from January 2007 to December 2020. Any new-onset AF during the index hospitalisation for CABG was defined as POAF. Figure 1 provides a flow chart of included and excluded patients. Exclusion criteria included patients who died during the index hospitalisation, had a history of AF or used OACs at the time of admission for CABG. Patients with POAF who received OAC at discharge were excluded from the risk factor analysis and the assessment of the risk stratification tools but included in the assessment of OAC prescription patterns. Patients who, after discharge and during the first year, started OAC were also excluded unless OAC was initiated after an ischaemic stroke. Patients were followed up until an ischaemic stroke occurred, emigration or the study period ended.

# Data sources

Four Swedish mandatory registries, the Cardiac Surgery Registry, Patient Registry, Dispensed Drug Registry and Cause of Death Registry, were used to collect individual patient data. Data were merged using the personal identification number received by all Swedish residents at birth or shortly after immigration. Patients were identified in the Cardiac Surgery Registry, which is part of the SWEDEHEART Registry.<sup>16</sup> The Cardiac Surgery Registry contains detailed information on cardiac surgical procedures with nearly 100% coverage since 1992.<sup>17</sup> Comorbidities,



Figure 1 Flow chart of included and excluded patients. AF, atrial fibrillation; CABG, coronary artery bypass grafting; OAC, oral anticoagulation; POAF, postoperative atrial fibrillation.

preoperative AF status and outcome events were obtained from the National Patient Registry using International Classification of Diseases V.10 codes reported since 1997 (online supplemental table 1). This registry has full coverage of all hospitalacquired diagnoses, with 85–95% validity.<sup>18</sup> Medications data were collected from the Dispensed Drug Registry, which covers all dispensed prescriptions in Sweden since July 2005.<sup>19</sup> The Anatomical Therapeutic Classification codes used are listed in online supplemental table 2. Mortality data were obtained from the Cause of Death Registry, which holds information on all deaths in Sweden, including date and cause of death.<sup>20</sup>

#### **Definitions and tools**

Ischaemic stroke was considered an outcome if it (1) occurred after discharge; (2) was reported in the National Patient Registry as either a principal or a contributing diagnosis; and (3) was associated with hospitalisation or death.

The CHA<sub>2</sub>DS<sub>2</sub>-VASc<sup>13</sup> is the most commonly used tool for stroke risk assessment in patients with non-surgical AF and is recommended by international guidelines.<sup>11 12</sup> Its main application is to identify patients with a low ischaemic stroke risk (<1%/year) for whom OAC is not recommended.

The ATRIA score, developed and validated to predict annual stroke risk in patients with non-surgical AF,<sup>14</sup> factors in age and prior ischaemic stroke as major risk determinants. Additional components—sex, diabetes, congestive heart failure, hypertension, proteinuria and estimated glomerular filtration rate and/or end-stage renal disease—are included but less heavily weighted. ATRIA classifies patients with AF into low (0–5 points), moderate (6 points) and high stroke risk (7–15 points) categories correlating to annual stroke rates of <1%, 1–2% and ≥2%, respectively. All patients in the present study were assigned zero point for proteinuria because of lack of information in the registries, as in a large-scale ATRIA validation study conducted in patients with AF.<sup>21</sup>

#### **Statistical analysis**

Descriptive statistics are presented as mean and SD, or median and IQR for continuous variables, and as number and percentage for categorical variables. For between-group testing of dichotomous variables, Fisher's exact test was used, while the Mantel-Haenszel  $\chi^2$  trend test was used for ordered categorical variables, the  $\chi^2$  test for non-ordered categorical variables, and the Mann-Whitney U test for continuous variables. The cumulative incidence function for ischaemic stroke during the complete follow-up is presented, adjusted for death as competing risk.

Unadjusted, age-adjusted and sex-adjusted, and multivariable logistic regression models, were applied to calculate the ischaemic stroke rate during the first year after hospital discharge. ORs with 95% CIs are presented along with the area under the receiver-operating characteristic curve (AUC-ROC).<sup>22</sup> Multiple testing was performed in the prognostic analysis of ischaemic stroke; p values were considered significant at the 0.05 level after Bonferroni-Holm adjustment for multiple comparisons.<sup>23</sup> Variables remaining significant after this correction were included in a stepwise (forward and backward) regression to obtain two multivariable models with independent predictors, one where age was included as a continuous variable, and the other where age (<65, 65–74,  $\geq$ 75 years) was included as categorical variable. Potential interactions between variables were investigated. The predictive accuracy of the CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores for ischaemic stroke at 1 year was assessed, and their AUC-ROCs were compared using DeLong, DeLong and Clarke-Pearson's method.<sup>24</sup> Goodness of fit was tested by Hosmer-Lemeshow test. A p value >0.05 indicated a good fit. A sensitivity analysis was conducted, using the same statistical methods as the main analysis. All tests were two-tailed, and analyses were performed using SAS Software V.9.4 (SAS Institute, Cary, New Carolina, USA).

#### Patient and public involvement

This study did not involve patients or the public in its design, conduct, reporting or dissemination plans.

## RESULTS

# General

Among 34914 CABG patients, 10435 patients with POAF were identified (29.9%). Out of these, 6903 (72.9%) patients did not receive OAC and were selected for assessing risk factors for ischaemic stroke and comparing risk stratification tools. Their mean age (SD) was 69.9 (7.9) years and 18.5% were women (table 1). In the first postoperative year, 211 patients (3.1%) experienced an ischaemic stroke. Over a median follow-up period of 6.2 years (IQR 3.0-9.4 years), ischaemic stroke was diagnosed in 750 patients (10.9%). The cumulative incidence of ischaemic stroke is presented in online supplemental figure 1. Patients who suffered an ischaemic stroke during the first year were generally older, had worse renal function, and more often history of myocardial infarction, cerebrovascular events (TIA, ischaemic stroke, or haemorrhagic stroke), hypertension, heart failure, peripheral vascular disease and higher CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores (table 1).

#### Factors associated with 1-year ischaemic stroke risk

The univariable and age-adjusted and sex-adjusted models for associations between patient characteristics and the occurrence of ischaemic stroke during the first postoperative year are presented in online supplemental table 3. Variables significantly associated with an increased risk for 1-year ischaemic stroke were identified in the age-adjusted and sex-adjusted analysis. After correction for multiple testing, advanced age, a history of myocardial infarction, prior ischaemic stroke, haemorrhagic stroke, TIA and heart failure remained statistically significant predictors of ischaemic stroke at 1 year (all p<0.001). These variables were included in the multivariable stepwise logistic regression models with age as a continuous variable (model 1) and as a categorical variable (model 2), including investigation of significant interactions (table 2).

A significant interaction between prior stroke and age (p < 0.001) was observed. Advanced age was a significant risk factor in patients without but not in patients with prior stroke. Model 1 showed that prior ischaemic stroke (eg, aOR at 70 years 10.51, 7.66–14.42), higher age for those with no prior ischaemic stroke (aOR 1.86 per 10-year increase, 1.45–2.38), history of myocardial infarction (aOR 1.55, 1.14–2.10) and heart failure (aOR 1.53, 1.06–2.21) were independent predictors of 1-year ischaemic stroke. The probability of 1-year ischaemic stroke, myocardial infarction and/or heart failure showed a higher incident stroke risk in patients with prior stroke (online supplemental figure 2). The interaction between age category and prior ischaemic stroke is illustrated in figure 2.

#### Sensitivity analysis

All 10435 patients with POAF, including those receiving OAC, were included. Patient characteristics, comorbidities and

 Table 1
 Demographic characteristics, comorbidities and medications at discharge in postoperative atrial fibrillation patients with no oral anticoagulation, with and without an ischaemic stroke event during the first year after hospital discharge

Variable	Total N=6903	No ischaemic stroke n=6692	lschaemic stroke n=211	P value	
Demographic characteristics					
Age (years)	69.9 (7.9)	69.8 (7.9)	72.7 (7.2)	<0.001	
Age category				<0.001	
18–54 years	271 (3.9%)	268 (4.0%)	3 (1.4%)		
55–64 years	1394 (20.2%)	1369 (20.5%)	25 (11.8%)		
65–74 years	3128 (45.3%)	3039 (45.4%)	89 (42.2%)		
75+ years	2110 (30.6%)	2016 (30.1%)	94 (44.5%)		
Female	1276 (18.5%)	1222 (18.3%)	54 (25.6%)	0.009	
Medical history and comorbidities					
Type of coronary artery disease				0.024	
STEMI	1108 (16.1%)	1066 (15.9%)	42 (19.9%)		
NSTEMI	2352 (34.1%)	2269 (33.9%)	83 (39.3%)		
Unstable angina	1595 (23.1%)	1548 (23.1%)	47 (22.3%)		
Stable angina	1848 (26.8%)	1809 (27.0%)	39 (18.5%)		
Previous myocardial infarction	3886 (56.3%)	3740 (55.9%)	146 (69.2%)	<0.001	
Previous stroke	498 (7.2%)	418 (6.2%)	80 (37.9%)	<0.001	
Previous ischaemic stroke	457 (6.6%)	378 (5.6%)	79 (37.4%)	<0.001	
Previous haemorrhagic stroke	53 (0.8%)	46 (0.7%)	7 (3.3%)	0.001	
Previous transient ischaemic attack	402 (5.8%)	369 (5.5%)	33 (15.6%)	<0.001	
Diabetes	2145 (31.1%)	2067 (30.9%)	78 (37.0%)	0.070	
Hypertension	5133 (74.4%)	4953 (74.0%)	180 (85.3%)	<0.001	
Heart failure	784 (11.4%)	743 (11.1%)	41 (19.4%)	<0.001	
Peripheral vascular disease	707 (10.2%)	673 (10.1%)	34 (16.1%)	0.008	
CHA <sub>2</sub> DS <sub>2</sub> -VASc score				<0.001	
Mean (SD)	3.6 (1.4)	3.6 (1.4)	4.8 (1.5)		
Median (IQR)	4 (3–5)	4 (3–4)	5 (4–6)		
ATRIA score				<0.001	
Mean (SD)	4.6 (2.5)	4.5 (2.4)	6.7 (2.5)		
Median (IQR)	5 (3–6)	5 (3–6)	7 (5–8)		
Left ventricular ejection fraction				0.002	
>50%	4770 (69.5%)	4646 (69.8%)	124 (59.3%)		
30–50%	1731 (25.2%)	1662 (25.0%)	69 (33.0%)		
<30%	367 (5.3%)	351 (5.3%)	16 (7.7%)		
Previous bleeding	831 (12.0%)	793 (11.8%)	38 (18.0%)	0.001	
eGFR (mL/min)	74.5 (18.5)	74.7 (18.4)	68.8 (19.2)	<0.001	
Renal failure	275 (4.0%)	258 (3.9%)	17 (8.1%)	0.006	
Renal replacement therapy	44 (0.6%)	40 (0.6%)	4 (1.9%)	0.044	
Cancer	1114 (16.1%)	1075 (16.1%)	39 (18.5%)	0.34	
Chronic respiratory disease	753 (10.9%)	717 (10.7%)	36 (17.1%)	0.007	
Medications at discharge					
Diuretics	3213 (46.5%)	3076 (46.0%)	137 (64.9%)	<0.001	
Mineralocorticoid receptorantagonist	815 (11.8%)	770 (11.5%)	45 (21.3%)	<0.001	
Beta-blockers	6396 (92.7%)	6204 (92.7%)	192 (91.0%)	0.35	
Calcium channel blockers	1956 (28.3%)	1894 (28.3%)	62 (29.4%)	0.76	
Renin-angiotensin antagonists	5317 (77.0%)	5164 (77.2%)	153 (72.5%)	0.110	
Lipid-lowering agents	6658 (96.5%)	6465 (96.6%)	193 (91.5%)	<0.001	
Insulin	933 (13.5%)	888 (13.3%)	45 (21.3%)	0.001	
Oral antidiabetics	1425 (20.6%)	1383 (20.7%)	42 (19.9%)	0.86	
Digoxin	94 (1.4%)	78 (1.2%)	16 (7.6%)	<0.001	
Sotalol	662 (9.6%)	645 (9.6%)	17 (8.1%)	0.55	
Amiodarone	704 (10.2%)	681 (10.2%)	23 (10.9%)	0.73	
Dual antiplatelet therapy	1673 (24.2%)	1620 (24.2%)	53 (25.1%)	0.74	
Antiplatelet therapy	6742 (97.7%)	6557 (98.0%)	185 (87.7%)	<0.001	
				Continued	

Table 1	Continued			
Variablo	Total	No ischaemic stroke	Ischaemic stroke	P valuo
Determine	N=0303	(	11-211	r value

Data are presented as mean (SD), median (IQR) or number (percentage).

ATRIA, Anticoagulation and Risk Factors in Atrial Fibrillation score; CHA<sub>2</sub>DS<sub>2</sub>-VASc, Congestive heart failure, Hypertension, Age  $\geq$ 75 years, Diabetes, previous Stroke/transient ischemic attack–Vascular disease, age 65–74 years, Sex category score; eGFR, estimated glomerular filtration rate; IQR, interquartile range; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.

medications are shown in online supplemental table 4. This analysis yielded results in line with the main analysis (online supplemental table 5).

# Discriminative accuracy of CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores for 1-year ischaemic stroke

The incidence of 1-year ischaemic stroke by the  $CHA_2DS_2$ -VASc and ATRIA scores in 6903 patients without OAC is depicted in figure 3. An annual stroke risk of >2% was observed in 3569 (51.7%) patients with a  $CHA_2DS_2$ -VASc score ≥4 and 2487 (36.0%) with an ATRIA score ≥6 points.

The AUC-ROC for ischaemic stroke during 1 year after discharge for  $CHA_2DS_2$ -VASc and ATRIA were 0.72 (0.69–0.76) and 0.74 (0.70–0.78), respectively (online supplemental figure 3). Both scores had a good fit (p>0.05). ATRIA demonstrated superior predictive accuracy compared with  $CHA_2DS_2$ -VASc, with a significant difference in AUC-ROC values (p=0.021).

# Oral anticoagulation at discharge

Out of 10435 patients with POAF, 2830 (27.1%) were discharged on OAC. Online supplemental table 6 details the characteristics of these patients. Those discharged on OAC were generally older, had higher CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores, and were more likely to have a history of cancer. No significant differences were found between the groups in terms of previous stroke, major bleeding, renal failure or heart failure. Figure 4

and online supplemental table 7 show OAC discharge rates by  $CHA_2DS_2$ -VASc score, ATRIA score, age and prior ischaemic stroke status. In patients with a  $CHA_2DS_2$ -VASc score  $\geq 4$  and an ATRIA score  $\geq 6$ , corresponding to an annual stroke risk  $\geq 2\%$ , 29.1% (n=1620/5576) and 30.1% (n=1187/3940) were discharged with OAC, respectively. In patients aged  $\geq 75$ , 37.7% received OAC at discharge, compared with 27.2% of those aged 65–74, and 19.9% for those <65. The rate of OAC use at discharge was 28.8% and 27.0%, in POAF patients with and without prior ischaemic stroke, respectively.

# DISCUSSION

The study's key findings were as follows: (1) prior ischaemic stroke, advancing age, heart failure and a history of myocardial infarction were independently associated with 1-year ischaemic stroke in patients with POAF after CABG; (2) CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores moderately predicted ischaemic stroke risk in patients with POAF (with ATRIA slightly outperforming in accuracy and identifying fewer high-risk patients); and (3) a minority of patients with presumably high stroke risk, based on risk factors and scores, were treated with OAC at discharge.

## Factors associated with ischaemic stroke

Current guidelines recommend long-term OAC for non-surgical AF patients with significant annual stroke risk, estimated using the CHA,DS,-VASc and ATRIA scores, and acceptable bleeding

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Table 2	Multivariable step	wise logistic regression models for the incid	lence of ischaemic	stroke during t	the first year after discharge

Model	Variables	Or (95% CI)	P value	AUC-ROC	Hosmer-Lemeshow goodness-of-fit test
Model 1	Age (per 10-year increase) for no previous ischaemic stroke	1.86 (1.45 to 2.38)	<0.001	0.75 (0.72–0.79)	0.41
	Age (per 10-year increase) for previous ischaemic stroke	1.05 (0.74 to 1.51)	0.77		
	Previous ischaemic stroke for age 60	18.56 (10.05 to 34.28)	<0.001		
	Previous ischaemic stroke for age 70	10.51 (7.66 to 14.42)	<0.001		
	Previous ischaemic stroke for age 80	5.95 (3.78 to 9.37)	<0.001		
	Previous myocardial infarction	1.55 (1.14 to 2.10)	0.005		
	Heart failure	1.53 (1.06 to 2.21)	0.023		
Model 2	Age 65–74 vs 18–64 for no previous ischaemic stroke	1.70 (0.98 to 2.95)	0.060	0.74 (0.71–0.78)	0.48
	Age 75+ vs 18–64 for no previous ischaemic stroke	2.99 (1.74 to 5.14)	<0.001		
	Age 65–74 vs 18–64 for previous ischaemic stroke	1.09 (0.52 to 2.29)	0.82		
	Age 75+ vs 18–64 for previous ischaemic stroke	1.16 (0.54 to 2.48)	0.70		
	Previous ischaemic stroke for age 18–64	16.71 (7.46 to 37.46)	<0.001		
	Previous ischaemic stroke for age 65–74	10.74 (6.85 to 16.86)	<0.001		
	Previous ischaemic stroke for age 75+	6.49 (4.08 to 10.33)	<0.001		
	Previous myocardial infarction	1.56 (1.15 to 2.12)	0.004		
	Heart failure	1.53 (1.06 to 2.21)	0.024		
*P value >0.05 means good model fit. AUC-ROC, area under the receiver-operating characteristic curve.					



Figure 2 Incidence of ischaemic stroke during the first postoperative year, by age category and previous ischaemic stroke.

risks.<sup>11-14</sup> However, assessing stroke risk in patients with POAF post-cardiac surgery is more complex. The European Society of Cardiology guidelines suggest considering OAC in these patients but provide no guidance on stroke risk assessment.<sup>11</sup> Similarly, the American College of Cardiology/American Heart Association guidelines recommend OAC for 60 days postoperatively for high stroke risk patients but lack criteria for identifying them.<sup>12</sup> Since the decision-making for long-term OAC treatment ideally should be based on stroke risk stratification, and on the potential benefit of OAC therapy, knowledge about which factors influence this risk in patients with POAF after cardiac surgery is crucial. Hitherto no large studies have addressed this issue. Addressing this gap, this study demonstrated that a history of ischaemic stroke, advanced age, heart failure and myocardial infarction were independently associated with increased ischaemic stroke risk during the first year after CABG. Notably,

previous stroke was, by far, the strongest risk factor regardless of age. An association between advancing age and increased stroke risk was only observed in patients without a history of previous stroke. A similar interaction between age and previous ischaemic stroke as risk factors for future stroke has also been observed in patients with non-surgical AF.<sup>14</sup>

# CHA2DS2-VASc and ATRIA

The ischaemic stroke risk factors identified in this study are also key components of non-surgical AF stroke risk stratification tools such as the CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores.<sup>13 14</sup> Societal guidelines recommend OAC in non-surgical AF patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq$ 3 for women and  $\geq$ 2 for men, corresponding to an annual stroke risk of  $\geq$ 2% (class I recommendation); in women with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 and men with



**Figure 3** Incidence of ischaemic stroke during the first postoperative year, by (A)  $CHA_2DS_2$ -VASc score and (B) ATRIA score. ATRIA, Anticoagulation and Risk Factors in Atrial Fibrillation;  $CHA_2DS_2$ -VASc, Congestive heart failure, Hypertension, Age  $\geq$ 75 years, Diabetes, previous Stroke/transient ischaemic attack–Vascular disease, Age 65–74 years, Sex category.



**Figure 4** Rates of oral anticoagulant (OAC) use at discharge in patients with new-onset postoperative atrial fibrillation after coronary artery bypass grafting in relation to (A)  $CHA_2DS_2$ -VASc score, (B) ATRIA score, (C) prior ischaemic stroke and (D) age. ATRIA, Anticoagulation and Risk Factors in Atrial Fibrillation score;  $CHA_2DS_2$ -VASc, Congestive heart failure, Hypertension, Age  $\geq$ 75 years, Diabetes, previous Stroke/transient ischaemic attack–Vascular disease, Age 65–74 years, Sex category score.

a score of 1 (stroke risk of 1–2%/year), treatment with OAC should be considered (class IIa recommendation).<sup>11 12</sup>

The applicability of these tools in patients with POAF remains underexplored. Benedetto *et al*, in a post-hoc analysis of the Arterial Revascularisation Trial (ART), showed no difference in stroke rate in patients with and without POAF and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score <4, while a score  $\geq$ 4 was associated with an increased stroke risk in patients with POAF only.<sup>25</sup> We found in a previous study, using a partially overlapping cohort, that a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\leq$ 3 was associated with  $\leq$ 1.5% annual stroke risk.<sup>26</sup> These findings suggest that if the CHA<sub>2</sub>DS<sub>2</sub>-VASc is used in guiding OAC prescription for patients with POAF, higher thresholds than in patients with non-surgical AF should probably be adopted. Notably, the CHA<sub>2</sub>DS<sub>2</sub>-VASc score in the current study cohort showed a similar or better discrimination accuracy for ischaemic stroke at 1 year (AUC 0.72) than that described in non-surgical AF cohorts (AUC 0.58–0.70).<sup>27</sup>

The ATRIA score untested patients with POAF until now, had a similar discrimination accuracy in the present study (AUC 0.74) to that seen in non-surgical AF cohorts  $(0.71-0.75)^{1421}$  and slightly outperformed the CHA<sub>2</sub>DS<sub>2</sub>-VASc. Additionally, compared with the CHA<sub>2</sub>DS<sub>2</sub>-VAS, the ATRIA score identified fewer patients with high stroke risk ( $\geq 2\%$ /year) during the first postoperative year (36% vs 52%), which may impact the patient selection for OAC. Despite its accuracy, ATRIA's complexity makes it less practical in clinical settings compared with CHA<sub>2</sub>DS<sub>2</sub>-VASc.

# OAC in patients with POAF

While some observational studies suggest a beneficial effect of OAC in patients with POAF,<sup>6,7</sup> others,<sup>4,9</sup> including a metaanalysis by Fragão-Marques *et al*,<sup>8</sup> have not confirmed this finding. Additionally, a recent analysis of around 39 000 patients with POAF from the Society of Thoracic Surgeons Adult Cardiac Surgery Database found that those with versus those without OAC at hospital discharge had a significantly increased risk for mortality and bleeding without a reduction in stroke risk regardless of CHA<sub>2</sub>DS<sub>2</sub>-VASc score.<sup>28</sup> These observations underscore the importance of identifying high-risk POAF patients who could potentially benefit from OAC.

In our study, one-third of patients with POAF were discharged on OAC, with those at higher stroke risk, based on CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA scores, had a slightly higher rate of OAC use, as illustrated in figure 4. Yet, over two-thirds of patients with an estimated stroke risk of >2% during the first year, according to the CHA<sub>2</sub>DS<sub>2</sub>-VASc or ATRIA scores, were not prescribed OAC at discharge. Furthermore, given the strong association between previous ischaemic stroke and recurrent stroke, it is noteworthy that >70% of patients with previous stroke did not receive OAC. Although it is conceivable that a proportion of patients with high stroke risk also had high bleeding risk, our results suggest that stroke risk alone had a limited influence on the decision to initiate OAC treatment in patients with POAF. Simultaneously, a considerable number of patients with a low risk of 1-year ischaemic stroke were discharged on OAC. This might explain why numerous studies have not observed a preventive effect of OAC on strokes in patients with POAF.

# **Strengths and limitations**

This study's strengths include the sizeable nationwide cohort of CABG patients and the use of high-quality registers that provide comprehensive information on patient demographics, comorbidities and outcomes. This study also has limitations, including the observational design with its inherent weaknesses. Additionally, all patients were assigned zero points for proteinuria in the ATRIA score calculation. While this might slightly affect the score's performance, the impact is likely minimal, as proteinuria is a minor component.

# Cardiac risk factors and prevention

Balancing stroke and bleeding risks is crucial when considering OAC, especially in post-cardiac surgery patients on antiplatelet therapy. This manuscript does not address bleeding complications which is a limitation. Clinical tools to assess bleeding risk and guide OAC decisions in patients with POAF after cardiac surgery are needed.

The POAF diagnosis was based on information from the SWEDEHEART Registry which may have failed to report episodes of silent AF. Additionally, there is a significant risk of AF recurrence in patients with POAF, particularly during the initial postoperative period,<sup>4</sup> which may affect the decision to start OAC. This current study did not examine the rate of AF recurrence or changes in OAC status after discharge. However, a previous study found no association between early AF recurrence in patients with POAF and all-cause mortality or thromboembolic events.<sup>29</sup> Furthermore, the external validity of our results needs to be confirmed in other patient cohorts.

# CONCLUSIONS

This large population-based study in patients with POAF after CABG identified prior ischaemic stroke, advanced age, myocardial infarction and heart failure as independent risk factors for ischaemic stroke during the first postoperative year. The CHA<sub>2</sub>DS<sub>2</sub>-VASc and ATRIA instruments demonstrated a moderate ability to predict ischaemic stroke within 1 year in patients with POAF; the predictability was similar as in patients with non-surgical AF. One-third of patients with POAF were discharged on OAC. However, factors associated with increased stroke risk appeared to have a low impact on the propensity to prescribe OAC in patients with POAF.

**Acknowledgements** This manuscript was part of Amar Taha's PhD thesis titled, 'New-onset atrial fibrillation after coronary surgery: epidemiology, risk factors and long-term prognosis' successfully defended on 17 May 2024, at Gothenburg University.

**Contributors** AT: Data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; writing—original draft; writing—review and editing. AM: Conceptualisation; funding acquisition review and editing. MR: Methodology, review and editing. SJN: Conceptualisation, funding acquisition, investigation, methodology, resources, software, review and editing. TG: Conceptualisation, review and editing. AP: Data curation, formal analysis, software, review and editing. FEMH: Investigation, methodology, review and editing. LB: Conceptualisation, supervision; writing—review and editing. A1: Conceptualisation, data curation, formal analysis, investigation, methodology, project administration, supervision; writing—review and editing. A2: Conceptualisation, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, writing—review and editing.

**Funding** This work was supported by grants from the Swedish Heart-Lung Foundation (20210433 to AJ), the Swedish state under the agreement between the Swedish government and the county councils concerning economic support of research and education of doctors (ALF agreement) (ALFGBG-977905 to AM, ALFGBG-942665 to SN and ALFGBG-966204 to AJ), Västra Götaland Region (VGFOUREG-969376 to AJ) and grant (VGFOUREG-648981 to AT), Wilhelm and Martina Lundgrens Foundation (grant 2019-3110 to AT) and grant from Emelle Foundation to AT. The funding organisations did not impact the analysis and interpretation of the data, the composition of the report or the decision to submit the manuscript for publication.

**Competing interests** AJ discloses financial relationships with AstraZeneca, Werfen, LFB Biotechnologies, Pharmacosmos, Boehringer-Ingelheim and Bayer unrelated to the present study. AT discloses a financial relationship with Bayer and Medtronic unrelated to the present study. LB reports personal fees from Bayer, Boehringer Ingelheim and Sanofi, outside the submitted work. No other disclosures were reported.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

#### Patient consent for publication Not applicable.

**Ethics approval** This study involves human participants and was approved by Swedish Ethical Review Authority (registration number 2021-00122, approved on 31

March 2021). The study was based on registry data and the Swedish Ethical Review Authority waived the need for individual patient consent.

Provenance and peer review Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. The used data will be provided on reasonable request and following approval by the SWEDEHEART Registry, the Swedish National Board of Health and Welfare, and the Ethical Review Authority.

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