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Original Article

Early Thromboembolic Stroke Risk of Postoperative Atrial Fibrillation Following Cardiac Surgery

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Objective: The authors aimed to study the association between postoperative atrial fibrillation (POAF) and thromboembolic stroke and to determine risk factors for thromboembolic stroke after cardiac surgery.
Design: The authors performed a secondary analysis from a randomized controlled trial (GRIP-COMPASS). The patients with thromboembolic stroke were compared with those without thromboembolic stroke, and the difference in the incidence of POAF between these groups was assessed. Odds ratios (OR) were calculated using logistic regression analyses. Brain imaging was studied for the occurrence of thromboembolic stroke during hospital admission, and POAF was monitored for seven days. To assess which characteristics were associated with occurrence of thromboembolic stroke, stepwise backward regression analysis was performed.
Participants: All adult consecutive cardiac surgery patients admitted postoperatively to the intensive care unit.
Setting: Academic tertiary care medical center.
Interventions: None.
Measurements and Main Results: Of the 910 patients included in this study, 26 patients (2.9%) had a thromboembolic stroke during hospital admission. The incidence of POAF during the first seven days after cardiac surgery in those with thromboembolic stroke was 65%, compared with 39% in those without thromboembolic stroke: adjusted OR 3.01 (95% confidence interval, 1.13-8.00). POAF, a history of peripheral vascular disease, a higher EuroSCORE, and a longer duration of surgery were associated with thromboembolic stroke.
Conclusions: POAF within seven days after cardiac surgery was associated with a three-fold increased risk for a thromboembolic stroke during hospital admission. Expeditious treatment of POAF may, therefore, reduce early stroke risk after cardiac surgery.

Key Words: stroke; atrial fibrillation; cardiac surgery

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ATRIAL FIBRILLATION and atrial flutter are the most common cardiac arrhythmias in both the general population and perioperatively in cardiac surgery patients admitted to the intensive care unit (ICU). Even in the latter environment the subclinical variant may have a few symptoms and short episodes can be missed. As a result, this condition may be underestimated and left untreated.[1,2]

Postoperative atrial fibrillation or flutter (POAF), preexisting or as a new-onset manifestation, occurs frequently after cardiac surgery. It has a reported incidence ranging from 10%-to-50%, and is associated with a two-fold increase in long-term cardiovascular mortality and morbidity.[3] POAF usually develops during the first week after cardiac surgery, with a peak incidence on the second day.[4,5] Cardiac surgery-related POAF mostly is self-limiting and usually without clinical consequences.[6] However, among other mechanisms, clot formation triggered by blood stasis due to POAF may lead to thromboembolic stroke.[7] Although atrial fibrillation is an established risk factor for stroke in the general population, it is less clear how and to what extent POAF directly contributes to thromboembolic stroke after cardiac surgery. Most studies on POAF focus on the effect on length of stay and mortality, and stroke occurrence rarely is differentiated between thromboembolic (cardioembolic) stroke and other stroke subtypes.[8] Risk factors, such as severe illness and advanced age, contribute to the incidence rate of POAF after cardiac surgery, but these also are risk factors for stroke.[9,10] Therefore, the causal relationship between POAF and thromboembolic stroke in this setting is ambiguous.

According to the European Society of Cardiology guidelines, anticoagulation administration should be considered in patients with POAF at higher risk of stroke, without a beneficial cutoff point based on POAF duration stated by the American College of Cardiology/American Heart Association guidelines, while assessing the risk of bleeding.[5] Therefore, adequate risk stratification potentially may be helpful for preventive measures in patients at risk for POAF and subsequent stroke directly after cardiac surgery.[11] If a clear increase of stroke risk in patients with POAF were established, this might indicate that POAF should be detected meticulously and treated expeditiously, or, preferably, prevented.

The primary aim of the current study was to establish thromboembolic stroke risk during hospital admission in patients with POAF in the first week after cardiac surgery in the authors' institution. The secondary aim was to study the association of clinical characteristics, including the occurrence of POAF, with the occurrence of thromboembolic stroke during hospital admission in patients after cardiac surgery.

Methods

Study Design and Inclusion Criteria

Data from a randomized controlled trial (GRIP-COMPASS study) were complemented with data from brain imaging. Inclusion and exclusion criteria were based on the GRIP-COMPASS trial's specific purposes. All patients admitted to the ICU after any type of cardiac surgery, regardless of its urgency, were included. Cardiac surgery was categorized as coronary artery bypass grafting (CABG), valve surgery (irrespective of CABG), or aortic surgery (irrespective of concomitant CABG or valve surgery).

Ethical approval was obtained from the Medical Ethics Committee of the University Medical Center Groningen and known under numbers METc 2009/096 (GRIP-COMPASS trial) and METc 2014/154. The Medical Ethics Committee waived the need for patient consent.

The GRIP-COMPASS trial was a prospective, double-blinded interventional study in 910 consecutive adult patients after cardiac surgery who were admitted to the ICU between 2009 and 2010 at the University Medical Center Groningen (UMCG), with the aim to determine the effect of two different potassium targets (4.0 mmol/L *v* 4.5 mmol/L) on the occurrence of POAF.[12,13] This was a neutral study with no differences in the incidence of POAF between the two allocated potassium regulation strategies. Occurrence of POAF was monitored continuously for seven days in the postoperative phase, using 12-lead electrocardiography at the ICU with rhythm recognition and ST-segment monitoring. After ICU discharge, patients at risk for developing arrhythmias were observed closely via telemetry. A duration of at least ten seconds was seen as a diagnostic threshold and the presence of POAF had to be confirmed with a 12-lead ECG.

In general, patients with confirmed POAF de novo initially were treated with amiodarone, aiming for rhythm control followed by electrical cardioversion within 72 hours of POAF onset indicated by the treating physician. In patients with a history of AF or in case of treatment-resistant POAF, beta-blocking agents were used for rate control, aiming for a heart frequency <100/min. Perioperative amiodarone or beta-blockers were not used routinely for prevention of atrial fibrillation.

Data Collection

Compared with the number of strokes mentioned in the GRIP-COMPASS trial, a more detailed stroke analysis, for example, thromboembolic or otherwise, was newly performed in this retrospective study. Only patients who had postoperative brain imaging, that is, computed tomography (CT) and/or magnetic resonance imaging, for suspected stroke during their hospital stay after cardiac surgery, were studied after being selected by means of radiologic codes used to invoice healthcare consumption in the authors' hospital.[14] The brain images were rated independently by the first (RP) and senior author (WMvdB) to distinguish according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria among hemorrhagic, thromboembolic, air embolism, or hemodynamic stroke and to determine if the clinical symptoms mentioned in the electronic patient files that triggered brain imaging correlated with the site and age of the lesion. Thromboembolic stroke was defined as a new ischemic lesion compatible with an arterial occlusion found on imaging, and was considered definitive if the findings on imaging were in concordance with the clinical findings. Findings on imaging were compared with previous imaging if available, but the conclusion that an ischemic lesion was (semi)recent was based on the latest brain images (eg, demarcation of lesion). Cardiac embolism or large-vessel atherosclerosis were not differentiated because it was assumed that all thromboembolic strokes were cardioembolic in this specific population.

Patient demographics were collected routinely during ICU admission, and specific perioperative data were obtained from anesthetic reports. In addition, all available variables, involving pre-, peri-, and postoperative values, affecting the cardiovascular system were analyzed. These included patients' characteristics and medical history, as well as risk stratification models (European System for Cardiac Operative Risk Evaluation [EuroSCORE], Acute Physiology and Chronic Health Evaluation [APACHE] III, and Simplified Acute Physiology Score [SAPS]), surgery, and ICU data. EuroSCORE is a risk model for predicting mortality after cardiac surgery, and APACHE and SAPS are scoring models predicting in-hospital death for the general ICU population.[15] CHA_2DS_2-VASc (congestive heart failure, hypertension, age [>75 = 2 points], diabetes, previous stroke/transient ischemic attack [2 points], vascular disease, and sex category) score is a well-known tool to predict short- and long-term stroke risk in the presence of atrial fibrillation. However, this scoring model was considered to be of insufficient value in a time window that spanned only hospital admission after cardiac surgery and was, therefore, not used in multivariate analyses in this study.[16]

Anticoagulation Management

Postoperative anticoagulation practice was as follows: within 24 hours after CABG, acetylsalicylic acid (ASA) 100 mg was (re)started, combined with clopidogrel 75 mg in case of a recent acute coronary syndrome or coronary stent in recent history, and prophylactic low-molecular-weight heparin (LMWH). Prophylactic dose of nadroparin, a LMWH, is always 2,850 IU once a day regardless of patient weight. Patients with a history of (paroxysmal) AF, deep venous thrombosis, pulmonary embolism, mechanical valve replacement, or mitral or tricuspid valve replacement or reconstruction were bridged with therapeutic LMWH, which usually was started the day after surgery, until (new) oral anticoagulants were (re)started before hospital discharge. Therapeutic dose of nadroparin is 3,600 IU if <60 kg, 5,700 IU if 60-to-80 kg, 7,600 IU if 80-to-100 kg, and 9,500 IU if >100 kg twice a day dependent on renal function. In case (dual) antiplatelet therapy with clopidogrel and ASA were both indicated next to anticoagulants, clopidogrel was used preferably above ASA because triple therapy is not recommended in the authors' medical center. After aortic surgery or bioprosthetic aortic valve replacement, ASA was started within 24 hours after surgery.

Apart from cardiac surgery-related anticoagulation, all patients with sustained (48-72 hours) POAF without contraindication, received per protocol anticoagulation with LMWH followed by oral anticoagulation. This may be lifelong or reconsidered and tapered at a later stage.

In case of new-onset POAF, patients were treated with therapeutic LMWH within 12-to-48 hours after AF onset. These patients were treated only with therapeutic LMWH more than 48 hours after cardiac surgery and after thoracic drains were removed. This therapy was followed by oral anticoagulation before hospital discharge, but usually only if POAF was sustained more than 24 hours.

The primary endpoint of this secondary analysis was thromboembolic stroke during hospital stay after cardiac surgery. Secondary endpoints included length of stay (ICU, hospital), and mortality (ICU, hospital, 90-day, one year).

Statistical Analyses

To study the association between POAF and thromboembolic stroke, the patients with thromboembolic stroke were compared with those without thromboembolic stroke, and the difference in the incidence of POAF in these groups was assessed. Odds ratios (ORs) were calculated with corresponding 95% confidence interval (CI) using logistic regression analyses. In additional multivariate analyses, the authors assessed the influence of adjustment of the crude ORs for potential confounders using all patient and baseline characteristics mentioned in Table 1 with the exception of a known history of atrial fibrillation and CHA_2DS_2-VASc. A subgroup analysis in which patients with a known history of atrial fibrillation were excluded, also was performed. A Kaplan-Meier survival curve was made for illustrative purposes.

To assess if patient or disease characteristics were associated with the occurrence of a thromboembolic stroke, stepwise logistic regression analysis was performed using a p value of 0.10 to eliminate variables with the backward method. The full model consisted of all patient and baseline characteristics mentioned in Table 1, again with exception of a known history of atrial fibrillation and CHA_2DS_2-VASc, but complemented by POAF occurrence during the first seven days after cardiac surgery. Thereafter, a risk score was calculated using the betas of the remaining variables in the model. Discrimination of the risk score for a thromboembolic stroke was calculated with the concordance C-statistic and corresponding receiver operating characteristic curve. Variables with more than 3% missing data are clarified in Table 1 but were not excluded from further analysis. Missing values were not imputed in the authors' analyses. To perform the statistical analyses, SPSS version 23 software was used.

Power Analysis

The study population consisted of a fixed sample size of 910 patients derived from the GRIP-COMPASS trial in which AF occurred in half of the patients and 26 patients had a thromboembolic stroke. Therefore, the minimal significant difference that was detected was RR 2.72 (95% CI, 1.15-6.41).

Data Availability

The data that supported the findings of this study are available from the corresponding author on reasonable request.

Table 1
Baseline Characteristics of 910 Patients Based on Having Thromboembolic Stroke (n = 26) After Cardiac Surgery or Not (n = 884)

Variable	Total (n = 910)N (%)	TE Stroke (n = 26, 2.9%)N (%)	No TE Stroke (n = 884, 97.1%)N (%)	p Value(Fisher Exact Test)
Age, y (mean)	66	69	66	0.18
Sex, female	299 (33%)	12 (46%)	287 (32%)	0.15
BMI (mean)	27	27	27	0.90
Previous cardiac surgery	55 (6%)	3 (12%)	52 (6%)	0.20
EuroSCORE (mean)	3.4	8.0	3.2	< 0.001
APACHE III score (mean)	43	58	43	< 0.001
SAPS (mean)	30	37	30	0.001
CHA_2DS_2-VASc (mean)	2.7	3.8	2.7	0.002
Type of cardiac surgery				0.016
CABG	440 (48%)	9 (35%)	431 (49%)	
Valve surgery	413 (45%)	12 (46%)	401 (45%)	
Aortic surgery	57 (6%)	5 (19%)	52 (6%)	0.019
Left ventricular function before surgery				0.376
EF >50%	508 (56%)	12 (46%)	496 (56%)	
EF 31%-50%	177 (20%)	8 (31%)	169 (19%)	
EF 21%-30%	90 (10%)	2 (7%)	88 (10%)	
EF <21%	57 (6%)	1 (4%)	77 (9%)	
CPB during surgery	594 (65%)	21 (81%)	573 (65%)	0.10
Duration surgery, min (mean)	243	320	241	< 0.001
AMI <3 mo prior to surgery	163 (18%)	6 (33%)	157 (18%)	0.44
History of stroke	103 (11%)	7 (27%)	96 (11%)	0.02
Diabetes mellitus	204 (22%)	6 (23%)	198 (22%)	> 0.99
COPD	110 (12%)	4 (15%)	106 (12%)	0.54
Hypertension	390 (43%)	14 (54%)	376 (43%)	0.32
Hypercholesterolemia	132 (15%)	5 (19%)	127 (14%)	0.57
Peripheral vascular disease	130 (14%)	11 (42%)	119 (13%)	< 0.001
History of renal failure	77 (9%)	1 (4%)	76 (9%)	0.72
History of malignancy	111 (12%)	4 (15%)	107 (12%)	0.55
History of atrial fibrillation/flutter	167 (18%)	5 (19%)	162 (18%)	0.80
Use of beta-blocking agents	578 (68%)*	12 (46%)	566 (64%)	0.25
Creatinine at ICU admission, μmol/L	94	87	94	0.60

Abbreviations: AMI, acute myocardial infarction; APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; CHA_2DS_2-VASc, congestive heart failure, hypertension, age (>75 = 2 points), diabetes, previous stroke/transient ischemic attack (2 points), vascular disease, and sex category; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; EuroSCORE, European System of Cardiac Operative Risk Evaluation; ICU, intensive care unit; SAPS, Simplified Acute Physiology Score; TE, thromboembolic.

* 58 (6.4%) missing (completely at random).

Results

Of the 910 patients included in this study, 26 patients (2.9%) had a thromboembolic stroke during hospital admission, of whom 21 patients (81%) had a postoperative thromboembolic stroke within seven days. No patients had symptoms resolving within 24 hours without ischemic lesions on brain imaging. POAF during the first seven days after cardiac surgery was detected in 17 patients (65%) among all patients with a thromboembolic stroke, and a total of 343 patients (39%) of the 884 patients (97.1%) without a stroke had POAF. About half (54%) of the patients with POAF had no history of atrial fibrillation.

Baseline Characteristics and Outcome Parameters

Patients with thromboembolic stroke had a higher EuroSCORE, APACHE III, SAPS, and CHA_2DS_2-VASc score, a longer duration of surgery, more often had surgery involving the aorta, and more often had a history of previous stroke or peripheral vascular disease (Table 1). There were no significant differences for age, sex, and body mass index between patients with and without a thromboembolic stroke. A history of atrial fibrillation (18% with stroke *v* 19% without stroke) and use of beta-blocking agents (46% with stroke *v* 64% without stroke) did not significantly differ between these groups. Patients with thromboembolic stroke had an average extended ICU stay of six days, an average extended hospital length of stay of nine days, and a higher ICU, hospital, 90-day, and one-year mortality (Table 2).

Primary and Secondary Outcomes

The incidence of POAF in those with a thromboembolic stroke was 65%, compared with 39% in those without a thromboembolic stroke: crude OR 2.98 (95% CI, 1.31-6.76) and confounder-adjusted OR 3.01 (95% CI, 1.13-8.00) (Table 3). All patient and baseline characteristics are in Table 1, with the exception of a known history of atrial fibrillation while investigating POAF, were considered to be potential thromboembolic

Table 2
Outcome Parameters of 910 Patients Based on Having Thromboembolic Stroke (n = 26) After Cardiac Surgery or Not (n = 884)

Variable	Total (n = 910)N (%)	TE Stroke (n = 26, 2.9%)N (%)	No TE Stroke (n = 884, 97.1%)N (%)	p ValueFisher Exact Test
POAF <7 d	360 (40%)	17 (65%)	343 (39%)	0.008
POAF hospital	389 (43%)	18 (69%)	371 (42%)	0.008
Days until first detection of POAF (mean)	5.8	4.7	5.9	0.04
Days until detection of stroke (mean)	4.8	4.8	-	-
Stroke <7 d	-	21 (81%)	-	-
LOS ICU, d (mean)	2.3	8.2	2.1	< 0.001
LOS ICU cumulative, d (mean)*	3.1	9.9	2.9	< 0.001
LOS hospital, d (mean)	14.5	23.1	14.2	0.001
ICU mortality	23 (3%)	3 (12%)	20 (2%)	0.025
Hospital mortality	38 (4%)	7 (27%)	31 (4%)	< 0.001
Mortality, 90 d	52 (6%)	7 (27%)	45 (5%)	< 0.001
Mortality, 1 y	64 (7%)	7 (27%)	57 (6%)	0.001

Abbreviations: EuroSCORE, European System of Cardiac Operative Risk Evaluation; ICU, intensive care unit; LOS, length of stay; POAF, postoperative atrial fibrillation; TE, thromboembolic.
* In case of 1 or more ICU readmissions.

stroke risk factors and, thus, included as confounders. Additional subgroup analysis in which patients with a known history of atrial fibrillation were excluded resulted in crude OR 3.59 (95% CI, 1.47-8.78) and confounder-adjusted OR 2.93 (95% CI, 1.01-8.55) (Table 3). To illustrate the thromboembolic stroke-free interval after cardiac surgery with or without POAF, survival curves are shown in Fig 1.

POAF, a history of peripheral vascular disease, a higher EuroSCORE, and a longer duration of surgery were associated independently with thromboembolic stroke, of which POAF was the strongest independent predictor (Table 4). The C-statistic (area under the curve of the receiver operating characteristic curve) for predicting thromboembolic stroke was 0.70 (95% CI, 0.60-0.79) (Fig 2).

Discussion

The main finding of the study was that patients with POAF within the first seven days after cardiac surgery had a three-fold increased risk for thromboembolic stroke during hospital admission based on the difference in the incidence of POAF between patients with and without thromboembolic stroke. Risk factors for the occurrence of thromboembolic stroke are POAF within seven days after cardiac surgery, a history of peripheral vascular disease, a higher EuroSCORE, and a longer duration of surgery, of which POAF is the strongest predictor. Another finding was that the occurrence of thromboembolic stroke had a negative impact on ICU and hospital length of stay and survival. Even though mortality after cardiac surgery is based on multifactorial risk profiles, reducing the risk for thromboembolic stroke may improve the outcome of cardiac surgery because POAF is an important and potentially preventable and treatable factor.

The findings were in line with several registry studies.[17,18] One study in which 49,264 patient records were extracted from a multiinstitutional database, aimed to examine the risk-adjusted impact of POAF on mortality, hospital readmission, and hospital costs.[17] POAF was found in 9,255 patients (19%), of whom 2.6% had a stroke, compared with 1.1% of the 40,009 patients (81%) without POAF (risk ratio 2.27; 95% CI, 1.94-2.66). POAF was associated with a two-fold increase in the adjusted odds of stroke after CABG and four-fold after valve replacement.

Another study totaling 19,497 patients investigated the impact of POAF on early and late outcomes after isolated CABG.[18] Postoperative atrial fibrillation was found in 5,547 patients (29%), of whom 1.3% had a permanent stroke compared with 0.7% of the patients without POAF (adjusted OR 1.80; 95% CI, 1.29-2.51).

The incidence of POAF and associated stroke risk in the authors' study was larger compared with the previously mentioned studies. This probably was due to a meticulous registration of POAF, and, moreover, the authors' primary analysis focused on thromboembolic stroke only, which was not specified in the previously mentioned studies.

Table 3
Odds Ratio for In-Hospital Thromboembolic Stroke With POAF in Fewer ThanSeven Days

Variable	Total (n = 910)N (%)	TE Stroke(n = 26, 2.9%) N (%)	No TE Stroke (n = 884, 97.1%)N (%)	OR (95% CI)	OR (95% CI)*
POAF <7 d	360 (40%)	17 (65%)	343 (39%)	2.98 (1.31-6.76) 3.01 (1.13-8.00)†	3.59 (1.47-8.78)* 2.93 (1.01-8.55)*,†

Abbreviations: CI, confidence interval; OR, odds ratio; POAF, postoperative atrial fibrillation; TE, thromboembolic.
* Additional subgroup analysis in which patients with a history of atrial fibrillation were excluded.
† Adjusted for all variables in Table 1 with exception of a history of atrial fibrillation and CHA_2DS_2-VASc.

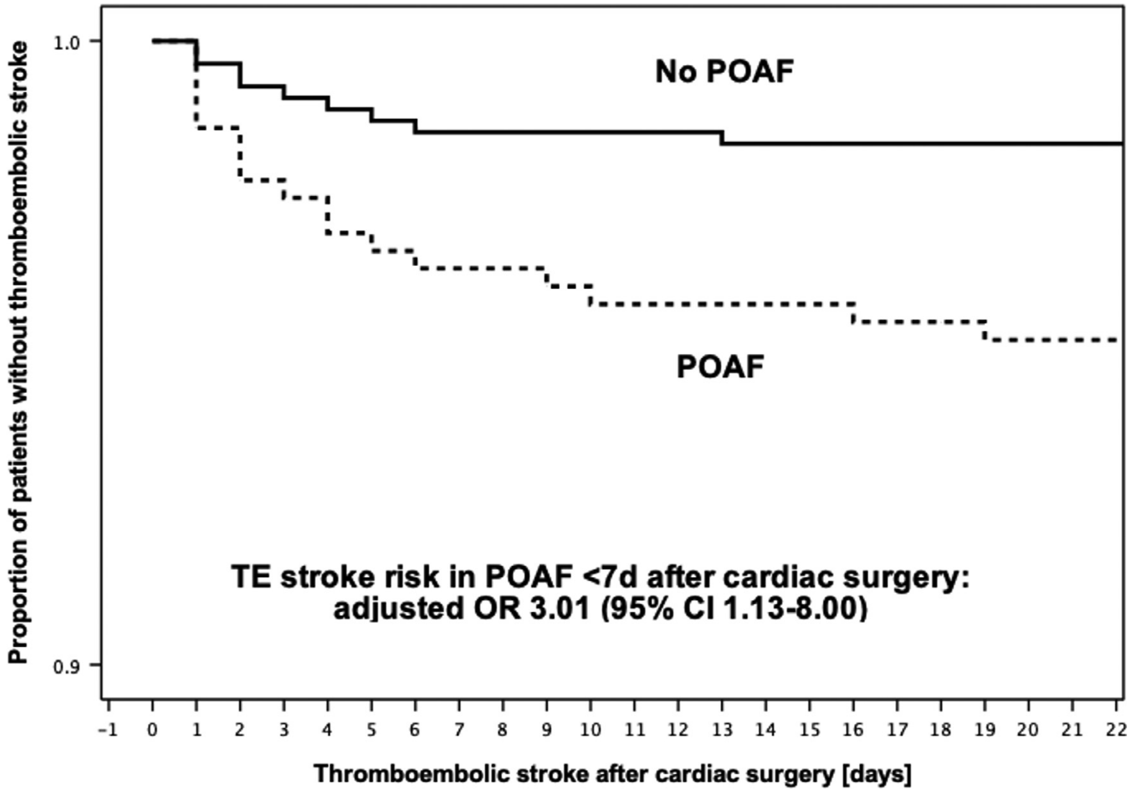

Fig 1. Thromboembolic stroke-free interval after cardiac surgery dependent on postoperative atrial fibrillation. OR, odds ratio; POAF, postoperative atrial fibrillation; TE, thromboembolic.

Some studies found no association between POAF and stroke.[19,20] One study aimed to explore the association between type and quantity of bypass grafts and cardiovascular outcomes in patients with POAF in a retrospective cross-sectional study of 3,068 patients undergoing CABG, with or without valve repair or replacement, and found no difference in the proportion of patients with postoperative stroke among patients with (5.7%) and without POAF (5.8%).[19] Again, stroke subtypes were not further specified.

Furthermore, an interesting finding in this study was the longer duration of surgery as an independent predictor for postoperative thromboembolic stroke. Cardiac surgery duration often correlates with the complexity of the procedure, which independently may predispose patients to well-known cardiac surgery-related stroke mechanisms such as emboli or hypoperfusion.[21]

Table 4
Chance for Thromboembolic Stroke Based on Stepwise Backward Logistic Regression

Variable	Beta	OR (95% CI)	p Value
POAF <7 d	1.096	2.99 (1.23-7.27)	0.016
Peripheral vascular disease	0.967	2.63 (1.05-6.61)	0.040
EuroSCORE	0.054	1.06 (1.00-1.11)	0.037
Duration of surgery, h	0.290	1.34 (1.10-1.62)	0.003

Abbreviations: CI, confidence interval; EuroSCORE, European System of Cardiac Operative Risk Evaluation; OR, odds ratio; POAF, postoperative atrial fibrillation.

Cardiac surgery-related POAF is considered as a different entity compared with atrial fibrillation in the general population in terms of onset mechanisms and complication risks.[22] However, analyzing these groups separately was not the purpose of this study and would dilute the power considerably given the relatively low number of thromboembolic strokes. Thereby, some patients with known (paroxysmal) atrial fibrillation did not show POAF during ICU admission. Additional subgroup analysis, in which patients with a known history of atrial fibrillation were excluded, had no significant impact on the results.

Of all included patients, 578 patients (68%) were treated with beta-blocking agents preoperatively, according to the recommended use of beta-blocking agents in this specific population. Beta-blocking agents were continued when already used preoperatively, but the authors did not routinely use perioperative beta-blockers or amiodarone for prevention of atrial fibrillation. This may have contributed to an increased incidence of POAF in the authors' population, although the overall effect on stroke incidence remains unclear.

Even though in the authors' study thromboembolic stroke mostly occurred in patients after the onset of POAF, the causal relation remains dubious, as in six patients (23%) thromboembolic stroke occurred prior to POAF detection. Affirming this, a cohort study in which 2,580 patients with a pacemaker or defibrillator and aged ≥65 years with a history of hypertension but without a history of AF, enrolled in long-term (three years) continuous heart rhythm monitoring, showed a cumulative incidence of device-detected subclinical AF (SCAF) of

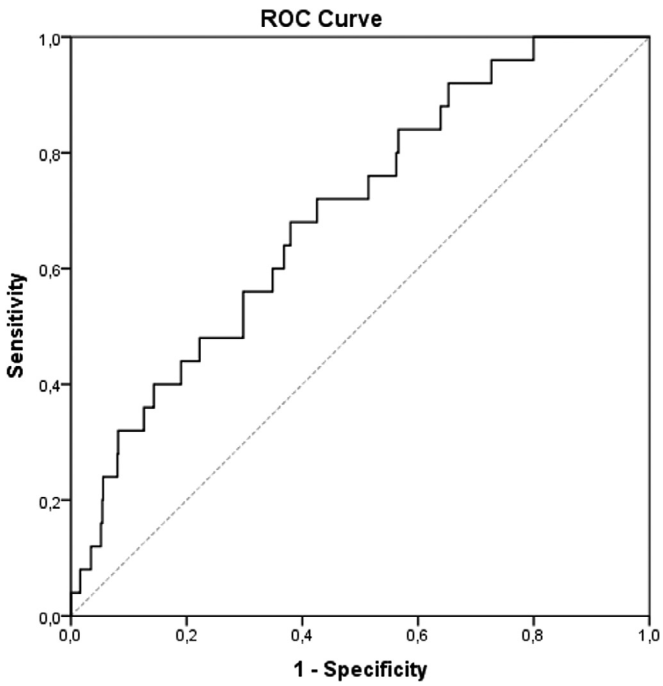

Fig 2. Receiver operating characteristic curve of risk score for thromboembolic stroke. AUC, area under the curve; ROC, receiver operating characteristic.

nearly 40%.[23] Only 15.6% of the patients who had a stroke showed evidence of SCAF within 30 days prior to the ischemic event.[24] Therefore, it is hypothesized that (subclinical) AF is rather a risk factor for stroke than a direct cause.

To reduce perioperative stroke risk, POAF should be further assessed. Studies on prophylactic interventions for POAF after cardiac surgery and the effect on subsequent stroke have been evaluated in a Cochrane Systematic Review.[25] The majority of studies followed patients until hospital discharge. The effect of pharmacologic treatment on POAF with amiodarone (OR 0.43; 95% CI, 0.34-0.54), magnesium (OR 0.55; 95% CI, 0.41-0.73), and beta-blockers (OR 0.33; 95% CI, 0.26-0.43) showed an overall lower incidence in the treatment group compared with the control group. However, the effect on postoperative stroke is not convincingly beneficial, as studies involving amiodarone showed only a borderline significant reduction in postoperative stroke and studies for magnesium and beta-blockers had insufficient data on postoperative stroke. Therefore, timely intervention of POAF by means of rhythm control or anticoagulation treatment also may have the potential to reduce the risk for thromboembolic stroke, as it occurred up to the third week after cardiac surgery in patients with POAF in the authors' study.[11,26]

Besides medical interventions, surgical risk reduction strategies also may be considered.[27] A small single-center randomized study found that closure of the left atrial appendage (LAA) during CABG, valve, or aorta surgery significantly reduced stroke risk within six years after cardiac surgery.[28] Most stroke cases had a late onset and likely were caused by thrombus formation in the LAA in the presence of AF. These findings warrant more research on this scarcely investigated procedure.

The authors' study had several limitations. First, the point estimate of the primary outcome thromboembolic stroke was low, which may limit the study's power, but was comparable with that described in the literature.[10] However, stroke frequency potentially could have been underestimated because brain imaging was not performed routinely in the absence of neurologic symptoms, which does not rule out the occurrence of minor events; for example, a TIA or lacunar infarction, although the latter is not associated with a cardioembolic source. Due to the absence of permanent neurologic deficits, they are less clinically relevant and had, therefore, no consequences for the interpretation of the study.[7,29] In addition, a few patients had magnetic resonance imaging, which underscores the heterogeneity of brain imaging. Alternative explanations, such as atherosclerotic plaques, were not ruled out systematically by means of CT angiography or carotid duplex in every patient. This limited the evidence for the authors' assumption that all perioperative thromboembolic strokes were cardiogenic embolisms. As continuous monitoring of POAF was not always performed after ICU discharge and short episodes could have been missed, the POAF incidence rate may have been underestimated. In addition, the total duration of POAF was not registered, so that a potential correlation with the severity of thromboembolic events could not be investigated. The retrospective nature of this study was the final limitation.

Postoperative atrial fibrillation within seven days after cardiac surgery was associated with a three-fold risk for a thromboembolic stroke during initial hospitalization. POAF, a history of peripheral vascular disease, a higher EuroSCORE, and a longer duration of surgery were independent risk factors for thromboembolic stroke directly after cardiac surgery, of which POAF was the most important and the only potentially modifiable factor. Preventing or treating cardiac surgery-related POAF, therefore, may reduce early stroke risk, but optimal strategies have yet to be determined.

Conflict of Interest

None.

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