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Association of New-Onset Atrial Fibrillation After Noncardiac Surgery With Subsequent Stroke and Transient Ischemic Attack

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IMPORTANCE Outcomes of postoperative atrial fibrillation (AF) after noncardiac surgery are not well defined.

OBJECTIVE To determine the association of new-onset postoperative AF vs no AF after noncardiac surgery with risk of nonfatal and fatal outcomes.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study in Olmsted County, Minnesota, involving 550 patients who had their first-ever documented AF within 30 days after undergoing a noncardiac surgery (postoperative AF) between 2000 and 2013. Of these patients, 452 were matched 1:1 on age, sex, year of surgery, and type of surgery to patients with noncardiac surgery who were not diagnosed with AF within 30 days following the surgery (no AF). The last date of follow-up was December 31, 2018.

EXPOSURES Postoperative AF vs no AF after noncardiac surgery.

MAIN OUTCOMES AND MEASURES The primary outcome was ischemic stroke or transient ischemic attack (TIA). Secondary outcomes included subsequent documented AF, all-cause mortality, and cardiovascular mortality.

RESULTS Among 904 patients included in the matched analysis, the median age was 75 years (IQR, 67-82 years) and 51.8% of patients were men. Patients with postoperative AF had significantly higher CHA_2DS_2-VASc scores vs the no AF group (median, 4 [IQR, 2-5] vs 3 [IQR, 2-5]; $P < .001$). Over a median follow-up of 5.4 years (IQR, 1.4-9.2 years), there were 71 ischemic strokes or TIAs, 266 subsequent documented AF episodes, and 571 deaths, of which 172 were cardiovascular related. Patients with postoperative AF had a statistically significantly higher risk of ischemic stroke or TIA vs those with no AF. Patients with postoperative AF had statistically significantly higher risks of subsequent documented AF and all-cause death. No significant difference in the risk of cardiovascular death was observed for patients with and without postoperative AF.

	Rate per 1000 person-years (95% CI)		Absolute risk difference at 5 y (95% CI), %	HR (95% CI)
	No AF	Postoperative AF		
Primary outcome: ischemic stroke/TIA	10.0 (6.7-14.4)	18.9 (13.6-25.6)	4.7 (1.0-8.4)	2.69 (1.35-5.37)
Subsequent AF	21.6 (16.5-27.8)	136.4 (118.4-156.5)	39.3 (33.6-45.0)	7.94 (4.85-12.98)
All-cause death	86.8 (76.5-98.0)	133.2 (118.9-148.8)	9.4 (4.9-13.7)	1.66 (1.32-2.09)
Cardiovascular death	25.0 (19.6-31.5)	42.5 (34.6-51.8)	6.2 (2.2-10.4)	1.51 (0.97-2.34)

CONCLUSIONS AND RELEVANCE Among patients undergoing noncardiac surgery, new-onset postoperative AF compared with no AF was associated with a significant increased risk of stroke or TIA. However, the implications of these findings for the management of postoperative AF, such as the need for anticoagulation therapy, require investigation in randomized trials.

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Atrial fibrillation (AF) occurring after noncardiac surgery has been considered to be triggered by the combination of postoperative stress and systemic inflammation, in addition to predisposing comorbidities.[1] However, it is unknown how often the arrhythmia is an isolated postoperative phenomenon or an arrhythmia that is likely to persist after the postoperative state resolves. Prior data suggest that it may identify a subset of patients at a greater risk of short-term and long-term adverse outcomes. In a retrospective cohort study involving about 1.7 million patients undergoing any surgery for which ascertainment of AF and outcomes was based on diagnostic billing codes, patients with postoperative AF following noncardiac surgery were at greater long-term risk of ischemic stroke than were patients with postoperative AF after cardiac surgery.[2] An improved understanding of the long-term prognosis of postoperative AF following noncardiac surgery on stroke and mortality may have clinical implications on management strategies and arrhythmia monitoring.

This community-based cohort study sought to compare the risks of stroke or transient ischemic attack (TIA) among patients with new-onset postoperative AF vs those without AF after noncardiac surgery. In secondary analyses, the risks of subsequent documented AF, all-cause mortality, and cardiovascular mortality between those with and without postoperative AF were compared.

Key Points

Question What is the prognostic significance of new-onset atrial fibrillation (AF) after noncardiac surgery?

Findings This retrospective cohort study included 904 participants who underwent noncardiac surgery. Comparing those with vs without postoperative AF, the hazard ratio for ischemic stroke or transient ischemic attack was 2.69, which was statistically significant.

Meaning New-onset AF after noncardiac surgery was significantly associated with increased risk of subsequent stroke or transient ischemic attack.

Methods

Study Design and Patient Population

The Mayo Clinic and Olmsted Medical Center institutional review boards approved this study. The study was considered minimal risk by both institutional review boards; therefore, the requirement for informed consent was waived. However, records of any patient who had not provided authorization for their medical records to be used for research were not reviewed pursuant on Minnesota statute 144.335.

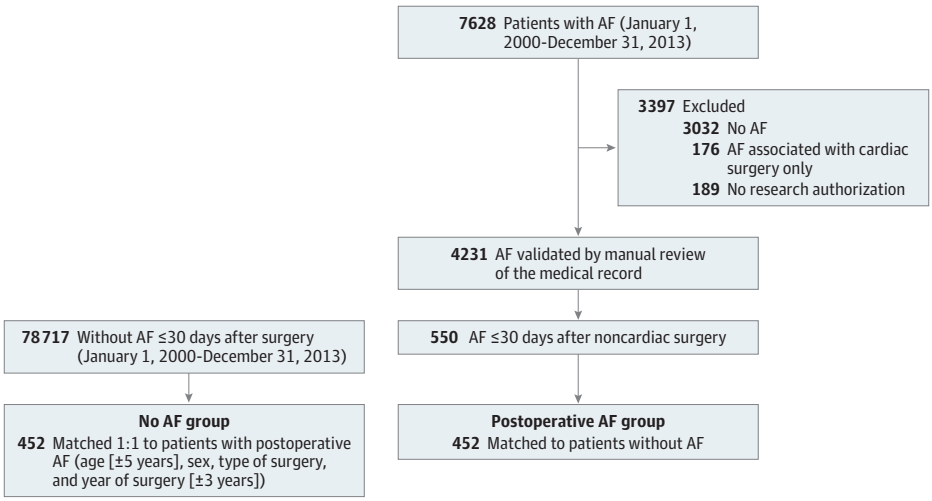
This study used the resources of the Rochester Epidemiology Project (REP), a medical records linkage system enabling nearly complete capture of all medical care delivered to residents of Olmsted County, Minnesota.[3,4] The comprehensive capture of medical care is possible because Olmsted County is relatively isolated from other urban centers, and only a few institutions (mainly Mayo Clinic, Olmsted Medical Center, and their affiliated hospitals) deliver health care to local residents. The study population consisted of adult residents (≥18 years) with first-known AF diagnosed between January 1, 2000, and December 31, 2013. *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9*) diagnostic codes 427.31 and 427.32 from all institutions in Olmsted County, and Mayo Clinic electrocardiograms (ECGs) indicating AF or atrial flutter were obtained from inpatient and outpatient encounters. All records of these patients with possible AF were manually reviewed to validate the diagnoses of AF or atrial flutter. One or more of the following were required to validate the first-ever AF events in either the inpatient or outpatient setting: (1) ECG or rhythm strip; (2) Holter monitor, event monitor, or telemetry; (3) monitor during an emergency department visit or hospitalization; (4) ECG during an echocardiogram; (5) pacemaker interrogation; or (6) physician diagnosis.[5] Patients with AF occurring within 30 days of heart or large thoracic vessel surgery were excluded. Also, any patient whose first-ever AF episode occurred prior to January 1, 2000, or after December 31, 2013, was excluded.

From the eligible patient population with AF, we selected patients with first-ever AF occurring within 30 days after a noncardiac surgical procedure (postoperative AF group; index date is the date of their AF occurence). Intraoperative AF events were also included. Patients with a history of AF prior to the surgery were not included in this group. The surgical procedures were identified using *ICD-9* procedure codes and *Current Procedural Terminology* (*CPT*) codes as defined by the Clinical Classifications Software (CCS) developed by the Agency for Healthcare Research and Quality.[6,7] Eligibility of noncardiac surgical procedures was defined to (1) include any inpatient or outpatient noncardiac surgery (open or laparoscopic) performed for diagnostic (such as open biopsies, exploratory laparotomy) or therapeutic purposes under general anesthesia and, (2) exclude minor surgeries such as endoscopic ear, nose, and throat (ENT) procedures; endoscopic gastrointestinal, urological, or pulmonary procedures; percutaneous vascular or nonvascular procedures; and minor skin, dental, ENT, and ophthalmologic procedures with only minimal sedation or local anesthesia.

Comparator Group

Outcomes for patients with postoperative AF were contrasted to a group of patients who had noncardiac surgery but did not have AF prior to or after surgery (within 30 days following the surgery or up to the date of last follow-up visit within the 30-day window; no AF group). The patients with no AF were matched 1:1 to the postoperative AF patients on age (±5 years), sex, year of surgery (±3 years), and type of surgery (ie, surgery that falls within the same CCS category; for those with multiple CCS categories on the same index surgical date, we matched on all categories). The index date for the no AF group was adjusted so that it was comparable with the postoperative AF group. For example, if a patient with postoperative AF developed AF 5 days after the noncardiac surgery, the index date for the matched patient without AF also began 5 days after the date of their surgery. In the same example, if the matched comparator patient died within 5 days after surgery, the matched patient was replaced with another comparator patient (**Figure 1**).

Figure 1. Flow Diagram of Olmsted County, Minnesota, Cohort Creation Process



AF indicates atrial fibrillation.

Data Collection

Patient demographics, comorbidities, outpatient prescriptions, and outcomes were obtained routinely on the AF cohort. Comorbidities diagnosed on or prior to the index date were electronically obtained using the *ICD-9* diagnostic codes, as previously defined.[5] In addition, the Charlson Comorbidity Index, $CHADS_2$ (congestive heart failure, hypertension, aged 75 years or older, diabetes, prior stroke or transient ischemic attack), and CHA_2DS_2-VASc (congestive heart failure, hypertension, age 75 years or older, diabetes, prior stroke or transient ischemic attack–vascular disease, age 65-74 years, sex category) scores were calculated.[8-10] Outpatient anticoagulant prescription data were routinely available from 2004 forward from Mayo Clinic and Olmsted Medical Center. Anticoagulant prescriptions included warfarin, heparin, and direct oral anticoagulants, such as dabigatran, rivaroxaban, and apixaban. We assessed the time from the first AF diagnosis to the first anticoagulant prescription and the time from prescription until discontinuation (defined as prescription nonrenewal or a >30-day gap between a prescription's estimated end date and subsequent prescription's start date).

Outcomes

The primary outcome was the composite of ischemic stroke or transient ischemic attack (TIA). Secondary, exploratory outcomes included subsequent documented AF (defined as AF documented >30 days after the index date), and death (all-cause and cardiovascularly related). Ischemic strokes and TIAs were identified using cardiovascular-related *ICD-9* diagnostic codes 433-436 and all records were manually reviewed to validate the diagnosis using previously published criteria.[9,11-13] For subsequent AF, the Mayo Clinic ECG database and *CPT* codes were used to identify patients who underwent an ECG with an AF diagnosis after the index date. Manual review of the records was completed to validate subsequent AF. Deaths from all causes were identified using death certificates from the Minnesota Department of Vital and Health Statistics, autopsy reports, and obituary notices. Deaths due to cardiovascular causes were defined using the American Heart Association classification.[14]

Statistical Analysis

Analyses were performed using SAS software, version 9.4 (SAS Institute Inc) and R software, version 3.4.2 (R Foundation for Statistical Computing). The incidence estimate of postoperative AF was age- and sex-adjusted to the US 2000 population. Baseline characteristics of the patients with and without postoperative AF were reported as frequencies and percentages for categorical variables and medians (interquartile range [IQR]) for continuous variables. Patient characteristics were compared using the McNemar test for categorical variables and the Wilcoxon signed rank test for continuous variables. The incidence of postoperative AF was age- and sex-standardized to the US 2000 population.

The same analytic approach was used for the primary outcome (ischemic stroke or TIA) and secondary exploratory outcomes (subsequently documented AF, all-cause mortality, and cardiovascular mortality). Patients were followed up from the index date until death, last follow-up while alive, or December 31, 2018, whichever occurred first. Cumulative incidence plots were constructed to visualize the occurrence of ischemic stroke or TIA, subsequently documented AF, and all-cause and cardiovascular mortality for patients with postoperative AF compared with those with no AF. Death was treated as a competing risk in the plots for ischemic stroke or TIA and subsequent documented AF, whereas noncardiovascular death was treated as a competing risk for the cardiovascular death plot. Absolute risk estimates and differences for patients with postoperative AF and patients with no AF were determined from Cox proportional hazards regression models. Stratified Cox models, which take into account the individual matching of patients with postoperative AF to patients with no AF, were used to estimate the hazard ratios (HRs) for each outcome for those with postoperative AF compared with those with no AF. Results were presented for unadjusted models and after adjustment for the Charlson Comorbidity Index. To account for residual confounding introduced by the nonexact match on

Table 1. Baseline Characteristics of Patients With Postoperative Atrial Fibrillation After Noncardiac Surgeries Matched to Patients Without Postoperative Atrial Fibrillation

	No. (%) of patients	
	Postoperative AF (n = 452)	No AF (n = 452)
Age, median (IQR), y	75 (67-82)	75 (67-82)
Sex		
Men	234 (51.8)	234 (51.8)
Women	218 (48.2)	218 (48.2)
Race		
White	436 (96.5)	427 (94.5)
Other or mixed	9 (2.0)	11 (2.4)
Asian	5 (1.1)	7 (1.5)
Black	1 (0.2)	7 (1.5)
American Indian	1 (0.2)	0
Hispanic ethnicity	3 (0.7)	5 (1.1)
BMI, median (IQR)	28.5 (24.2-33.1)	27.3 (24.0-31.9)
Hypertension	348 (77.0)	322 (71.2)
Malignancy	147 (32.5)	139 (30.8)
Diabetes	130 (28.8)	122 (27.0)
Chronic pulmonary disease	100 (22.1)	71 (15.7)
Heart failure	106 (23.5)	59 (13.1)
Myocardial infarction	76 (16.8)	55 (12.2)
Ischemic stroke or TIA	67 (14.8)	59 (13.1)
Peripheral vascular disease	62 (13.7)	55 (12.2)
Metastatic solid tumor	49 (10.8)	50 (10.8)
Renal disease	49 (10.8)	44 (9.7)
Aortic atherosclerotic disease	40 (8.8)	21 (4.6)
Rheumatologic disease	32 (7.1)	26 (5.8)
Dementia	25 (5.5)	22 (4.9)
Hemiplegia or paraplegia	18 (4.0)	16 (3.5)
Liver disease	17 (3.8)	10 (2.2)
Charlson Comorbidity Index, median (IQR)[a]	2 (1-5)	2 (1-4)
$CHADS_2$ score, median (IQR)[b]	2 (1-3)	2 (1-3)
CHA_2DS_2-VASc score, median (IQR)[c]	4 (2-5)	3 (2-5)

Abbreviations: AF, atrial fibrillation; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; IQR, interquartile range; TIA, transient ischemic attack.

[a] The Charlson Comorbidity Index is a weighted score indicating comorbidity burden that includes 17 comorbidities with the total score ranging from 0 to 33. Higher values indicate higher numbers of comorbidities. A value of 2 indicates the presence of 2 comorbidities.

[b] The $CHADS_2$ (congestive heart failure, hypertension, aged 75 years or older, diabetes, prior stroke or transient ischemic attack) score is a weighted risk score (range, 0-6) for ischemic stroke among patients with AF. Higher values indicate a greater risk. A score of 2 indicates a moderate risk; 3 or more, high risk.

[c] The CHA_2DS_2-VASc (congestive heart failure, hypertension, age 75 years or older, diabetes, prior stroke or transient ischemic attack–vascular disease, age 65-74 years, sex category) is a weighted risk score (range, 0-9) for ischemic stroke among patients with AF. Higher values indicate a greater risk. A score of 2 or higher indicates a moderate to high risk of stroke.

age, we further adjusted for age. For all Cox models, the proportional hazards assumption was tested using the scaled Schoenfeld residuals and found to be valid. No variables included in the models had missing values. The statistical significance threshold was set at $P < .05$ (2-sided). Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary end points should be interpreted as exploratory.

Results

Characteristics of the Patient Population

A total of 4231 patients with a new AF diagnosis were identified in the study period, of whom 550 patients (13.0%) had postoperative AF as their first-ever documented AF presentation, corresponding to a crude percentage of patients with postoperative AF of 0.7%, and an age- and sex-adjusted incidence of 38.6 (95% CI, 35.3-41.8) per 100 000 patients undergoing noncardiac surgery. Of the 550 patients, 144 (26.2%) underwent orthopedic , 128 (23.3%) gastrointestinal , 113 (20.5%) respiratory, 38 (6.9%) urogenital, and 35 (6.4%) nervous system procedures and 92 (16.7%) underwent other procedures. Among all postoperative AF diagnoses, 82% and 90% occurred within 7 and 14 days after surgery, respectively (median time from surgery to AF diagnosis, 2 days [IQR, 1-5 days]).

Of these 550 patients, 452 were 1:1 matched to patients with no AF. The median age was 75 years (IQR, 67-82 years), and 51.8% of study patients were men in both groups. Missing data were observed for body mass index (n = 36 patients) whereas complete data were available for all other patient characteristics. Patients with postoperative AF had higher prevalence of comorbidities including hypertension, diabetes, myocardial infarction, aortic atherosclerotic disease, chronic pulmonary disease, peripheral vascular disease, liver disease, and renal disease (all $P < .05$) compared with patients with no AF (**Table 1**). The median CHA_2DS_2-VASc score was 4 (IQR, 2-5) for patients with postoperative AF and 3 (IQR, 2-5) for patients with no AF ($P < .001$).

Follow-up and Clinical Events

Among the 452 matched pairs, over a median follow-up of 5.4 years (IQR, 1.4-9.2 years; range, 0-19.0 years), 71 patients

Table 2. Rates, Absolute Risk Differences, and Hazard Ratios for Outcomes in Patients With Noncardiac Surgeries With and Without Postoperative Atrial Fibrillation

	No. events		Incidence rate per 1000 person-years (95% CI)		Unadjusted (95% CI)				Adjusted for age and Charlson Comorbidity Index (95% CI)			
					Absolute risk at 5 y, %				Absolute risk at 5 y, %			
	No AF (n = 452)	Postoperative AF (n = 452)	No AF	Postoperative AF	No AF (n = 452)	Postoperative AF (n = 452)	Absolute RD at 5 y, %[a]	HR	No AF (n = 452)	Postoperative AF (n = 452)	Absolute RD at 5 y, %[b]	HR
Primary outcome												
Ischemic stroke or TIA	29	42	10.0 (6.7-14.4)	18.9 (13.6-25.6)	5.3 (3.2-7.4)	9.7 (6.4-12.8)	4.4 (1.0-7.8)	2.75 (1.42-5.32)	6.0 (3.5-8.4)	10.7 (7.1-14.2)	4.7 (1.0-8.4)	2.69 (1.35-5.37)
Secondary outcomes												
Subsequent AF	61	205	21.6 (16.5-27.8)	136.4 (118.4-156.5)	11.4 (8.5-14.3)	50.3 (44.5-55.4)	38.9 (33.1-44.5)	6.87 (4.44-10.64)	12.1 (9.0-15.1)	51.4 (45.8-56.4)	39.3 (33.6-45.0)	7.94 (4.85-12.98)
All-cause death	258	313	86.8 (76.5-98.0)	133.2 (118.9-148.8)	36.3 (32.2-40.1)	48.5 (44.0-52.6)	12.2 (7.0-17.4)	1.75 (1.41-2.17)	37.2 (33.5-40.8)	46.6 (42.8-50.1)	9.4 (4.9-13.7)	1.66 (1.32-2.09)
Cardiovascular-related death	73	99	25.0 (19.6-31.5)	42.5 (34.6-51.8)	11.3 (8.4-14.1)	18.0 (14.2-21.6)	6.7 (2.6-10.8)	1.53 (1.02-2.27)	13.0 (9.8-16.0)	19.2 (15.4-22.8)	6.2 (2.2-10.4)	1.51 (0.97-2.34)

Abbreviations: AF, atrial fibrillation; RD, risk difference; HR, hazard ratio; TIA, transient ischemic attack.

[a] Absolute risk difference is absolute risk of postoperative atrial fibrillation minus absolute risk of no atrial fibrillation.

experienced an ischemic stroke or TIA, 266 patients experienced a subsequent documented AF event, and 571 patients died. Of these, 14 had missing cause of death and of the remaining 557 deaths, 172 (30.9%) were cardiovascular related. The rates of all outcomes were higher for patients with postoperative AF than for those with no AF (**Table 2**; **Figure 2**).

Associations of Postoperative AF With Clinical Events

After adjustment for age and Charlson Comorbidity Index, a statistically significant increased risk of ischemic stroke or TIA was observed for patients with postoperative AF compared with those with no AF. The absolute risk at 5 years for patients with postoperative AF was 10.7% (95% CI, 7.1%-14.2%) vs 6.0% (95% CI, 3.5%-8.4%) for those with no AF. The absolute risk difference [RD] at 5 years was 4.7% (95% CI, 1.0%-8.4%), and the HR was 2.69 (95% CI, 1.35-5.37). In addition, a statistically significant increased risk of subsequent documented AF was observed for the postoperative AF group compared with the no AF group. The absolute risk at 5 years for the postoperative AF group was 51.4% (95% CI, 45.8%-56.4%) vs 12.1% (95% CI, 9.0%-15.1%) for the no AF group. The absolute RD at 5 years was 39.3% (95% CI, 33.6%-45.0%), and the HR was 7.94 (95% CI, 4.85-12.98).

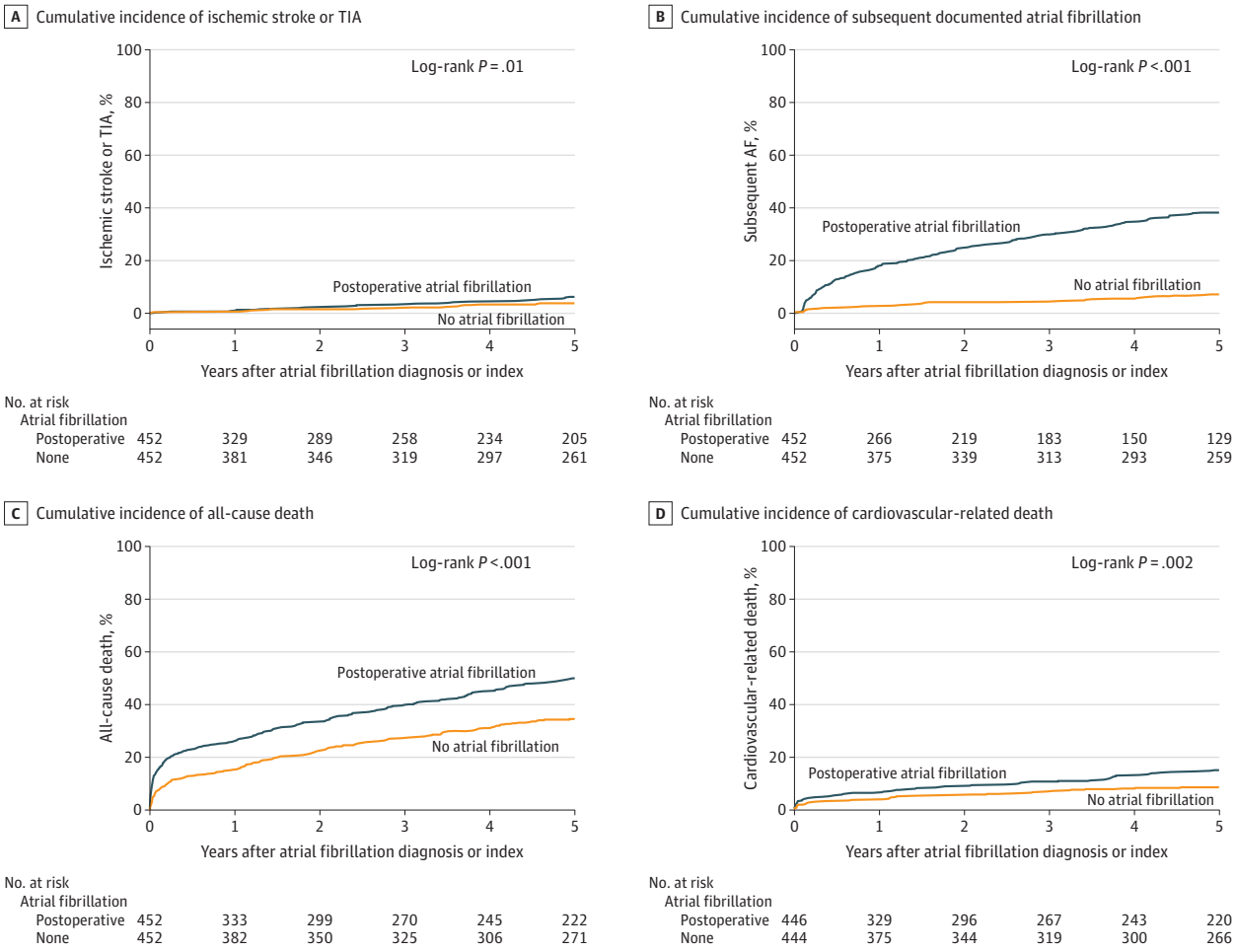
Similarly, a statistically significant increased risk of all-cause death was observed for patients with postoperative AF compared with those with no AF. The absolute risk at 5 years for those with postoperative AF was 46.6% (95% CI, 42.8%-50.1%) vs 37.2% (95% CI, 33.5%-40.8%) for those with no AF. The absolute RD at 5 years was 9.4% (95% CI, 4.9%-13.7%), and the HR was 1.66 (95% CI, 1.32-2.09). However, there was no statistically significant difference in the risk of cardiovascular death between groups. The absolute risk at 5 years was 19.2% (95% CI, 15.4%-22.8%) for those with AF vs 13.0% (95% CI, 9.8%-16.0%) for those with no AF. The absolute RD at 5 years was 6.2% (95% CI, 2.2%-10.4%), and the HR, 1.51 (95% CI, 0.97-2.34).

Anticoagulation Therapy

Among the 550 patients with postoperative AF, 437 had their index postoperative AF diagnosis in 2004 or later when outpatient prescription data became routinely available. Of them, 216 (49.4%) were prescribed an anticoagulant during follow-up. The median time from AF diagnosis to the first anticoagulant prescription was 37 days (IQR, 5-683 days). The median time spent taking anticoagulation agents was 60 days (IQR, 7-365 days). The cumulative incidence of anticoagulant prescriptions at 30 days and 1 year after the index AF diagnosis were 23.6% (95% CI, 19.7%-27.5%) and 34.6% (95% CI, 30.1%-39.1%), respectively.

In the postoperative AF group, 56 patients had a stroke or TIA during follow-up. The median CHA_2DS_2-VASc score of these patients was 4 (IQR, 3-4), and 91.1% had CHA_2DS_2-VASc score of 2 or more at the time of the postoperative AF diagnosis. In comparison, patients with postoperative AF without a stroke or TIA had a bmedian CHA_2DS_2-VASc score of 4 (IQR, 2-5), and 86.2% had CHA_2DS_2-VASc score of 2 or higher (P = .68 for comparing the medians). Among patients with postoperative AF during the period when prescription data were available, 46 patients had a stroke or TIA, and among these, only 9 patients

Figure 2. Cumulative Incidence of Primary and Secondary Outcomes Among Patients With Postoperative Atrial Fibrillation and Without Atrial Fibrillation



The median observation times for ischemic stroke or transient ischemic attack were 4.2 years (IQR, 0.7-7.3 years) for those with postoperative atrial fibrillation (AF) and 6.0 years (IQR, 2.2-10.1 years) for those with no AF; for subsequent documented AF, 1.8 years (IQR, 0.2-5.4 years) for those with postoperative AF and 5.9 years (IQR, 2.0-9.6 years) for those with no AF; and for all-cause and cardiovascular-related death, 4.9 years (IQR, 0.8-7.9 years) for those with postoperative AF and 6.3 years (IQR, 2.3-10.3 years) for those with no AF. TIA indicates transient ischemic attack.

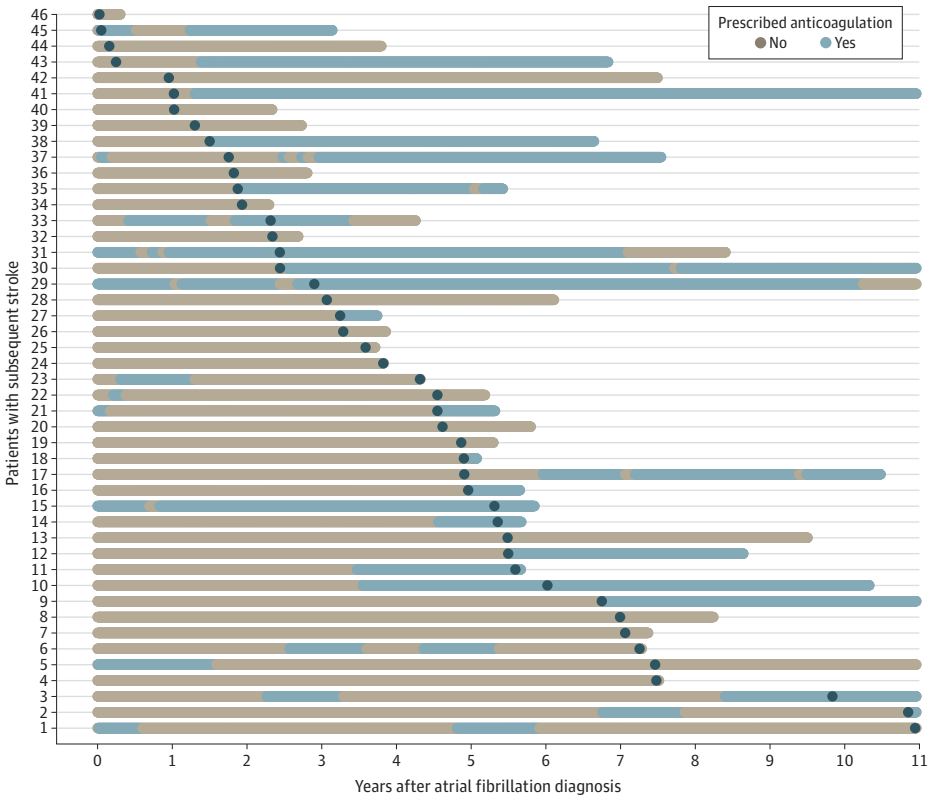
were prescribed anticoagulation agents at the time of the stroke or TIA (**Figure 3**).

Discussion

Among patients undergoing noncardiac surgery followed up for a median of 5.4 years, the presence of postoperative AF compared with no documented AF was associated with a significantly increased risk of stroke or TIA. There was also a significant association with all-cause mortality and subsequent documented AF. These findings might have rhythm monitoring and treatment implications and suggest that, for many patients, AF after noncardiac surgery is not a transient arrhythmia simply dependent on resolution of the postoperative state. Rather, the postoperative state may be considered a "stress test" for the manifestation of AF. A subset of patients with new diagnoses of postoperative AF may also represent previously undiagnosed AF that is detected due to more intensive rhythm monitoring postoperatively.

Associations between postoperative AF and outcomes have been extensively studied after cardiac surgery with studies indicating an increased risk of subsequent AF and increased short-term risk of stroke,[15-18] whereas results have been conflicting regarding long-term stroke risk.[19,20] It is critical to clarify these associations for postoperative AF after noncardiac surgery. The current study expands on recent evidence suggesting an increased risk of thromboembolism in patients with AF after noncardiac surgery. In an administrative claims analysis from California hospitals using diagnosis codes for ascertainment of AF and clinical events, AF after noncardiac surgery was associated with incident stroke with an HR of 2.0 (95% CI, 1.7-2.3).[2] Similar results were reported in a secondary analysis of the Perioperative Ischemic Evaluation Study (POISE) trials in which patients with postoperative AF had a significantly increased risk of stroke at 1 year.[21] This present analysis, using manually ascertained AF and outcomes

Figure 3. Anticoagulation Prescriptions After the Diagnosis of Atrial Fibrillation Among Patients With Postoperative Atrial Fibrillation Who Had a Stroke or Transient Ischemic Attack During Follow-up



Black dots indicate the time of the first stroke or transient ischemic attack event among patients with postoperative atrial fibrillation who had a stroke or transient ischemic attack during follow-up.

and even longer follow-up, supports and strengthens the validity of these findings. Furthermore, a unique aspect of this study is that the comparator group without AF was exactly matched to the type of surgery in the AF group, thus reducing the potential confounding by type of surgery.

The mechanisms mediating the association of AF after noncardiac surgery with thromboembolism merit consideration. Postoperative AF may identify a subset of patients who have a substrate for thromboembolism regardless of the arrhythmia. However, the novel finding of this study that postoperative AF is not a transient, self-limited event provides further insights into the association with long-term thromboembolic risk that may be partially mediated by the recurrent nature of the arrhythmia and its persistence as a thromboembolism risk factor in a large proportion of patients. Thus, increased monitoring for detection of AF recurrence in patients with postoperative AF may be warranted. Whether anticoagulation can help prevent thromboembolic events in patients with postoperative AF is unknown and would require a randomized trial. In the current analysis, anticoagulation was used in a minority of patients with postoperative AF, and most patients with subsequent strokes were not taking anticoagulation agents at the time of stroke. These data support the notion that anticoagulation may warrant consideration in postoperative AF. However, the decision to initiate anticoagulation in the postoperative setting is a complex one. The high bleeding risk in the early postoperative period may outweigh any thromboembolic protection benefits with anticoagulation, particularly considering the small absolute risk of stroke or TIA over the brief postoperative period. Also, the unknown required duration of anticoagulant therapy for postoperative AF poses another limitation to its routine implementation in clinical practice.

An increased risk of all-cause mortality was identified in patients with postoperative AF compared with those without AF after similar types of surgery. A similar observation was made in the POISE trial.[21] It is possible that AF and its complications (thromboembolism, heart failure), as well as the downstream treatments for AF, contribute to some extent to the increased mortality. However, this increase in mortality may also largely reflect the worse risk profile of the patients experiencing postoperative AF, such that postoperative AF is a marker of poor postsurgical outcome. AF can precede or follow the development of other cardiac and noncardiac complications after noncardiac surgery in high-risk patients, such as those undergoing surgery for malignancy.[22]

Limitations

This study has several limitations. First, the Olmsted County population consists predominantly of White individuals and extrapolating to other more heterogeneous populations should be done with caution. Second, information regarding the number and duration of subsequent AF episodes, including the distinction between paroxysmal and persistent AF, was not available. Third, a detailed classification of strokes as cardioembolic

vs other was not feasible. Fourth, it is possible that postoperative AF may have alerted physicians to increase monitoring for subsequent AF, which could introduce an ascertainment bias in favor of increased detection (rather than increased incidence) in this population. Fifth, given the observational nature of the analysis, the possibility of residual confounding in the associations cannot be completely eliminated despite statistical adjustments and matching of patient cohorts on several characteristics.

Conclusions

Among patients undergoing noncardiac surgery, new-onset postoperative AF compared with no documented AF was associated with a significant increased risk of stroke or TIA. However, the implications of these findings for the management of postoperative AF, such as the need for anticoagulation therapy, require investigation in randomized trials.

ARTICLE INFORMATION

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Author Contributions: Dr Chamberlain had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Siontis, Gersh, Kashou, Roger, Noseworthy, Chamberlain.
Acquisition, analysis, or interpretation of data: Siontis, Weston, Jiang, Chamberlain.
Drafting of the manuscript: Siontis, Kashou, Chamberlain.
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