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Association of Preceding Antithrombotic Treatment With Acute Ischemic Stroke Severity and In-Hospital Outcomes Among Patients With Atrial Fibrillation

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IMPORTANCE Antithrombotic therapies are known to prevent stroke for patients with atrial fibrillation (AF) but are often underused in community practice.

OBJECTIVES To examine the prevalence of patients with acute ischemic stroke with known history of AF who were not receiving guideline-recommended antithrombotic treatment before stroke and to determine the association of preceding antithrombotic therapy with stroke severity and in-hospital outcomes.

DESIGN, SETTING, AND PARTICIPANTS Retrospective observational study of 94 474 patients with acute ischemic stroke and known history of AF admitted from October 2012 through March 2015 to 1622 hospitals participating in the Get With the Guidelines–Stroke program.

EXPOSURES Antithrombotic therapy before stroke.

MAIN OUTCOMES AND MEASURES Stroke severity as measured by the National Institutes of Health Stroke Scale (NIHSS; range of 0-42, with a higher score indicating greater stroke severity and a score ≥16 indicating moderate or severe stroke), and in-hospital mortality.

RESULTS Of 94 474 patients (mean [SD] age, 79.9 [11.0] years; 57.0% women), 7176 (7.6%) were receiving therapeutic warfarin (international normalized ratio [INR] ≥2) and 8290 (8.8%) were receiving non–vitamin K antagonist oral anticoagulants (NOACs) preceding the stroke. A total of 79 008 patients (83.6%) were not receiving therapeutic anticoagulation; 12 751 (13.5%) had subtherapeutic warfarin anticoagulation (INR <2) at the time of stroke, 37 674 (39.9%) were receiving antiplatelet therapy only, and 28 583 (30.3%) were not receiving any antithrombotic treatment. Among 91 155 high-risk patients (prestroke CHA_2DS_2-VASc score ≥2), 76 071 (83.5%) were not receiving therapeutic warfarin or NOACs before stroke. The unadjusted rates of moderate or severe stroke were lower among patients receiving therapeutic warfarin (15.8% [95% CI, 14.8%-16.7%]) and NOACs (17.5% [95% CI, 16.6%-18.4%]) than among those receiving no antithrombotic therapy (27.1% [95% CI, 26.6%-27.7%]), antiplatelet therapy only (24.8% [95% CI, 24.3%-25.3%]), or subtherapeutic warfarin (25.8% [95% CI, 25.0%-26.6%]); unadjusted rates of in-hospital mortality also were lower for those receiving therapeutic warfarin (6.4% [95% CI, 5.8%-7.0%]) and NOACs (6.3% [95% CI, 5.7%-6.8%]) compared with those receiving no antithrombotic therapy (9.3% [95% CI, 8.9%-9.6%]), antiplatelet therapy only (8.1% [95% CI, 7.8%-8.3%]), or subtherapeutic warfarin (8.8% [95% CI, 8.3%-9.3%]). After adjusting for potential confounders, compared with no antithrombotic treatment, preceding use of therapeutic warfarin, NOACs, or antiplatelet therapy was associated with lower odds of moderate or severe stroke (adjusted odds ratio [95% CI], 0.56 [0.51-0.60], 0.65 [0.61-0.71], and 0.88 [0.84-0.92], respectively) and in-hospital mortality (adjusted odds ratio [95% CI], 0.75 [0.67-0.85], 0.79 [0.72-0.88], and 0.83 [0.78-0.88], respectively).

CONCLUSIONS AND RELEVANCE Among patients with atrial fibrillation who had experienced an acute ischemic stroke, inadequate therapeutic anticoagulation preceding the stroke was prevalent. Therapeutic anticoagulation was associated with lower odds of moderate or severe stroke and lower odds of in-hospital mortality.

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Atrial fibrillation (AF) is an independent risk factor for stroke, increases stroke risk by a factor of 4 to 5, and accounts for 10% to 15% of all ischemic strokes.[1,2] While the burden of AF-related stroke is high, AF is a potentially treatable risk factor. Numerous studies have demonstrated that vitamin K antagonists, such as warfarin, or non–vitamin K antagonist oral anticoagulants (NOACs), such as dabigatran, rivaroxaban, apixaban, and edoxaban, reduce the risk of ischemic stroke.[3-8] Based on these data, current guidelines recommend adjusted-dose warfarin or NOACs over aspirin for stroke prevention in high-risk patients with AF.[1,9]

Despite guideline recommendations, oral anticoagulants such as warfarin are often underused in community practice.[10,11] Several studies have reported that warfarin might also reduce stroke severity if stroke occurs.[12-14] Nonetheless, these findings are based on select patients from a single health plan or a local health system before the era of NOACs. More importantly, stroke severity either was assessed at discharge, which might have been affected by in-hospital treatment, or was not assessed using the National Institutes of Health Stroke Scale (NIHSS), which is considered the reference standard. With the rapid adoption of NOACs in clinical practice, there is a lack of contemporary data on a national scope regarding the prevalence of preceding antithrombotic treatment among patients with known history of AF who develop acute ischemic stroke and how stroke severity and outcomes differ by such treatment.

The goals of the study were to examine the prevalence of preceding antithrombotic treatment among patients with AF who had experienced an acute ischemic stroke and to assess the association between preceding antithrombotic treatment with initial stroke severity, in-hospital mortality, and functional outcomes at discharge.

Key Points

Question What is the prevalence of preceding antithrombotic treatment in patients with atrial fibrillation who had experienced an ischemic stroke, and what is its association with stroke severity and in-hospital outcomes?

Findings In this observational study of 94 474 patients with acute ischemic stroke who had a known history of atrial fibrillation, 84% did not receive guideline-recommended therapeutic anticoagulation preceding the stroke. Therapeutic anticoagulation with warfarin or non–vitamin K antagonist oral anticoagulants was significantly associated with lesser stroke severity and lower odds of in-hospital mortality.

Meaning Among patients with atrial fibrillation who had experienced an acute ischemic stroke, inadequate therapeutic anticoagulation preceding the stroke was prevalent.

Methods

Study Design and Data Sources

Details of the design and conduct of the Patient-Centered Research Into Outcomes Stroke Patients Prefer and Effectiveness Research (PROSPER) study have been previously described.[15-18] Briefly, PROSPER is a Patient-Centered Outcomes Research Institute (PCORI)-sponsored project designed to help patients, physicians, and other stakeholders make informed decisions about stroke care and improve patient outcomes. The study was conceived and designed by the multidisciplinary PROSPER team, composed of researchers partnering with patient investigators and stakeholders.

PROSPER builds on the American Heart Association (AHA)/American Stroke Association (ASA) Get With the Guidelines–Stroke (GWTG-Stroke) Registry program, which is an ongoing, voluntary, national stroke registry and quality-improvement initiative sponsored by the AHA/ASA.[19,20] Standardized data collection includes patient demographic characteristics, medical history, medications prior to admission, diagnostic testing, brain imaging, in-hospital treatment, and outcomes. Data elements for dabigatran and rivaroxaban use prior to admission were added to the registry in October 2012, followed by apixaban in October 2013 and edoxaban in September 2015. The validity and reliability of data collection have been reported previously.[21] Each participating hospital received either human research approval to enroll patients without individual patient consent under the Common Rule or a waiver of authorization and exemption from subsequent review by their institutional review board. Quintiles Inc serves as the data collection and coordination center. The Duke Clinical Research Institute serves as the data analysis center and has an agreement to analyze the aggregate deidentified data for research purposes. This study was approved by the institutional review board of Duke University.

Study Population and Variables of Interest

This is a retrospective analysis of patients with known history of AF or atrial flutter who had experienced an acute ischemic stroke and were admitted from October 2012 through March 2015 to hospitals participating in GWTG-Stroke. History of AF or atrial flutter was defined as AF or atrial flutter known to exist prior to the index acute ischemic stroke admission and documented in the medical record. Preceding antithrombotic treatment was defined as documentation of patients receiving an antithrombotic agent within 7 days before hospital arrival. For the purpose of the study, antithrombotic treatments were categorized into 5 mutually exclusive groups: (1) no antithrombotic therapy (none) as the reference; (2) antiplatelet therapy only (aspirin, clopidogrel, or dual antiplatelet therapy with aspirin and clopidogrel); (3) subtherapeutic warfarin with an admission international normalized ratio (INR) less than 2; (4) therapeutic warfarin with an INR of 2 or higher; and (5) NOACs (dabigatran, rivaroxaban, or apixaban). Edoxaban was approved by the US Food and Drug Administration in January 2015; therefore, information on edoxaban was not collected in this registry during the study period.

Reasons for no anticoagulation prior to the index hospitalization were not collected in this registry. Because contraindications or reasons for no anticoagulation are likely to persist after stroke, documented reasons for no anticoagulation at discharge were analyzed to gain insights into potential reasons anticoagulation was not provided prior to admission. Reasons for not prescribing anticoagulation at hospital discharge

were documented in the medical record by a physician, advanced practice nurse, or physician assistant.

The primary outcomes were the initial stroke severity at admission and in-hospital mortality. The NIHSS score was used as a measure of stroke severity (range of 0-42, with a higher score indicating greater stroke severity). Patients with an NIHSS score of 16 or higher were classified as having a moderate or severe stroke.[22,23] The secondary outcome was functional outcome at discharge as measured by the modified Rankin Scale (mRS) score (range of 0 [no symptoms] to 6 [death]).[24] Patients with an mRS score of 0 or 1 were classified as having excellent recovery and those with an mRS score of 0 to 2 were classified as having functional independence.

Statistical Analysis

Medians (interquartile ranges [IQRs]) and percentages were used to describe the distribution of continuous and categorical variables, respectively. Baseline characteristics were compared across 5 preceding antithrombotic treatment groups using the Pearson χ^2 test for categorical variables and Kruskal-Wallis test for continuous variables. Multivariable logistic regression models were performed to investigate the relationships between preceding antithrombotic therapies with each clinical outcome measure: stroke severity at admission, in-hospital mortality, and mRS score at discharge. These analyses adjusted for baseline demographic and clinical variables prior to the index stroke event, including age, sex, race/ethnicity (admission staff, medical staff, or both recorded the patient's self-reported race/ethnicity, usually during the registration; prior studies have suggested differences in outcomes from acute ischemic stroke related to race/ethnicity), insurance, medical history (coronary artery disease [CAD] or prior myocardial infarction [MI], prior stroke or transient ischemic attack [TIA], prosthetic heart valve, carotid stenosis, heart failure, hypertension, diabetes mellitus, dyslipidemia, peripheral vascular disease, and smoking status), and use of antihypertensive, cholesterol-lowering, or antidiabetic medication prior to admission. The preceding antithrombotic treatment was included as an independent variable, with no antithrombotic therapy as the reference group.

In addition, administration of intravenous tissue plasminogen activator, intra-arterial catheter-based treatment, and hospital characteristics (number of beds, academic status, primary stroke center, annual ischemic stroke volume, annual tissue plasminogen activator volume, hospital region, and rural location) were included in the mortality and mRS models because these variables are expected to be predictive of in-hospital outcomes but not initial stroke severity. Generalized estimating equations with exchangeable correlation matrix were used to account for within-hospital clustering. Because it is inappropriate to impute outcome measure, complete case analyses were performed for stroke severity, in-hospital mortality, and mRS models.

In addition to the overall population, prespecified stratified analyses were performed in clinically relevant subgroups by age (<80 and ≥80 years); sex; history of previous stroke or TIA; CAD or MI; and prestroke CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes, stroke/TIA/thromboembolism [doubled], vascular disease [prior MI, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]) because these variables are expected to influence the decision of antithrombotic treatment. Interactions between antithrombotic treatment and each subgroup variable were formally tested by including the interaction terms in the logistic regression model. A CHA_2DS_2-VASc score of 0 or 1 corresponds to low to moderate thromboembolic risk and 2 or higher indicates high risk prior to the index stroke event.[25-27] Except for patients receiving warfarin or NOACs with a prestroke CHA_2DS_2-VASc score of 0 or 1, this analysis had more than 80% statistical power for each subgroup.

All statistical analyses were performed using SAS version 9.4 statistical software (SAS Institute Inc). All P values are 2-sided, with $P < .05$ considered statistically significant.

Results

A total of 120 260 patients with known history of AF who had experienced an acute ischemic stroke were admitted from October 2012 through March 2015 to hospitals participating in the GWTG-Stroke program. Of these, 16 933 patients transferred from another hospital were excluded because in-hospital care from the transferring hospital could not be tracked after transfer. In addition, patients receiving warfarin with missing information on INR at admission (n = 6686) and patients who were receiving unfractionated heparin, low-molecular-weight heparin, argatroban, desirudin, fondaparinux, lepirudin, aspirin-dipyridamole, prasugrel, ticagrelor, or ticlopidine (n = 2167) were also excluded. After these exclusions, the final study population consisted of 94 474 patients admitted to 1622 hospitals in the United States (eFigure in the Supplement). For the outcome measures, data were available for stroke severity (for 81.7% of cases), in-hospital mortality (98.0%), and mRS score (52.0%).

Preceding Antithrombotic Treatment and Baseline Characteristics

Of 94 474 patients with acute ischemic stroke who had a history of AF (mean [SD] age, 79.9 [11.0] years; 57.0% women), 79 008 (83.6%) were not receiving therapeutic anticoagulation prior to stroke, 7176 (7.6%) were receiving therapeutic warfarin, and 8290 (8.8%) were receiving NOACs (**Table 1**). A total of 12 751 (13.5%) had a subtherapeutic warfarin with an INR less than 2 at the time of stroke, 37 674 (39.9%) were receiving antiplatelet therapy only, and 28 583 (30.3%) were not receiving any antithrombotic treatment prior to stroke. A total of 91 155 patients (96.5%) had a prestroke CHA_2DS_2-VASc score of 2 or higher (ie, high risk); of these patients, 76 071 (83.5%) were not receiving adequate therapeutic anticoagulation prior to stroke (Table 1).

Patients receiving warfarin or NOACs were slightly younger, were less likely to be female, and had a higher prevalence of previous stroke or TIA than those receiving antiplatelet therapy only or receiving no antithrombotic treatment ($P < .001$;

Table 1. Baseline Characteristics by Preceding Antithrombotic Treatment Among 94 474 Patients With AF and Acute Ischemic Stroke

Characteristic[a]	Preceding Antithrombotic Therapy				
	None (n = 28 583)	Antiplatelet Therapy Only (n = 37 674)	Warfarin, INR <2 (n = 12 751)	Warfarin, INR ≥2 (n = 7176)	NOACs (n = 8290)
Age, median (IQR), y	82 (73-88)	83 (75-89)	81 (73-87)	81 (73-86)	79 (70-85)
Women, No. (%)	16 856 (59.0)	21 945 (58.2)	7213 (56.6)	3561 (49.6)	4303 (51.9)
Race and ethnicity, No. (%)					
Non-Hispanic white	22 287 (78.0)	30 953 (82.2)	10 021 (78.6)	6039 (84.2)	6611 (79.8)
Non-Hispanic black	2731 (9.6)	3140 (8.3)	1438 (11.3)	573 (8.0)	823 (9.9)
Hispanic	1575 (5.5)	1568 (4.2)	636 (5.0)	245 (3.4)	435 (5.3)
Other	1920 (6.7)	1958 (5.2)	656 (5.1)	301 (4.2)	405 (4.9)
Insurance, No. (%)					
Private	8066 (28.2)	14 140 (37.5)	5093 (39.9)	3100 (43.2)	3434 (41.4)
Medicare	17 124 (59.9)	20 230 (53.7)	6386 (50.1)	3503 (48.8)	4129 (49.8)
Medicaid	1953 (6.8)	2526 (6.7)	983 (7.7)	474 (6.6)	523 (6.3)
Self-pay	450 (1.6)	381 (1.0)	207 (1.6)	74 (1.0)	67 (0.8)
Medical history, No. (%)					
AF or atrial flutter	28 583 (100)	37 674 (100)	12 751 (100)	7176 (100)	8290 (100)
Prosthetic heart valve	479 (1.7)	782 (2.1)	600 (4.7)	586 (8.2)	134 (1.6)
Previous stroke or TIA	8176 (28.6)	13 508 (35.9)	5270 (41.3)	3383 (47.1)	3722 (44.9)
Carotid stenosis	903 (3.2)	1862 (4.9)	473 (3.7)	392 (5.5)	395 (4.8)
CAD or MI	7603 (26.6)	14 664 (38.9)	4563 (35.8)	2942 (41.0)	2982 (36.0)
Heart failure	5600 (19.6)	8521 (22.6)	3159 (24.8)	1782 (24.8)	1663 (20.1)
Hypertension	21 910 (76.7)	31 064 (82.5)	10 666 (83.7)	5928 (82.6)	6880 (83.0)
Dyslipidemia	11 474 (40.1)	19 314 (51.3)	6492 (50.9)	3954 (55.1)	4397 (53.0)
PVD	1446 (5.1)	2799 (7.4)	926 (7.3)	623 (8.7)	541 (6.5)
Diabetes mellitus	7641 (26.7)	10 981 (29.2)	4270 (33.5)	2513 (35.0)	2756 (33.2)
Smoker	2289 (8.0)	2561 (6.8)	862 (6.8)	451 (6.3)	631 (7.6)
Prestroke CHA_2DS_2-VASc score, No. (%)[b]					
0	404 (1.4)	215 (0.6)	41 (0.3)	16 (0.2)	49 (0.6)
1	1186 (4.1)	904 (2.4)	187 (1.5)	91 (1.3)	226 (2.7)
≥2	26 993 (94.4)	36 555 (97.0)	12 523 (98.2)	7069 (98.5)	8015 (96.7)
Preadmission medication, No. (%)					
Antihypertensive	14 068 (49.2)	28 535 (75.7)	11 395 (89.4)	6462 (90.1)	6482 (78.2)
Cholesterol-lowering	10 425 (36.5)	20 613 (54.7)	7316 (57.4)	4487 (62.5)	5016 (60.5)
Antidiabetic	3325 (11.6)	7210 (19.1)	3406 (26.7)	2073 (28.9)	1930 (23.3)
INR, median (IQR)	1.1 (1.0-1.1)	1.1 (1.0-1.1)	1.4 (1.2-1.6)	2.5 (2.2-3.1)	1.2 (1.1-1.4)
In-hospital treatment, No. (%)					
Intravenous tPA	3943 (13.8)	5683 (15.1)	1491 (11.7)	31 (0.4)	268 (3.3)
Intra-arterial catheter-based treatment	545 (1.9)	691 (1.8)	354 (2.8)	106 (1.5)	215 (2.6)
Hospital characteristics					
Bed size, median (IQR), No.	347 (231-523)	353 (240-531)	357 (244-527)	348 (235-509)	365 (248-550)
Academic center, No. (%)	15 090 (52.8)	20 764 (55.1)	6910 (54.2)	3821 (53.3)	4366 (52.7)
Primary stroke center, No. (%)	12 969 (45.4)	17 150 (45.5)	5733 (45.0)	3328 (46.4)	3705 (44.7)
Annual ischemic stroke volume, median (IQR), No.	213 (144-319)	215 (144-326)	218 (144-326)	215 (143-326)	218 (147-331)
Annual tPA volume, median (IQR), No. of patients/y	17 (10-27)	16 (9-27)	17 (10-27)	16 (9-26)	17 (10-29)
Hospital region, No. (%)					
West	7126 (24.9)	7845 (20.8)	2429 (19.1)	1311 (18.3)	1465 (17.7)
South	9922 (34.7)	12 260 (32.5)	4067 (31.9)	1967 (27.4)	3205 (38.7)
Midwest	4454 (15.6)	7087 (18.8)	2351 (18.4)	1487 (20.7)	1262 (15.2)
Northeast	7081 (24.8)	10 482 (27.8)	3904 (30.6)	2411 (33.6)	2358 (28.4)
Rural hospital, No. (%)	1245 (4.4)	1872 (5.0)	603 (4.7)	380 (5.3)	365 (4.4)

Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, stroke/transient ischemic attack/thromboembolism (doubled), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65-75 years, sex category (female); INR, international normalized ratio; IQR, interquartile range; MI, myocardial infarction; NOACs, non–vitamin K antagonist oral anticoagulants; PVD, peripheral vascular disease; TIA, transient ischemic attack; tPA tissue plasminogen activator.

[a] Except for primary stroke center ($P = .23$) and annual ischemic stroke volume ($P = .002$), all differences were statistically significant with $P < .001$.

[b] CHA_2DS_2-VASc is a prediction tool for estimating the risk of stroke in patients with AF, ranging from 0 to 9. A CHA_2DS_2-VASc score of 0 or 1 corresponds to low to moderate risk; 2 or higher, high stroke risk.

Table 2. Association of Preceding Antithrombotic Treatment With Stroke Severity and In-Hospital Outcomes

	Preceding Antithrombotic Therapy				
Measure	None	Antiplatelet Therapy Only	Warfarin, INR <2	Warfarin, INR ≥2	NOACs
NIHSS score, median (IQR)	7 (2-16)	6 (2-15)	6 (2-16)	4 (1-10)	4 (1-11)
Moderate or severe stroke[a]					
No./Total No.	6189/22 811	7693/31 022	2766/10 716	900/5706	1208/6886
% (95% CI)	27.1 (26.6-27.7)	24.8 (24.3-25.3)	25.8 (25.0-26.6)	15.8 (14.8-16.7)	17.5 (16.6-18.4)
AOR (95% CI)	1 [Reference]	0.88 (0.84-0.92)	0.98 (0.92-1.04)	0.56 (0.51-0.60)	0.65 (0.61-0.71)
In-hospital mortality[b]					
No./Total No.	2588/27 977	2980/37 000	1092/12 446	451/7037	509/8144
% (95% CI)	9.3 (8.9-9.6)	8.1 (7.8-8.3)	8.8 (8.3-9.3)	6.4 (5.8-7.0)	6.3 (5.7-6.8)
AOR (95% CI)	1 [Reference]	0.83 (0.78-0.88)	0.97 (0.89-1.05)	0.75 (0.67-0.85)	0.79 (0.72-0.88)
mRS score of 0 or 1[c]					
No./Total No.	2077/12 964	3607/20 053	1339/7426	885/4115	1040/4528
% (95% CI)	16.0 (15.4-16.7)	18.0 (17.5-18.5)	18.0 (17.2-18.9)	21.5 (20.3-22.8)	23.0 (21.7-24.2)
AOR (95% CI)	1 [Reference]	1.29 (1.20-1.38)	1.24 (1.13-1.35)	1.43 (1.28-1.59)	1.37 (1.24-1.51)
mRS score of 0-2[c]					
No./Total No.	2994/12 964	5151/20 053	1945/7426	1290/4115	1487/4528
% (95% CI)	23.1 (22.4-23.8)	25.7 (25.1-26.3)	26.2 (25.2-27.2)	31.3 (29.9-32.8)	32.8 (31.5-34.2)
AOR (95% CI)	1 [Reference]	1.27 (1.20-1.35)	1.24 (1.15-1.34)	1.50 (1.36-1.65)	1.43 (1.32-1.55)

Abbreviations: AOR, adjusted odds ratio; INR, international normalized ratio; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; NOACs, non–vitamin K antagonist oral anticoagulants.

[a] Excluding 18.3% with missing records. The NIHSS is a measure of stroke severity, ranging from 0 to 42, with a higher score indicating greater stroke severity. An NIHSS score of 16 or higher indicates moderate or severe stroke. The stroke severity model adjusts for baseline demographic and clinical variables prior to the index stroke event, including age, sex, race/ethnicity, insurance, medical history, and use of antihypertensive, cholesterol-lowering, or antidiabetic medication prior to admission.

[b] Excluding 2.0% of transfer-out or discharge disposition missing records. The in-hospital mortality model adjusts for the same variables as the stroke severity model plus administration of tissue plasminogen activator, intra-arterial catheter-based treatment, and hospital characteristics including hospital bed size, academic, primary stroke center, annual ischemic stroke volume, annual tissue plasminogen activator volume, hospital region, and rural location.

[c] Excluding 48.0% with missing mRS scores. The mRS is a measure of degree of disability and functional outcomes, ranging from 0 (no symptoms) to 6 (death). An mRS score of 0 or 1 indicates excellent recovery; 0 to 2, functional independence after stroke. The mRS model adjusts for the same variables as the in-hospital mortality model.

Table 1). The overall median INR at admission was 1.7 (IQR, 1.3-2.3) in all warfarin-treated patients, with a median INR of 1.4 (IQR, 1.2-1.6) in patients receiving subtherapeutic warfarin and 2.5 (IQR, 2.2-3.1) in those receiving therapeutic warfarin (all these differences were statistically significant with $P < .001$).

Stroke Severity and In-Hospital Outcomes

The distribution of NIHSS scores and the proportion of patients presenting with moderate or severe stroke (NIHSS score ≥16) are shown in **Table 2**. The median initial NIHSS scores were significantly higher among patients not receiving antithrombotic medication (7 [IQR, 2-16]), antiplatelet therapy only (6 [IQR, 2-15]), or subtherapeutic warfarin (6 [IQR, 2-16]) compared with those receiving therapeutic warfarin (4 [IQR, 1-10]) and NOACs (4 [IQR, 1-11]) ($P < .001$). Similarly, patients receiving no antithrombotic treatment (27.1% [95% CI, 26.6%-27.7%]), antiplatelet therapy only (24.8% [95% CI, 24.3%-25.3%]), or subtherapeutic warfarin (25.8% [95% CI, 25.0%-26.6%]) were more likely to present with moderate or severe stroke than those receiving therapeutic warfarin (15.8% [95% CI, 14.8%-16.7%]) or NOACs (17.5% [95% CI, 16.6%-18.4%]) ($P < .001$). Compared with no antithrombotic treatment, therapeutic warfarin (adjusted odds ratio [AOR] = 0.56 [95% CI, 0.51-0.60]), NOACs (AOR = 0.65 [95% CI, 0.61-0.71]), and antiplatelet therapy only (AOR = 0.88 [95% CI, 0.84-0.92]) were associated with lower odds of moderate or severe stroke (Table 2 and **Figure 1**).

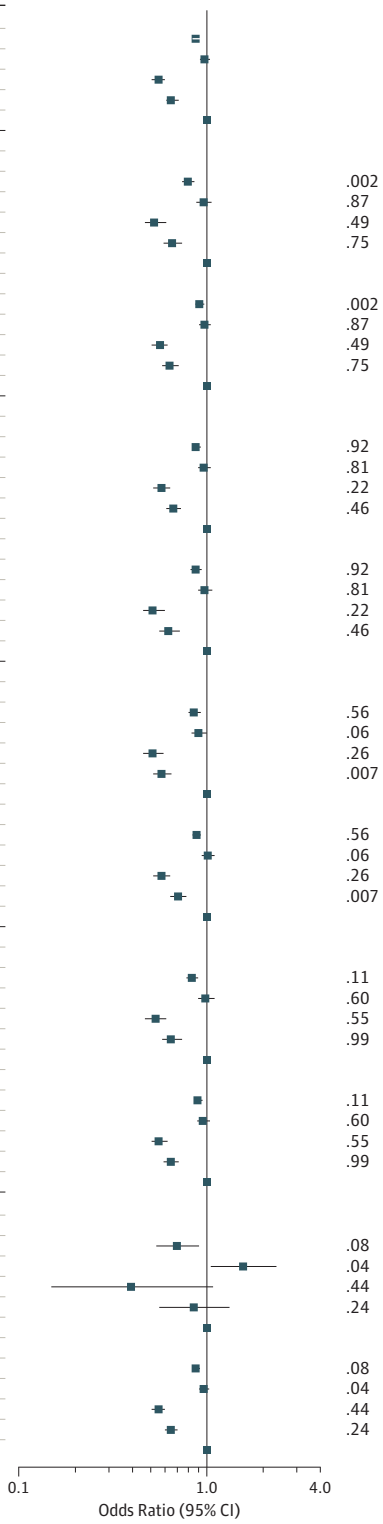
The unadjusted rates of in-hospital mortality were highest in patients not receiving antithrombotic treatment (9.3% [95% CI, 8.9%-9.6%]), followed by subtherapeutic warfarin (8.8% [95% CI, 8.3%-9.3%]), antiplatelet treatment only (8.1% [95% CI, 7.8%-8.3%]), therapeutic warfarin (6.4% [95% CI, 5.8%-7.0%]), and NOACs (6.3% [95% CI, 5.7%-6.8%]) ($P < .001$; Table 2). After multivariable adjustment, therapeutic warfarin (AOR = 0.75 [95% CI, 0.67-0.85]), NOACs (AOR = 0.79 [95% CI, 0.72-0.88]), and antiplatelet therapy only (AOR = 0.83 [95% CI, 0.78-0.88]) were associated with lower odds of in-hospital mortality compared with no antithrombotic treatment (Table 2 and **Figure 2**). Similarly, patients receiving preceding antithrombotic treatment had higher odds of having better functional outcomes (mRS score of 0-1 or 0-2) at discharge (Table 2).

Subgroup Analyses

Of 94 474 patients with AF who had experienced acute ischemic stroke, 55 553 (58.8%) were aged 80 years or older, 53 878 (57.0%) were women, 34 059 (36.1%) had a history of prior

Figure 1. Association Between Preceding Antithrombotic Treatment and Stroke Severity

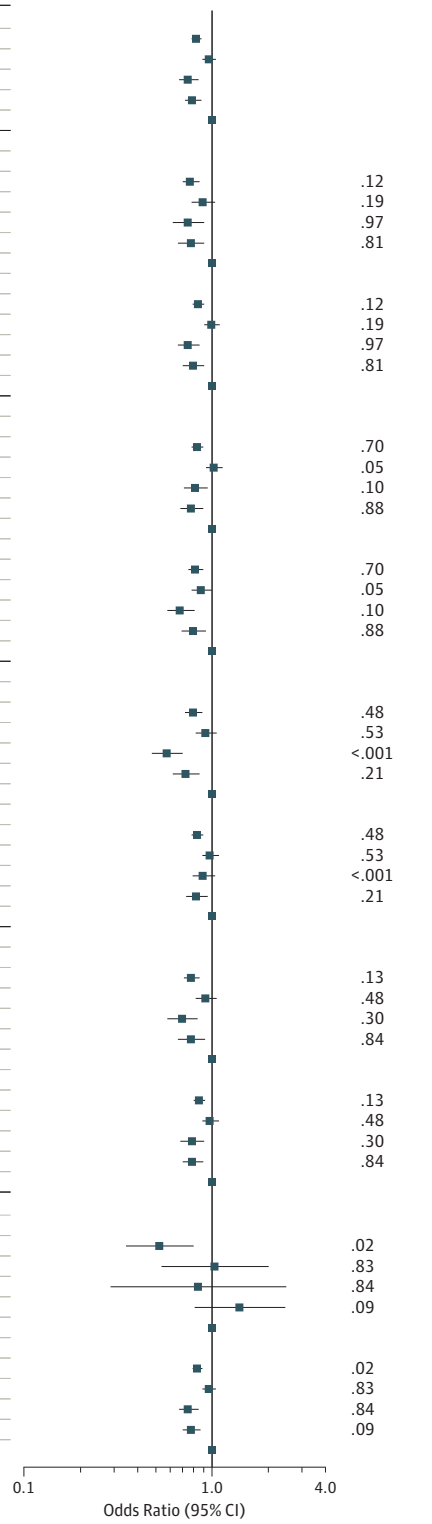
Preceding Antithrombotic Treatment	Unadjusted No. of Patients With Moderate or Severe Stroke/Total No. (%)	Adjusted Analysis of Moderate or Severe Stroke, Odds Ratio (95% CI)	*P* for Interaction
Overall cohort			
Antiplatelet only	7693/31 022 (24.8)	0.88 (0.84-0.92)	
Warfarin with INR <2	2766/10 716 (25.8)	0.98 (0.92-1.04)	
Warfarin with INR ≥2	900/5706 (15.8)	0.56 (0.51-0.60)	
NOACs	1208/6886 (17.5)	0.65 (0.61-0.71)	
None	6189/22 811 (27.1)	1 [Reference]	
Age, y			
<80			
Antiplatelet only	1919/11 460 (16.7)	0.80 (0.74-0.86)	.002
Warfarin with INR <2	955/4674 (20.4)	0.97 (0.88-1.06)	.87
Warfarin with INR ≥2	301/2514 (12.0)	0.53 (0.47-0.61)	.49
NOACs	527/3727 (14.1)	0.66 (0.59-0.74)	.75
None	1981/9584 (20.7)	1 [Reference]	
≥80			
Antiplatelet only	5774/19 562 (29.5)	0.92 (0.87-0.97)	.002
Warfarin with INR <2	1811/6042 (30.0)	0.98 (0.91-1.05)	.87
Warfarin with INR ≥2	599/3192 (18.8)	0.57 (0.51-0.62)	.49
NOACs	681/3159 (21.6)	0.64 (0.58-0.71)	.75
None	4208/13 227 (31.8)	1 [Reference]	
Sex			
Female			
Antiplatelet only	5197/17 949 (29.0)	0.88 (0.84-0.93)	.92
Warfarin with INR <2	1809/6046 (29.9)	0.97 (0.90-1.05)	.81
Warfarin with INR ≥2	554/2836 (19.5)	0.58 (0.52-0.64)	.22
NOACs	767/3565 (21.5)	0.67 (0.61-0.73)	.46
None	4210/13 511 (31.2)	1 [Reference]	
Male			
Antiplatelet only	2496/13 063 (19.1)	0.88 (0.82-0.94)	.92
Warfarin with INR <2	956/4666 (20.5)	0.98 (0.90-1.07)	.81
Warfarin with INR ≥2	345/2867 (12.0)	0.52 (0.46-0.60)	.22
NOACs	440/3318 (13.3)	0.63 (0.56-0.72)	.46
None	1977/9294 (21.3)	1 [Reference]	
Prior stroke or TIA			
Yes			
Antiplatelet only	2955/11 061 (26.7)	0.86 (0.80-0.93)	.56
Warfarin with INR <2	1147/4377 (26.2)	0.91 (0.83-1.00)	.06
Warfarin with INR ≥2	428/2682 (16.0)	0.52 (0.46-0.59)	.26
NOACs	534/3117 (17.1)	0.58 (0.52-0.65)	.007
None	1918/6538 (29.3)	1 [Reference]	
No			
Antiplatelet only	4738/19 961 (23.7)	0.89 (0.84-0.93)	.56
Warfarin with INR <2	1619/6339 (25.5)	1.02 (0.94-1.10)	.06
Warfarin with INR ≥2	472/3024 (15.6)	0.58 (0.52-0.64)	.26
NOACs	674/3769 (17.9)	0.71 (0.64-0.78)	.007
None	4271/16 273 (26.2)	1 [Reference]	
CAD or prior MI			
Yes			
Antiplatelet only	2789/12 105 (23.0)	0.84 (0.78-0.90)	.11
Warfarin with INR <2	971/3832 (25.3)	0.99 (0.90-1.10)	.60
Warfarin with INR ≥2	345/2328 (14.8)	0.54 (0.47-0.61)	.55
NOACs	422/2473 (17.1)	0.65 (0.58-0.74)	.99
None	1607/5928 (27.1)	1 [Reference]	
No			
Antiplatelet only	4904/18 917 (25.9)	0.90 (0.86-0.95)	.11
Warfarin with INR <2	1795/6884 (26.1)	0.96 (0.89-1.04)	.60
Warfarin with INR ≥2	555/3378 (16.4)	0.56 (0.51-0.62)	.55
NOACs	786/4413 (17.8)	0.65 (0.59-0.71)	.99
None	4582/16 883 (27.1)	1 [Reference]	
CHA_2DS_2-VASc score			
0-1			
Antiplatelet only	99/947 (10.5)	0.70 (0.54-0.91)	.08
Warfarin with INR <2	40/196 (20.4)	1.57 (1.05-2.34)	.04
Warfarin with INR ≥2	5/77 (6.5)	0.40 (0.15-1.08)	.44
NOACs	27/221 (12.2)	0.86 (0.56-1.32)	.24
None	187/1280 (14.6)	1 [Reference]	
≥2			
Antiplatelet only	7594/30 075 (25.3)	0.88 (0.85-0.92)	.08
Warfarin with INR <2	2726/10 520 (25.9)	0.97 (0.91-1.03)	.04
Warfarin with INR ≥2	895/5629 (15.9)	0.56 (0.51-0.60)	.44
NOACs	1181/6665 (17.7)	0.65 (0.60-0.70)	.24
None	6002/21 531 (27.9)	1 [Reference]	



CAD indicates coronary artery disease; INR, international normalized ratio; MI, myocardial infarction; NOACs, non–vitamin K antagonist oral anticoagulants; and TIA, transient ischemic attack. The CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes, stroke/TIA/thromboembolism [doubled], vascular disease [prior MI, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]) is a prediction tool for estimating the risk of stroke in patients with atrial fibrillation, ranging from 0 to 9. A CHA_2DS_2-VASc score of 0 or 1 corresponds to low to moderate stroke risk; 2 or higher, high stroke risk.

Figure 2. Association Between Preceding Antithrombotic Treatment and In-Hospital Mortality

Preceding Antithrombotic Treatment	Unadjusted No. of Patients With In-Hospital Mortality/Total No. (%)	Adjusted Analysis of In-Hospital Mortality, Odds Ratio (95% CI)	*P* for Interaction
Overall cohort			
Antiplatelet only	2980/37 000 (8.1)	0.83 (0.78-0.88)	
Warfarin with INR <2	1092/12 446 (8.8)	0.97 (0.89-1.05)	
Warfarin with INR ≥2	451/7037 (6.4)	0.75 (0.67-0.85)	
NOACs	509/8144 (6.3)	0.79 (0.72-0.88)	
None	2588/27 977 (9.3)	1 [Reference]	
Age, y			
<80			
Antiplatelet only	746/13 433 (5.6)	0.77 (0.70-0.86)	.12
Warfarin with INR <2	356/5372 (6.6)	0.90 (0.78-1.04)	.19
Warfarin with INR ≥2	152/3054 (5.0)	0.75 (0.62-0.91)	.97
NOACs	220/4347 (5.1)	0.78 (0.66-0.91)	.81
None	802/11 623 (6.9)	1 [Reference]	
≥80			
Antiplatelet only	2234/23 567 (9.5)	0.85 (0.79-0.91)	.12
Warfarin with INR <2	736/7074 (10.4)	1.00 (0.91-1.10)	.19
Warfarin with INR ≥2	299/3983 (7.5)	0.75 (0.66-0.86)	.97
NOACs	289/3797 (7.6)	0.80 (0.70-0.91)	.81
None	1786/16 354 (10.9)	1 [Reference]	
Sex			
Female			
Antiplatelet only	1804/21 607 (8.3)	0.84 (0.78-0.90)	.70
Warfarin with INR <2	670/7056 (9.5)	1.03 (0.93-1.14)	.05
Warfarin with INR ≥2	240/3494 (6.9)	0.82 (0.71-0.95)	.10
NOACs	275/4248 (6.5)	0.78 (0.68-0.90)	.88
None	1581/16 529 (9.6)	1 [Reference]	
Male			
Antiplatelet only	1176/15 379 (7.6)	0.82 (0.75-0.90)	.70
Warfarin with INR <2	421/5384 (7.8)	0.88 (0.78-1.00)	.05
Warfarin with INR ≥2	210/3539 (5.9)	0.68 (0.58-0.81)	.10
NOACs	233/3893 (6.0)	0.80 (0.69-0.93)	.88
None	1005/11 438 (8.8)	1 [Reference]	
Prior stroke or TIA			
Yes			
Antiplatelet only	1085/13 278 (8.2)	0.80 (0.72-0.89)	.48
Warfarin with INR <2	447/5187 (8.6)	0.93 (0.82-1.06)	.53
Warfarin with INR ≥2	170/3326 (5.1)	0.58 (0.48-0.70)	<.001
NOACs	214/3654 (5.9)	0.73 (0.62-0.86)	.21
None	781/8031 (9.7)	1 [Reference]	
No			
Antiplatelet only	1895/23 722 (8.0)	0.84 (0.78-0.90)	.48
Warfarin with INR <2	645/7259 (8.9)	0.98 (0.89-1.09)	.53
Warfarin with INR ≥2	281/3711 (7.6)	0.90 (0.79-1.04)	<.001
NOACs	295/4490 (6.6)	0.83 (0.73-0.95)	.21
None	1807/19 946 (9.1)	1 [Reference]	
CAD or prior MI			
Yes			
Antiplatelet only	1212/14 426 (8.4)	0.78 (0.71-0.86)	.13
Warfarin with INR <2	418/4451 (9.4)	0.93 (0.82-1.06)	.48
Warfarin with INR ≥2	193/2895 (6.7)	0.70 (0.58-0.84)	.30
NOACs	202/2926 (6.9)	0.78 (0.66-0.92)	.84
None	793/7466 (10.6)	1 [Reference]	
No			
Antiplatelet only	1768/22 574 (7.8)	0.86 (0.80-0.92)	.13
Warfarin with INR <2	674/7995 (8.4)	0.98 (0.89-1.09)	.48
Warfarin with INR ≥2	258/4142 (6.2)	0.79 (0.68-0.91)	.30
NOACs	307/5218 (5.9)	0.79 (0.70-0.90)	.84
None	1795/20 511 (8.8)	1 [Reference]	
CHA_2DS_2-VASc score			
0-1			
Antiplatelet only	29/1087 (2.7)	0.53 (0.35-0.80)	.02
Warfarin with INR <2	11/218 (5.0)	1.04 (0.54-2.00)	.83
Warfarin with INR ≥2	4/103 (3.9)	0.85 (0.29-2.48)	.84
NOACs	17/271 (6.3)	1.41 (0.81-2.45)	.09
None	75/1541 (4.9)	1 [Reference]	
≥2			
Antiplatelet only	2951/35 913 (8.2)	0.84 (0.79-0.89)	.02
Warfarin with INR <2	1081/12 228 (8.8)	0.97 (0.89-1.05)	.83
Warfarin with INR ≥2	447/6934 (6.4)	0.75 (0.67-0.85)	.84
NOACs	492/7873 (6.2)	0.78 (0.70-0.87)	.09
None	2513/26 436 (9.5)	1 [Reference]	



CAD indicates coronary artery disease; INR, international normalized ratio; MI, myocardial infarction; NOACs, non–vitamin K antagonist oral anticoagulants; and TIA, transient ischemic attack. The CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes, stroke/TIA/thromboembolism [doubled], vascular disease [prior MI, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]) is a prediction tool for estimating the risk of stroke in patients with atrial fibrillation, ranging from 0 to 9. A CHA_2DS_2-VASc score of 0 or 1 corresponds to low to moderate stroke risk; 2 or higher, high stroke risk.

Table 3. Documented Reasons for No Anticoagulation Use at the Time of Hospital Discharge Among Patients With a Prestroke CHA_2DS_2-VASc Score of 2 or Higher and Not Receiving Any Anticoagulation Before Stroke

Documented Reason[a]	No. (%) (n = 58 084)
Risk of bleeding	9476 (16.3)
Risk of falls	5968 (10.3)
Allergy to or complication with warfarin or heparin	341 (0.6)
Serious adverse effect of medication	583 (1.0)
Patient or family refusal	2476 (4.3)
Mental status	652 (1.1)
Terminal illness	3616 (6.2)
≥1 Documented reason	19 835 (34.2)
No documented reason	38 249 (65.8)

Abbreviation: CHA_2DS_2-VASc, congestive heart failure, hypertension, age greater than or equal to 75 years (doubled), diabetes, stroke/transient ischemic attack/thromboembolism (doubled), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65 to 75 years, sex category (female).

[a] Patients could have more than 1 reason.

stroke or TIA, and 32 754 (34.7%) had CAD or MI. Statistical tests for interaction were not significant (*P* for interaction > .05) for most subgroups. The exceptions were age and antiplatelet therapy (*P* for interaction = .002); prior stroke and NOACs (*P* for interaction = .007); CHA_2DS_2-VASc score and subtherapeutic warfarin (*P* for interaction = .04) with respect to stroke severity; sex and subtherapeutic warfarin (*P* for interaction = .05); prior stroke and therapeutic warfarin (*P* for interaction < .001); and CHA_2DS_2-VASc score and antiplatelet therapy (*P* for interaction = .02) with respect to mortality (Figure 1 and Figure 2).

Subgroup analyses stratified by age, sex, medical history of prior stroke or TIA, and CAD or MI found lower odds of moderate or severe stroke and mortality among patients receiving therapeutic warfarin, NOACs, or only antiplatelet therapy (Figure 1 and Figure 2). Nonetheless, the lower odds of moderate or severe stroke associated with use of antiplatelet therapy alone were less than those associated with use of therapeutic warfarin and NOACs in most subgroups. There were no statistically significant differences in terms of stroke severity and mortality between use of subtherapeutic warfarin and no antithrombotic therapy.

The relationship between preceding antithrombotic therapy and outcomes remained essentially the same in the subgroup analyses of patients with a CHA_2DS_2-VASc score of 2 or higher (Figure 1 and Figure 2). However, only antiplatelet treatment was associated with significantly lower odds of moderate or severe stroke (AOR = 0.70 [95% CI, 0.54-0.91]) and death (AOR = 0.53 [95% CI, 0.35-0.80]) among patients with a CHA_2DS_2-VASc score of 0 or 1.

Reasons for No Anticoagulation

Documented reasons for no oral anticoagulation at discharge among 58 084 survivors who had a prestroke CHA_2DS_2-VASc score of 2 or higher and were not receiving oral anticoagulants prior to admission are shown in **Table 3**. The most common reasons were risk of bleeding (16.3%), risk of falls (10.3%), terminal illness (6.2%), patient or family refusal (4.3%), mental status (1.1%), medication adverse effects (1.0%), or allergy (0.6%). However, 38 249 of the 58 084 patients (65.8%) did not have a documented reason for not receiving oral anticoagulation.

Discussion

In this large, nationwide, contemporary registry of patients with a known history of AF who had experienced an acute ischemic stroke, 30% were receiving some form of oral anticoagulants before their stroke. Moreover, 64% of warfarin-treated patients were receiving subtherapeutic warfarin. Collectively, 84% of patients were not receiving guideline-recommended anticoagulation or had anticoagulation levels that were not in the therapeutic range, even among those with high thromboembolic risk before stroke.

Atrial fibrillation is a highly prevalent and important, but treatable, risk factor for stroke. Despite numerous international guideline recommendations, many patients fail to receive proper treatment for stroke prevention. A systematic review of 54 studies from 11 countries in Europe, North America, and South America found consistent patterns of oral anticoagulation underuse in patients with AF who had an elevated risk of stroke.[28] In a contemporary outpatient cardiac quality-improvement registry in the United States, 60% of patients with a $CHADS_2$ score (congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/TIA/thromboembolism [doubled]) of 2 or higher were treated with warfarin or NOACs.[29] Unlike previous studies that evaluated the prevalence of antithrombotic therapy in patients at risk for stroke, this analysis examined the other end of the spectrum: how patients presenting with acute ischemic stroke were treated prior to their stroke event. This approach has implications for clinical practice because it identifies potentially preventable strokes in high-risk patients with AF who either were not treated with anticoagulants or did not receive adequate anticoagulation. Each year, nearly 700 000 individuals in the United States experience a new or recurrent ischemic stroke, and 10% to 15% of these strokes are estimated to be of cardioembolic origin.[2,30] Based on results from pivotal anticoagulation trials and the prevalence of inadequate therapeutic anticoagulation observed in our study, a substantial number of strokes may be due to underuse of or inadequate anticoagulation in AF.

There have been concerns that some patients with AF may not be ideal candidates for oral anticoagulants, and the selection of an antithrombotic agent should be individualized on the basis of patient risk factors, preference, and other clinical characteristics. It is possible that warfarin or other NOACs might have been contraindicated in some patients. Although the data in this study preclude direct assessment of eligibility for antithrombotic therapy before stroke, reasons for no anticoagulation at discharge among survivors of stroke were reported in order to gain insights into potential reasons anticoagulation was not provided prior to admission. Up to two-thirds of patients with a prestroke CHA_2DS_2-VASc score of 2 or higher

did not have a documented reason for nonuse of antithrombotic therapy. While the absence of documentation of reasons for nonuse does not mean the absence of a legitimate reason for nonuse, all of these patients had AF diagnosed with high thromboembolic risk before their stroke. Therefore, these patients should have been treated with anticoagulation if treatment was not contraindicated. Among those with a documented reason for not using antithrombotic therapy, 16% of nonuse was due to risk of bleeding, 10% to risk of falls, and 4% to patient or family refusal. Although risks of bleeding and falls may be considered to make a patient ineligible for anticoagulation therapy, some studies suggested that the perceived risk of bleeding and falls may have been overestimated, especially in elderly individuals.[31-33] Even if patients were unable to use oral anticoagulants due to contraindications, antiplatelet therapy could have been considered.[1,9] Nevertheless, 30% of high-risk patients in this study were not receiving any form of antithrombotic therapy before stroke, highlighting the opportunities for stroke prevention by improving appropriate AF treatment.

Prior studies have demonstrated that warfarin therapy reduces the incidence of stroke and also reduces the risk of severe stroke even when stroke occurs.[12,13] Unlike previous research that relied on nonstandard severity measures at discharge, the current study reports NIHSS score at baseline, which is considered the reference standard,[22,23] and may better reflect contemporary use and nonuse of antithrombotic therapy in the United States for patients with AF who had experienced an acute ischemic stroke. Therapeutic warfarin was associated with less severe stroke and fewer deaths. By contrast, the outcomes were almost equally poor in warfarin-treated patients with a subtherapeutic INR and patients not receiving any antithrombotic agents. These findings reinforce the importance of INR monitoring and dose adjustment to improve compliance and keep the INR in the therapeutic range for patients receiving warfarin.

Use of NOACs also was associated with reduced odds of stroke severity, disability, and in-hospital mortality, with point estimates similar to the odds ratios for therapeutic warfarin. These results seem plausible based on the understanding of the mechanisms in NOACs and given how these results align with data from clinical trials. However, there could be bias in a direct comparison of preceding warfarin and NOAC therapy for outcomes that these treatments are meant to prevent. It is challenging to address the treatment selection bias in a population that already experienced a stroke. Nevertheless, a direct comparison of stroke severity and outcomes in patients with ischemic stroke receiving warfarin vs NOACs is challenging because of the efficacy of oral anticoagulants and low event rates in patients receiving oral anticoagulants. A total of 8290 patients in this study experienced an ischemic stroke while receiving NOACs. In contrast, there were 1150 strokes among patients treated with NOACs in 4 pivotal NOAC trials.[5-8]

In this study, in addition to therapeutic warfarin and NOACs, antiplatelet treatment was also associated with less severe stroke and lower mortality in patients with a prestroke CHA_2DS_2-VASc score of 2 or higher. The lower severity of stroke and lower odds of in-hospital mortality were limited to patients receiving only antiplatelet treatment and were not observed in warfarin- or NOAC-treated patients presenting with a prestroke CHA_2DS_2-VASc score less than 2. In addition, only 3% of patients in the study cohort had a prestroke CHA_2DS_2-VASc score of 0 or 1. These findings provide further evidence supporting the use of the CHA_2DS_2-VASc score for risk stratification and selecting treatment based on an individual's risk for cardioembolic events.

This study had several limitations. First, this was a retrospective observational analysis. Treatment selection and unmeasured confounding could affect the validity of study findings. It is impossible to randomize patients with stroke to different antithrombotic regimens because treatment was given prior to the stroke. Furthermore, given the low event rates in stroke prevention trials,[5-8] the numbers of patients with stroke would probably be too small to assess the relationship of preceding anticoagulation therapy with stroke severity and outcomes. Second, the GWTG-Stroke registry database used in this study included only patients who had a stroke. Patients with AF treated with different antithrombotic regimens who did not have a stroke were not included in the registry. Therefore, the absence of a cohort or case-control design with patients who had AF and defined by anticoagulant exposure and subsequent stroke incidence measurement precludes assessment of the potential protective effect of adequate anticoagulation, and conversely the harm of inadequate anticoagulation.

Third, this registry did not collect Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification during the study period. Noncardioembolic stroke could possibly have accounted for some cases, especially among those receiving therapeutic warfarin (36.0% of warfarin-treated patients) or NOACs. Fourth, reasons for nonuse of anticoagulation documented at discharge were used as a proxy for reasons of nonuse prior to stroke. As a result, reasons for no anticoagulation could not be assessed among deceased patients and were potentially overestimated or underestimated in survivors of stroke. It is unlikely that comorbidities or other conditions that might have influenced eligibility will disappear after the stroke. Medical records were used rather than the recollection by patients who might have experienced memory loss or cognitive impairment after stroke; therefore, reasons for nonuse are less subject to recall bias. Having a stroke substantially changes the context of evaluation for anticoagulation eligibility; the reasons are likely to be different, with poor care quality, lack of patient interest, underestimation of stroke risks, and overestimation of the bleeding risks likely to be much more frequent in the outpatient setting prior to stroke. Therefore, the reasons for no oral anticoagulation could have been overestimated and fewer cases of warfarin or NOAC nonuse would be justifiable.

Fifth, some patients did not have NIHSS (18.3%) or mRS (48.0%) scores documented in the medical record. Because it is inappropriate to impute outcome measures, these patients were excluded from the stroke severity or functional outcome models. Excluding missing values might bias this analysis; however, it is unlikely that physicians will report stroke severity and functional outcomes differently according to antithrombotic treatment prior to stroke. Sixth, hospitals

participated in this registry based on their level of interest in quality improvement in stroke care and their capacity to fulfill the requirements. Data from this registry and these study results might not be able to be extrapolated to patients treated in hospitals not participating in this registry or to patients in other countries. A previous study had demonstrated that patients included in the registry used in this study are representative of patients with ischemic stroke in the United States, at least among patients with Medicare fee-for-service coverage.[34] Even though some patients previously received care at a hospital in this stroke registry, many more patients may have been receiving outpatient care at another health care facility prior to their stroke, then had an ischemic stroke, and then were admitted to a hospital in this registry. As a result, this study is more reflective of national patterns of preceding antithrombotic treatment rather than patterns limited to these hospitals.

Conclusions

Among patients with AF who had experienced an acute ischemic stroke, inadequate therapeutic anticoagulation preceding the stroke was prevalent. Therapeutic anticoagulation was associated with lower odds of moderate or severe stroke and lower odds of in-hospital mortality.

ARTICLE INFORMATION

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