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Effect of New Oral Anticoagulants on Prescribing Practices for Atrial Fibrillation in Older Adults

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Abstract

BACKGROUND—Warfarin is effective in preventing stroke and systemic embolism in atrial fibrillation (AF) but has several limitations. The new oral anticoagulants (NOACs) address many of these limitations but their impact on prescribing practices in older adults with AF is unknown.

DESIGN—Retrospective observational cohort study

SETTING—Academic medical center in St. Louis, MO, USA

PARTICIPANTS—Patients age ≥75 with AF admitted from October 2010 through September 2015 (N=6568, 50% female, 15% non-white).

MEASUREMENTS—NOACs and warfarin prescribed at discharge were obtained from hospital discharge summaries. Linear regression was used to examine quarterly trends in use of these agents. Multivariable logistic regression was used to assess independent predictors of anticoagulant use.

RESULTS—NOAC use increased over time (correlation coefficient $[r]=0.87$, $p<0.001$), warfarin use did not change ($r=-0.16$, $p=0.500$), and overall anticoagulant use (NOACs and warfarin) increased ($r=0.68$, $p=0.001$). NOAC use increased over time in all age groups (ages 75–79, 80–84, 85–89) except age ≥90, but the rate of NOAC uptake was attenuated by increasing age. There was no consistent relationship between age and warfarin or overall anticoagulant use, except patients age ≥90 had consistently lower use. Overall, <45% of patients were prescribed an anticoagulant. In multivariable analysis, younger age, white race, female gender, higher hemoglobin, higher creatinine clearance, being on a medical service, hypertension, stroke/TIA, no history of intracranial hemorrhage and modified HAS-BLED score <3 increased the likelihood of receiving NOACs.

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CONCLUSION—Prescription of anticoagulants for AF increased in older adults primarily due to an increase in the use of NOACs. Nonetheless, less than 45% of patients were prescribed an anticoagulant. Additional research is needed to optimize prescribing practices for older adults with AF.

Keywords

oral anticoagulants; new oral anticoagulants; atrial fibrillation; CHA₂DS₂-VASc score; race; creatinine clearance; dementia; warfarin

INTRODUCTION

Warfarin is an effective therapy for preventing stroke and systemic embolism in patients with atrial fibrillation (AF), and prior to 2010 it was the only oral anticoagulant available in the U.S. for this purpose. Warfarin has many advantages, including low cost, relative ease of monitoring, and availability of reversal agents, but it also has several disadvantages, including slow onset of action, narrow therapeutic index requiring close monitoring, numerous food and drug interactions, and relatively high risk for major bleeding complications.^{1, 2} In part for these reasons, warfarin is underutilized in a substantial proportion of patients with AF, and increasing age is associated with a progressive decline in warfarin use.^{3, 4}

Introduction of several new oral anticoagulants (NOACs) has addressed some of these disadvantages. As a group, NOACs have a rapid onset of action with more predictable pharmacokinetics and no need for routine monitoring.^{2, 5} In addition, the NOACs are at least as effective as warfarin for prevention of ischemic stroke and are associated with lower risk of intracranial hemorrhage,⁶ an advantage of particular relevance to older adults. For these reasons, NOACs are now recommended as alternative first-line therapy for prevention of stroke and systemic emboli in nonvalvular AF.⁷ Conversely, limitations to use of NOACs include higher cost, lack of readily accessible monitoring tests and reversal agents, and contraindications in patients with severe kidney or liver disease.²

Although several studies have examined trends in NOAC use in the general population,^{8–11} to our knowledge no study has assessed NOAC use in older adults. The purpose of this study, therefore, was to examine changes in anticoagulation prescribing practices for older adults with AF since the introduction of NOACs in 2010, with particular attention to the associations of age, sex, race, comorbidities, and socioeconomic status with overall utilization of anticoagulation and trends in uptake of NOACs. We hypothesized that there would be a net increase in anticoagulant use over time driven primarily by increased use of NOACs, and that uptake in NOAC use would be affected by age, kidney function, dementia diagnosis and income but not by sex or race.

METHODS

Study Population and Inclusion Criteria

This was a retrospective observational study. We included patients ≥75 years old with AF admitted to Barnes-Jewish Hospital (a large tertiary academic medical center in St. Louis,

MO) from October 2010 through September 2015 and discharged alive. Based on age alone, all patients had a CHA₂DS₂-VASc (congestive heart failure, hypertension, age ≥ 75, diabetes, stroke/TIA, vascular disease (peripheral vascular disease or coronary artery disease), age 65–74, sex category (female sex)) score¹² of at least 2 and were therefore candidates for anticoagulation. A total of 7012 unique patients met the inclusion criteria; 444 patients with missing data on discharge medications were excluded, yielding 6568 patients for the final analysis. For 2029 patients with multiple admissions, only the last available discharge record with medication data was retained for analysis. Patients were grouped into calendar year quarters based on discharge date. The study was approved by the institutional review board at the Washington University in St. Louis.

Data Collection

Patients fulfilling the inclusion criteria were identified using a searchable electronic medical record database, the Clinical Investigation Data Exploration Repository (CIDER), maintained by the Washington University in St. Louis Center for Biomedical Informatics. Data were collected on patient demographics (age, sex and race), height, weight, selected laboratory (hemoglobin and creatinine) and service type (medical and surgical). Medical services included general medicine, neurology and psychiatry. Surgical services included general surgery, cardiothoracic surgery, gynecology, neurosurgery, ophthalmology, orthopedic surgery, otolaryngology, plastic surgery, trauma surgery and urology. Medical comorbidities were derived from ICD-9 codes and included heart failure, hypertension, diabetes, stroke, transient ischemic attack (TIA), cerebrovascular disease, peripheral vascular disease, coronary artery disease, dementia, liver disease, bleeding, gastrointestinal bleeding, intracranial bleeding, lung/thoracic bleeding, soft tissue hematoma, alcohol abuse and history of fall. Residential zip codes were used as a surrogate for economic status. Discharge medications including NOACs (dabigatran, rivaroxaban, apixaban), warfarin, aspirin, clopidogrel, prasugrel and ticagrelor were obtained from hospital discharge summaries.

Other Variables

Creatinine clearance was calculated using the Cockcroft-Gault equation.¹³ Body mass index (BMI) was calculated as (height in meters)/(weight in kilograms)². A modified HAS-BLED score¹⁴ was calculated that included hypertension, kidney disease, liver disease, stroke, bleeding history, elderly (age ≥ 65 years), drugs (aspirin, clopidogrel, prasugrel or ticagrelor) and alcohol abuse but excluded labile international normalized ratio (INR) and non-steroidal anti-inflammatory drugs (NSAIDs) because data for these were not available. Zip codes were used to obtain median income estimates from the United States Census Bureau website (<http://factfinder.census.gov/faces/nav/jsf/pages/searchresults.xhtml?refresh=t>) and classified in tertiles (\$12,589–40,413, \$40,460–55,876, and \$55,938–205,169).

Statistical Methods

Patient characteristics were summarized by age category (75–79, 80–84, 85–89, ≥ 90 years) using the mean ± standard deviation or frequency count (percent) for continuous and categorical variables, respectively. Continuous variables were compared using one-way analysis of variance. The chi-square or Fisher's exact test was used to compare categorical

variables. Non-normal and ordinal variables were summarized by the median (1st quartile, 3rd quartile) and compared using the Kruskal-Wallis test.

The linear trend in medication prescribed over time was examined using linear regression with quarter of the year as the independent variable and percent medication as the dependent variable. For this analysis, quarter was treated as a continuous variable with values ranging from 1 to 20 (first quarter October-December 2010; last available quarter July-September 2015). The Pearson correlation coefficient was created to describe strength of linear trend. To compare trends across patient subgroups, separate models were created that included the interaction between time and subgroup. The linear model assumptions of normal and homogeneous errors were evaluated by examination of residual and normal probability plots. No significant deviations were noted.

A multivariable logistic regression model was built to examine independent predictors of NOAC and anticoagulant use. Variables were chosen a priori based on prior literature and clinical experience, including factors affecting risk of stroke, bleeding or likelihood of prescribing anticoagulation (age, race, gender, BMI, hemoglobin and creatinine clearance) or based on results from univariate analysis ($p < 0.1$, see supplementary Tables S1 and S2) and components of the CHA₂DS₂-VASc score. To adjust for time, a quarterly time variable was included and treated as a continuous variable. When conducting the multivariable analysis, missing data were imputed. Multiple data sets (5) were created, each using a sequential imputation algorithm (see supplementary materials S1).

All statistical analyses were conducted in SAS v9.4 (SAS Institute Inc., Cary, NC). A two tailed $p < 0.05$ was considered statistically significant.

RESULTS

Baseline Characteristics

Baseline characteristics of the cohort stratified by age group are summarized in Table 1. Of 6568 total patients, 36%, 31%, 22% and 11% were aged 75 to 79, 80 to 84, 85 to 89 and 90 years, respectively. Women comprised 50% of the cohort and 85% of the patients with available race data were white. The percentage of women increased with increasing age ($p < 0.001$). The median income of the cohort was \$52,306. The median CHADS₂ (congestive heart failure, hypertension, age 75, diabetes, stroke/TIA)¹⁵ and CHA₂DS₂-VASc¹² scores were 3 and 4 respectively. The prevalence of comorbidities varied by age group as shown in Table 1. Baseline characteristics of the cohort stratified by anticoagulation use are shown in Supplementary Table S3.

Quarterly Trends in Use of Anticoagulation

Quarterly trends in NOAC, warfarin and overall anticoagulant use are summarized in Figures 1A, 1B and 1C respectively. NOAC use significantly increased over time (correlation coefficient [r] 0.87, $p < 0.001$). There was no significant change in warfarin use over time ($r = -0.16$, $p = 0.500$). Overall anticoagulant use increased over time ($r = 0.68$, $p = 0.001$), but remained $< 45\%$ throughout the study period.

Quarterly Trends in Use of Anticoagulants by Age Group

Quarterly trends in NOAC, warfarin and anticoagulant use by age group are summarized in Figures 2A, 2B and 2C respectively. Although uptake of NOACs increased significantly over time for all age groups except age 90, the rate of uptake was attenuated by increasing age (p for interaction = 0.007). Use of warfarin increased only in patients aged 85–89 (remaining unchanged in the other age groups), while overall use of anticoagulants increased only in patients aged 75–79 and 85–89 (remaining unchanged in the other age groups). Overall, there was no consistent association between age and prescription of warfarin or any anticoagulant, except that patients 90 years had consistently lower use. There were significant differences in trends of warfarin and anticoagulant use over time across age groups (p for interaction 0.028 and <0.001 , respectively).

Quarterly Trends in Use of NOACs for Other Subgroups

Quarterly trends by gender, race, renal function, dementia diagnosis and income are summarized in Supplementary Figures S1 through S5. NOAC use increased over time in women and men, whites and non-whites, patients without dementia (no change in patients with dementia), patients in all renal function categories (except stage V chronic kidney disease), and patients in all tertiles of median income. There were no significant differences in rate of NOAC uptake between men and women (p for interaction = 0.93), whites and non-whites ($p = 0.51$), patients with and without dementia diagnosis ($p = 0.05$) or across income tertiles ($p = 0.70$). Lower renal function was associated with lower NOAC use over time ($p < 0.001$).

Factors Predictive of NOAC Use

Factors independently predictive of NOAC use are summarized in Table 2. In the multivariable model that included age, gender, race, median income, BMI, hemoglobin, creatinine clearance, service type, heart failure, hypertension, diabetes, stroke/TIA, peripheral vascular disease, coronary artery disease, dementia, gastrointestinal bleeding, intracranial bleeding, modified HAS-BLED score and time, 11 factors independently affected the likelihood of NOAC use. These included age (compared to age group 75–79, age group 80–84 [OR 0.675, $p = 0.001$], 85–89 [OR 0.665, $p = 0.003$] and 90 [OR 0.390, $p < 0.001$]), female gender (OR 1.335, $p = 0.005$), white race (OR 1.501, $p = 0.018$), hemoglobin (OR per 1 g/dl increase 1.196, $p < 0.001$), creatinine clearance (>50 vs <50 mL/min, OR 1.368, $p = 0.010$), medical service (vs surgical service, OR 1.260, $p = 0.041$), hypertension (OR 1.323, $p = 0.044$), stroke/TIA (OR 1.573, $p = 0.016$), history of intracranial bleeding (OR 0.386, $p = 0.043$), HAS-BLED score ≥ 3 (vs <3 OR 0.744, $p = 0.015$) and time from start of the analysis (OR 1.081 per 1 quarter increase, $p < 0.001$).

Factors Predictive of Anticoagulant Use

Factors independently predictive of anticoagulant use are summarized in Supplementary Table S4. In the multivariable model, 15 factors independently affected the likelihood of anticoagulant use. These included age (compared to age group 75–79, age group 90 [OR 0.549, $p < 0.001$]), race (OR for white vs. other 1.495, $p < 0.001$), median income (1st tertile vs. 3rd tertile [OR 1.179, $p = 0.017$]), BMI (compared to BMI <25 , BMI 25 to <30 [OR 1.266,

$p<0.001$] and BMI ≥ 30 [OR 1.406, $p<0.001$]), hemoglobin (OR per 1 g/dl increase 1.134, $p<0.001$), medical service (vs. surgical service OR 1.317, $p<0.001$), heart failure (OR 1.150, $p<0.001$), cerebrovascular disease (OR 0.522, $p=0.016$), dementia (OR 0.515, $p<0.001$), liver disease (OR 0.567, $p=0.001$), gastrointestinal bleeding (OR 0.635, $p=0.009$), intracranial bleeding (OR 0.265, $p<0.001$), history of fall (OR 0.598, $p<0.001$), modified HAS-BLED score ≥ 3 (vs <3 , OR 0.811, $p=0.003$) and time from start of the analysis (OR 1.018 per 1 quarter increase, $p<0.001$).

DISCUSSION

Over a period of 5 years, NOAC use in older adults with AF admitted to a tertiary academic medical center increased progressively, whereas warfarin use remained stable, resulting in an overall increase in prescription of anticoagulants. The overall trend was generally consistent across demographic subgroups defined by age, sex, and race, but the rate of NOAC uptake declined significantly with increasing age.

Prior studies have assessed the effect of the introduction of NOACs on AF treatment patterns in various populations, but no study has assessed treatment patterns specifically in older adults. In one study of newly diagnosed AF patients with a mean age of 69 years evaluated over a similar period of time (2010 to 2015), the authors reported an increase in anticoagulation therapy driven primarily by prescription of NOACs.¹⁶ Another study in AF patients hospitalized with TIA or stroke conducted in the first two years after the introduction of NOACs showed no change in anticoagulant use but a trend towards switching from warfarin to NOACs.¹⁷ The increase in use of NOACs observed in these studies, including ours, reflects increased familiarity with NOACs and better understanding among physicians of indications for their use. We anticipate that this trend will continue, especially as prices of these drugs decline and with approval of novel reversal agents.

An important finding of our study is that NOAC use increased over time in all age groups except patients ≥ 90 years, and the rate of new use declined with increasing age. Warfarin and overall anticoagulant use increased only in patients age 85–89, most likely representing a chance finding, and there were no clear trends in usage over time as a function of age, except that patients ≥ 90 years were less likely to receive treatment.

Although age is a potent risk factor for stroke and systemic embolization in patients with AF, anticoagulation is underutilized in older adults.^{3, 4} We found that even with the availability of NOACs, overall use of anticoagulation was less than 45% throughout the study period. Factors associated with low utilization rates in our population include non-white race, low income, low BMI, low hemoglobin, being on a surgical service, not having heart failure, cerebrovascular disease, dementia, liver disease, gastrointestinal bleeding, intracranial bleeding, history of fall and a modified HAS-BLED score ≥ 3 . For warfarin, drug and dietary interactions and requirement for close monitoring with frequent blood tests likely also contributed to low utilization rates. Our results suggest that these and other concerns are especially pronounced in patients ≥ 90 years old. Alternatively, NOACs may have abated these concerns to a greater extent in patients age 75–79 years than in those ≥ 90

years. Nevertheless, our data indicate that there is considerable opportunity to improve use of anticoagulation in the high-risk group of older adults with AF.

As anticipated, there were no differences in the rate of NOAC uptake between women and men or between whites and non-whites (non-significant p-values for time interaction). However, both gender and race were found to be predictors of NOAC prescription after adjusting for time and other factors. Women were more likely to be prescribed a NOAC compared to men (OR=1.335, p=0.005) and whites were more likely to be prescribed a NOAC compared to non-whites (OR=1.501, p=0.018). In other words, although rate of NOAC uptake did not differ by gender or race, overall use was higher in women and whites than in men and non-whites, respectively, as illustrated in Supplementary Figures S1 and S2.

Also as expected, there was a difference in NOAC use based on renal function, such that patients with higher creatinine clearance were more likely to be prescribed NOACs. In bivariate analysis, NOAC use increased over time in patients without dementia but not in patients with dementia. However, the difference between groups was only marginally significant (p=0.05). After adjusting for time and other factors, dementia diagnosis did not affect the likelihood of being prescribed a NOAC but was associated with lower overall anticoagulant use. Other studies have also shown lower use of anticoagulation in patients with cognitive impairment.^{18, 19} This may be due to a perception of potentially lower net benefit of anticoagulation in this group, such that the benefit may no longer outweigh an increased risk of bleeding and other side effects. However, this view has been challenged by a recent study showing that discontinuation of warfarin following a diagnosis of dementia is associated with increased risk of stroke and death.²⁰ Of note, having a history of falling was also associated with lower use of anticoagulation overall but not with uptake of NOACs. This may be due to the associated lower risk of intracranial hemorrhage with NOACs.⁶ NOAC use increased over time in all tertiles of income, but contrary to expectations there was no difference in the rate of uptake across income tertiles after adjusting for time and other variables. Given the higher cost of NOACs, we had expected higher use in patients with higher incomes.

Limitations of study

Our study has several limitations. It is based on data from a single center and may not be representative of other populations. The retrospective design and use of hospital records may be associated with coding errors and other inaccuracies in the data. Specifically, geriatric syndromes such as falls and cognitive impairment are likely undercoded. Other factors not included in our analysis such as education level or marital status may have affected prescription of warfarin and NOACs; in particular, we did not have information on reasons for non-prescription of anticoagulants in individual patients, which may include both physician and patient factors. We used zip code as a surrogate for income, but this may not accurately reflect an individual's socioeconomic status. However, all patients were potentially eligible for Medicare, which may reduce disparities in ability to pay for medications.

Conclusion

In patients 75 years of age or older admitted to a large academic hospital, the introduction of NOACs was associated with an increase in the use of oral anticoagulation for AF.

Nonetheless, despite high risk for stroke based on the CHA₂DS₂-VASc score, less than 45% of patients in this cohort were discharged on an anticoagulant. Additional research is needed to optimize prescribing practices for older adults with AF, including a better understanding of the reasons for not using anticoagulants in a high proportion of patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(A) Quarterly trend in NOAC use (correlation coefficient [r] 0.87, $p < 0.001$). (B) Quarterly trend in warfarin use ($r -0.16$, $p = 0.500$). (C) Quarterly trend in anticoagulant use ($r 0.68$, $p = 0.001$).

Figure 2.

(A) Quarterly trends in NOAC use by age group. 75–79 (r 0.86, $p < 0.001$), 80–84 (r 0.62, $p = 0.003$), 85–89 (r 0.67, $p = 0.001$), 90 (r 0.23, $p = 0.340$); p -value for interaction = 0.007. (B) Quarterly trends in warfarin use by age group. 75–79 (r -0.07 , $p = 0.750$), 80–84 (r -0.32 , $p = 0.170$), 85–89 (r 0.48, $p = 0.032$), 90 (r -0.41 , $p = 0.070$); p -value for interaction = 0.028. (C) Quarterly trends in anticoagulant use by age group. 75–79 (r 0.58, $p = 0.008$), 80–84 (r 0.02, $p = 0.930$), 85–89 (r 0.81, $p < 0.001$) and 90

Table 1

Baseline Characteristics of the Study Cohort Stratified by Age Group

Characteristic	Overall (N=6568)	Age 75–79 (N=2345)	Age 80–84 (N=2024)	Age 85–89 (N=1445)	Age 90 (N=754)	P-value
Women, n (%)	3303 (50%)	1040 (44%)	989 (49%)	795 (55%)	479 (64%)	<0.001
White, n (%)	5298 (85%)	1953 (86%)	1627 (85%)	1175 (86%)	543 (78%)	<0.001
Median income, \$	52306 ± 21239	51393 ± 20310	52375 ± 20898	53720 ± 21869	52202 ± 23456	0.015
Body mass index, n (%)						<0.001
< 25	2487 (38%)	685 (29%)	769 (38%)	633 (44%)	400 (53%)	
25 to < 30	2484 (38%)	922 (39%)	772 (38%)	529 (37%)	261 (35%)	
30	1597 (24%)	738 (31%)	483 (24%)	283 (20%)	93 (12%)	
Hemoglobin, g/dl	10.7 ± 1.8	10.7 ± 1.9	10.8 ± 1.8	10.7 ± 1.8	10.8 ± 1.8	0.24
Creatinine clearance, n (%)						<0.001
0 to <15	169 (3%)	47 (2%)	44 (2%)	47 (4%)	31 (4%)	
15 to <50	2454 (41%)	561 (27%)	707 (39%)	679 (51%)	507 (73%)	
50	3336 (56%)	1498 (71%)	1083 (59%)	598 (45%)	157 (23%)	
Medical Service, n (%)	4270 (65%)	1432 (61%)	1326 (66%)	961 (67%)	551 (73%)	<0.001
Heart failure, n (%)	3065 (47%)	968 (41%)	962 (48%)	714 (49%)	421 (56%)	<0.001
Hypertension, n (%)	5269 (80%)	1856 (79%)	1615 (80%)	1180 (82%)	618 (82%)	0.15
Diabetes, n (%)	1990 (30%)	804 (34%)	613 (30%)	424 (29%)	149 (20%)	<0.001
Stroke/TIA, n (%)	391 (6%)	104 (4%)	130 (6%)	98 (7%)	59 (8%)	<0.001
Cerebrovascular disease, n (%)	91 (1%)	22 (1%)	36 (2%)	26 (2%)	7 (1%)	0.032
Peripheral vascular disease, n (%)	1077 (16%)	399 (17%)	316 (16%)	237 (16%)	125 (17%)	0.66
Coronary artery disease, n (%)	3208 (49%)	1129 (48%)	1005 (50%)	727 (50%)	347 (46%)	0.20
Dementia, n (%)	769 (12%)	152 (6%)	217 (11%)	235 (16%)	165 (22%)	<0.001
Liver disease, n (%)	213 (3%)	100 (4%)	59 (3%)	42 (3%)	12 (2%)	0.001
Gastrointestinal bleeding, n (%)	199 (3%)	72 (3%)	65 (3%)	43 (3%)	19 (3%)	0.84
Intracranial bleeding, n (%)	157 (2%)	40 (2%)	56 (3%)	45 (3%)	16 (2%)	0.022
History of fall, n (%)	350 (5%)	77 (3%)	88 (4%)	111 (8%)	74 (10%)	<0.001
CHADS ₂ score, median (Q1, Q3) *	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	0.007

Characteristic	Overall (N=6568)	Age 75–79 (N=2345)	Age 80–84 (N=2024)	Age 85–89 (N=1445)	Age 90 (N=754)	P-value
CHA ₂ DS ₂ -VASc score, median (Q1, Q3) *	4.0 (4.0, 5.0)	4.0 (3.0, 5.0)	4.0 (4.0, 5.0)	4.0 (4.0, 5.0)	4.0 (4.0, 5.0)	<0.001
Modified HAS-BLED score 3, n (%)	4179 (64%)	1459 (62%)	1273 (63%)	938 (65%)	509 (68%)	0.038

* (1st quartile, 3rd quartile). All percentages indicate the proportion of patients with available data. CHADS₂: congestive heart failure, hypertension, age 75, diabetes, stroke/TIA. CHA₂DS₂-VASc: congestive heart failure, hypertension, age 75, diabetes, stroke/TIA, vascular disease (peripheral vascular disease or coronary artery disease), age 65–74, sex category (female sex). NOAC: new oral anticoagulant; TIA: transient ischemic attack. Modified HAS-BLED: hypertension, kidney disease, liver disease, stroke, bleeding history (bleeding or gastrointestinal bleeding or intracranial bleeding or lung/thoracic bleeding or soft tissue hematoma), elderly (age >65), drugs (aspirin or clopidogrel or prasugrel or ticagrelor), alcohol abuse.

Table 2

Independent Predictors of NOAC Use

Characteristic	OR*	95% CI	P-value
Age (vs. 75–79)			
80–84	0.675	(0.536, 0.852)	0.001
85–89	0.665	(0.507, 0.873)	0.003
90	0.390	(0.254, 0.599)	<0.001
Women (vs. men)	1.335	(1.090, 1.636)	0.005
White (vs. non-white)	1.501	(1.073, 2.099)	0.018
Median income (vs. 1 st tertile)			
2 nd tertile	0.957	(0.851, 1.354)	0.74
3 rd tertile	1.257	(0.737, 1.258)	0.07
Body mass index (vs. < 25)			
25 to < 30	1.074	(0.851, 1.354)	0.55
30	0.963	(0.737, 1.258)	0.78
Hemoglobin (per 1 g/dl increase)	1.196	(1.132, 1.263)	<0.001
Creatinine Clearance, 50 (vs. < 50)	1.368	(1.077, 1.736)	0.010
Medical service (vs. surgical service)	1.260	(0.737, 1.258)	0.041
Heart failure, yes (vs. no)	1.097	(1.132, 1.263)	0.39
Hypertension, yes (vs. no)	1.323	(0.851, 1.354)	0.044
Diabetes, yes (vs. no)	0.795	(1.077, 1.736)	0.05
Stroke/TIA yes (vs. no)	1.573	(1.062, 1.101)	0.016
Peripheral vascular disease, yes (vs. no)	0.930	(0.851, 1.354)	0.61
Coronary artery disease, yes (vs. no)	0.872	(0.737, 1.258)	0.21
Dementia, yes (vs. no)	0.780	(1.132, 1.263)	0.15
Gastrointestinal bleeding, yes (vs. no)	0.746	(1.077, 1.736)	0.43
Intracranial bleeding, yes (vs. no)	0.386	(1.062, 1.101)	0.043
Modified HAS-BLED score, 3 yes (vs. <3)	0.744	(1.132, 1.263)	0.015
Time point (per 1 quarter increase)	1.081	(1.062, 1.101)	<0.001

* Adjusted odds ratio of being prescribed a NOAC

NOAC: new oral anticoagulant; TIA: transient ischemic attack. Modified HAS-BLED: hypertension, kidney disease, liver disease, stroke, bleeding history (bleeding or gastrointestinal bleeding or intracranial bleeding or lung/thoracic bleeding or soft tissue hematoma), elderly (age >65), drugs (aspirin or clopidogrel or prasugrel or ticagrelor), alcohol abuse.