

Barriers to Prescribing Oral Anticoagulants To Inpatients Aged 80 Years and Older With Nonvalvular Atrial Fibrillation: A Cross-Sectional Study

Xin Xia

The Center of Gerontology and Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University

Lishuang Wang

College of Pharmacy, Macau University of Science and Technology

Taiping Lin

The Center of Gerontology and Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University

Jirong Yue

The Center of Gerontology and Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University

Zhonghua Yang

The Center of Gerontology and Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University

Chongqing Mi

Shenqiu County People's Hospital

Zaibo Liao

The Center of Gerontology and Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University

Yanyu Chen

The Center of Gerontology and Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University

Ning Ge (✉ grace7733@163.com)

The Center of Gerontology and Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University

Chenkai Wu

Global Health Research Center, Duke Kunshan University

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Abstract

Background: To investigate the temporal trend of prevalence of anticoagulation treatment and explore the factors associated with under prescription of oral anti-coagulants (OACs) among inpatients aged ≥ 80 years with nonvalvular atrial fibrillation (NVAF).

Methods: We retrospectively reviewed the medical records of inpatients with a discharge diagnosis of NVAF from a medical database. We used the Pearson chi-square or Fisher's exact test to compare categorical variables between patients with and without OACs prescription. Logistic regression analysis was used to assess the association between risk factors and under prescription of OACs.

Results: A total of 4375 patients aged ≥ 80 years with AF were assessed in the largest academic hospital in China from August 1, 2016, to July 31, 2020, 3165 NVAF patients were included. The prevalence of OACs use was 20.9% in 2017, 28.7% in 2018, 35.6% in 2019, and 43.9% in 2020. Of all participants with $\text{CHA}_2\text{DS}_2\text{-VASc} \geq 2$, 1,027 (32.4%) were prescribed OACs; 33.7% and 31.8% of patients with and without prior stroke received OACs, respectively. Age, clinical department where patients were discharged, use of antiplatelets, and history of stroke and dementia were significantly associated with not prescribing OACs.

Conclusions: The prevalence of OACs use increased over the past several years. The rate of prescription of OACs was lower among NVAF patients who were older, prescribed antiplatelets, discharged from non-departmental cardiology, and suffered from comorbidities. This study found the iatrogenic factors affecting the use of OACs in the inpatients aged ≥ 80 years, providing clues and basis for the standardized use of OACs in the inpatients.

Background

Nonvalvular atrial fibrillation (NVAF), a common type of atrial fibrillation (AF) that can cause stroke and other serious complications, is prevalent among older adults in China. The number of older adults with AF in China is projected to be twice as high as that in the US by 2050^{1,2}. Stroke is one of the most serious complications associated with AF and affects approximately one-third of older AF patients in China³.

Antithrombotic agents have been consistently shown to be effective in reducing the risk of stroke among patients with AF. Although there has been a surge in the number of prescriptions for anticoagulants since direct and nonvitamin K antagonist oral anticoagulants (DOACs/NOACs) entered the Chinese market in 2009 and 2013, respectively, anticoagulation medications were still severely underutilized among patients with NVAF, with a prescription rate of less than 30%⁴⁻⁷. It is therefore important to identify risk factors for low utilization of anticoagulation treatment in older patients who have AF. In addition to patients' sociodemographic, health, and clinical characteristics, physicians' perceptions about anticoagulation therapy for NVAF among older patients may also explain the low prescription rate.

The purpose of the present study were to investigate the temporal trend of prevalence of anticoagulation treatment and to identify the factors that lead to underprescription of anticoagulation among NVAF patients aged 80 years and older.

Methods

Participants

This retrospective study was carried out in a tertiary teaching hospital with over 4,000 beds in western China. A total of 4,375 participants aged 80 years and over were recruited from the hospital database, and patients were discharged between August 1, 2016 and July 31, 2020 with a discharge diagnosis of AF. The study was approved by the Ethical Review Committee of West China Hospital of Sichuan University with the committee's reference number 2015(150). The ethical committee approved the research protocol and waived the need for informed consent, because of the retrospective nature of this study and waiving informed consent will not adversely affect the rights and health of the subject. The regulations followed Declarations of Helsinki and ethical review of biomedical research involving people in China.

The study excluded participants who (i) underwent invasive procedures (n=337); (ii) absolute contraindications to anticoagulation (n = 828); and (iii) mitral valve stenosis or previous prosthetic valve replacement (n = 45). These selection criteria resulted in a sample of 3,165 eligible participants. The flow of participants through each stage of selection based on exclusion criteria is shown in Fig. 1.

Data collection

Patient information was extracted from their medical records by trained hospital personnel. Demographics included age, sex. Clinical variables included departments where they were discharged from, years of hospitalization, history of diabetes, medical conditions (hypertension, congestive heart failure, prior stroke, coronary heart disease (CHD), thromboembolic events, atherosclerosis, liver and renal function, medications administered during hospitalization, and bleeding events during hospitalization), value of international normalized ratio (INR) and monitoring pattern, antithrombotic medications administered, and the Charlson comorbidity index (CCI). All methods were carried out in accordance with relevant guidelines and regulations.

Thromboembolic and bleeding risk assessment

We estimated the risk of stroke using the CHA₂DS₂-VASc, a common method for predicting thromboembolic risk in patients with AF⁸⁻¹⁰. Seven risk factors were included: heart failure, hypertension, age, diabetes, history of stroke/transient ischemic attack (TIA), vascular diseases (peripheral arterial disease, previous myocardial infarction, and aortic atheroma), and female sex. Each risk factor receives one point except age 75 years and history stroke/TIA, which receive 2 points. The total CHA₂DS₂-VASc score ranges from 0 to 9 (highest risk).

We evaluated the risk of bleeding using the HAS-BLED score, in which 1 point was assigned to uncontrolled hypertension (systolic blood pressure >160 mmHg), abnormal renal or liver function, previous stroke, bleeding history, labile international normalized ratio, age >65 years, and use of drugs (antiplatelet/anticoagulation) or alcohol (>8 drinks/week). A HAS-BLED score of 3 points or more indicates a high risk of bleeding.

Antithrombotic medications review

We identified prescriptions of antithrombotic medications administered from the electronic medical chart during stay in the hospital, which were stratified into four exclusive groups: oral anticoagulants (OACs), lower molecular weight heparins (LMWH), heparin, and antiplatelets. OACs consisted of vitamin K antagonists (VKAs) and DOACs/NOACs. NOACs include dabigatran, rivaroxaban, and apixaban, which have been gradually introduced to

China since 2012. Antiplatelet therapy involved the use of aspirin, clopidogrel, ticlopidine, ticagrelor, dipyridamole, and tirofiban.

Statistical analysis

We used means and SDs or medians and interquartile ranges to describe continuous variables and counts and percentages to describe count variables of the entire sample. Baseline characteristics of patients were compared and summarized by means of the independent-sample t test for continuous variables and the Pearson chi-square test or Fisher's exact test for categorical variables between patients with and without prescription of OACs. Subsequently, we used simultaneous univariate logistic regression analysis and multivariable logistic regression analysis adjusted for relevant factors to examine the risk factors that were associated with anticoagulation states. To test for differences in stroke on anticoagulants, we stratified for stroke and then performed logistic regression analysis using the same method as above.

The cutoff of the P value for testing significance was set at 0.05. All statistical analyses were conducted using the R Project for Statistical Computing (R-4.0.5-win, University of Science and Technology of China; 2021-03-31).

Results

Sample Characteristics

A total of 3,165 patients were included in the analysis. The mean age was 85.3 ± 4.3 years; 1,342 (42.4%) were females (Table 1). Of all participants, 1,027 (32.4%) were prescribed OACs, and 2,138 (67.6%) were not. Patients prescribed OACs were younger and more likely to be female than those without OACs. The average HAS-BLED score was significantly lower among patients prescribed OACs than among those without OACs (3.9 vs. 4.1). Patients prescribed OACs had lower comorbidity scores and a lower prevalence of cognitive impairment. The prevalence of antiplatelet use was 35.4% among patients prescribed OACs and 48.1% among those not using any anticoagulants.

Table 1
Demographic and clinical characteristics of the study population.

Characteristics	Characteristics of the sample Count (%) / Mean (±SD) N=3165	Prevalence within subgroup Count (%) / Mean (±SD)		P value
		No Anticoagulation N=2138 (67.6%)	Anticoagulation N=1027(32.4%)	
Age(years), Mean	85.3(4.3)	85.7(4.5)	84.3(3.5)	<0.001
Age(years), N(%)				<0.001
80-84	1588(50.2)	977(45.7)	611(59.5)	
85-89	1083(34.2)	761(35.6)	322(31.4)	
90+	494(15.6)	400(18.7)	94(9.2)	
Sex, N(%)				<0.001
Male	1824(57.6)	1301(60.9)	523(50.9)	
Female	1341(42.4)	837(39.1)	504(49.1)	
CHA2DS2-VASC Score*, Mean	4.1(1.3)	4.1(1.3)	4.2(1.3)	0.006
CHA2DS2-VASC*, Median	4(3-5)	4(3-5)	4(3-5)	0.007
HAS- BLED Score*, Mean	4(1.2)	4.1(1.3)	3.9(1.1)	<0.001
HAS- BLED Score*, Median	4(3-5)	4(3-5)	4(3-5)	<0.001
HAS- BLED Score, N(%)				<0.001
HAS- BLED Score<3	308(9.7)	205(9.6)	103(10)	
3<=HAS- BLED Score<=4	1771(56)	1148(53.7)	623(60.7)	
HAS- BLED Score>=5	1086(34.3)	785(36.7)	301(29.3)	
Clinical department, N(%)				<0.001
Cardiology	786(24.8)	383(17.9)	403(39.2)	
Geriatrics	1129(35.7)	834(39)	295(28.7)	

Note. Data are shown using count (percentage) or mean (standard deviation). P values were calculated with chi-squared tests and Student's t tests for categorical and continuous variables, respectively.

* These variables are also presented as medians (interquartile ranges), and their p values were calculated with the Wilcoxon rank sum test.

Characteristics	Characteristics of the sample Count (%) / Mean (±SD) N=3165	Prevalence within subgroup Count (%) / Mean (±SD)		P value
		No Anticoagulation N=2138 (67.6%)	Anticoagulation N=1027(32.4%)	
Neurology	311(9.8)	169(7.9)	142(13.8)	
Others	939(29.7)	752(35.2)	187(18.2)	
Use of antiplatelets, Yes, N(%)	1392(44)	1028(48.1)	364(35.4)	<0.001
ASA, Yes, N(%)	739(23.3)	504(23.6)	235(22.9)	0.7
Clopidogrel, Yes, N(%)	1014(32)	767(35.9)	247(24.1)	<0.001
CCI*, Mean	1.9(2)	2.1(2.1)	1.6(1.7)	<0.001
CCI*, Median	1(1-3)	2(1-3)	1(0-2)	<0.001
CCI				<0.001
CCI: 0	687(21.7)	424(19.8)	263(25.6)	
CCI: 1-2	1663(52.5)	1096(51.3)	567(55.2)	
CCI: 3+	815(25.8)	618(28.9)	197(19.2)	
Hypertension, Yes, N(%)	2168(68.5)	1460(68.3)	708(68.9)	0.743
Diabetes, Yes, N(%)	859(27.1)	570(26.7)	289(28.1)	0.404
Stroke, Yes, N(%)	1065(33.6)	706(33)	359(35)	0.299
CHD, Yes, N(%)	1393(44)	934(43.7)	459(44.7)	0.62
Thromboembolic disease, Yes, N(%)	876(27.7)	576(26.9)	300(29.2)	0.196
Dementia, Yes, N(%)	283(8.9)	229(10.7)	54(5.3)	<0.001
Years of hospitalization, N(%)				<0.001
2016-2017	722(22.8)	571(26.7)	151(14.7)	
2017-2018	826(26.1)	589(27.5)	237(23.1)	
2018-2019	851(26.9)	548(25.6)	303(29.5)	
2019-2020	766(24.2)	430(20.1)	336(32.7)	

Note. Data are shown using count (percentage) or mean (standard deviation). P values were calculated with chi-squared tests and Student's t tests for categorical and continuous variables, respectively.

* These variables are also presented as medians (interquartile ranges), and their p values were calculated with the Wilcoxon rank sum test.

Of all patients, 2,055 (64.9%) were prescribed antithrombotic medications (OACs, antiplatelets), and 1110 (35.1%) did not use any antithrombotic medications (Fig. 2). A total of 663 (20.9%) patients received OACs (warfarin or NOACs) monotherapy, 32.5% were prescribed antiplatelet agents only, and 11.5% used both OACs and antiplatelets.

Predictors for Anticoagulation Therapy Use

Model 1: In univariate analysis, age, sex, clinical department where patients were discharged from, $\text{CHA}_2\text{DS}_2\text{-VASc}$, use of antiplatelets, use of clopidogrel, CCI, dementia and the year of hospitalization were significantly associated with OACs use among AF patients (Table 2). Patients aged 85-89 and ≥ 90 years had 48% and 166% higher odds of not using OACs, respectively, than those aged 80-84 years. The odds ratios of not using OACs among patients discharged from geriatric, neurological, and other departments were 2.97 (95% CI: 2.45-3.61), 1.25 (95% CI: 0.96-1.63), and 4.23 (95% CI: 3.43-5.24), respectively, compared to those discharged from the cardiology department. The use of antiplatelets was associated with higher odds of not using OACs (OR=1.69, 95% CI: 1.45-1.97). Patients with a CCI ≥ 3 were associated with a higher odds of not using OACs (2.02, 95% CI: 1.62-2.53) than those with a CCI = 0. **Model 2:** In multivariable logistic regression analysis adjusted by age and sex, clinical department, the year of hospitalization, use of antiplatelets, use of clopidogrel, CCI, dementia and prior stroke were associated with OACs use (Table 2). **Model 3:** In multivariable logistic regression analysis adjusted by age, sex, clinical department and the year of hospitalization, use of antiplatelets, use of clopidogrel, CCI and dementia were associated with OACs use. In particular, the difference in the influence of the HAS-BLED score in model 3 was significant (Table 2).

Table 2
Factors associated with underprescription oral anticoagulants

Characteristics	Model1 [OR(95%CI)]	Model2 [OR(95%CI)]	Model3 [OR(95%CI)]
Age(years),80-84	Ref.	-	-
Age(years),85-89	1.48(1.25,1.74)	-	-
Age(years),90+	2.66(2.09,3.42)	-	-
Sex, Female	0.67(0.57,0.78)	-	-
Clinical department, Cardiology	Ref.	Ref.	-
Clinical department, Geriatrics	2.97(2.45,3.61)	2.2(1.78,2.71)	-
Clinical department, Neurology	1.25(0.96,1.63)	1.21(0.92,1.57)	-
Clinical department, Others	4.23(3.43,5.24)	4.2(3.39,5.21)	-
Year, 2016-2017	Ref.	Ref.	-
Year, 2017-2018	0.66(0.52,0.83)	0.65(0.51,0.83)	-
Year, 2018-2019	0.48(0.38,0.6)	0.47(0.37,0.6)	-
Year, 2019-2020	0.34(0.27,0.42)	0.32(0.25,0.4)	-
CHA2DS2-VASC Score	0.92(0.87,0.98)	0.94(0.88,1)	1(0.93,1.07)
HAS- BLED Score<3	Ref.	Ref.	Ref.
3<=HAS- BLED Score<=4	0.93(0.71,1.19)	0.86(0.66,1.11)	1.11(0.84,1.46)
HAS- BLED Score>=5	1.31(1,1.72)	1.08(0.82,1.43)	1.89(1.38,2.57)
Prescription of antiplatelets, Y	1.69(1.45,1.97)	1.57(1.35,1.84)	2.21(1.85,2.63)
Clopidogrel, Y	1.77(1.49,2.09)	1.59(1.34,1.89)	2.1(1.75,2.54)
CCI, 0	Ref.	Ref.	Ref.
CCI 1-2	1.2(0.99,1.44)	1.08(0.89,1.3)	1(0.82,1.23)
CCI 3+	2.02(1.62,2.53)	1.68(1.34,2.11)	1.39(1.09,1.78)
Dementia, Y	2.16(1.6,2.96)	1.68(1.24,2.33)	1.48(1.07,2.07)
Thromboembolic disease, Y	1.12(0.86,1.47)	1.14(0.88,1.5)	0.74(0.56,1)
Stroke, Y	0.92(0.78,1.07)	0.83(0.71,0.98)	0.89(0.74,1.08)

Note.

Model 1: Univariate logistic regression analysis between no anticoagulation and characteristic variables.

Model 2: Multivariate logistic regression analysis between no anticoagulation and characteristic variables adjusted by age and sex.

Model 3: Multivariate logistic regression analysis between no anticoagulation and characteristic variables adjusted by age, sex, clinical department and year.

Characteristics	Model1 [OR(95%CI)]	Model2 [OR(95%CI)]	Model3 [OR(95%CI)]
Hypertension, Y	0.97(0.83,1.14)	0.96(0.81,1.13)	0.98(0.82,1.16)
Diabetes, Y	0.93(0.79,1.1)	0.91(0.77,1.08)	0.97(0.82,1.17)
CHD, Y	0.96(0.83,1.12)	0.87(0.74,1.01)	1.01(0.86,1.19)
Note.			
Model 1: Univariate logistic regression analysis between no anticoagulation and characteristic variables.			
Model 2: Multivariate logistic regression analysis between no anticoagulation and characteristic variables adjusted by age and sex.			
Model 3: Multivariate logistic regression analysis between no anticoagulation and characteristic variables adjusted by age, sex, clinical department and year.			

Primary versus secondary prevention of stroke in elderly patients with NVAf

Overall, 25.4% of patients with previous stroke and 40% of patients without a history of stroke with CHA2DS2-VASc \geq 2 were not receiving any antithrombotic therapy. A total of 40.8% of patients were using antiplatelet monotherapy for secondary prevention of stroke, and 28.2% of AF octogenarians were prescribed antiplatelet monotherapy for primary prevention of stroke. A total of 19.7% of patients with prior stroke versus 21.6% of patients without prior stroke were receiving anticoagulant monotherapy. A total of 14.0% of octogenarian patients with previous stroke versus 10.2% of AF octogenarian patients without prior stroke were prescribed a combination of anticoagulants and antiplatelets.

Of participants aged 90 years or above, 37.0% were not prescribed any antithrombotic medication (including antiplatelets or OACs) for primary prevention compared to patients aged 80-84 and 85-89 years (42.2% and 37.4%, respectively; Fig. 3). Only 19.1% of patients \geq 90 years without a history of stroke were receiving OACs (11.8% OAC monotherapy and 7.3% combination of OACs and antiplatelets) compared to those aged 80-84 and 85-89 years (36.3% and 29.2%, respectively). In secondary prevention, patients \geq 90 years had a higher antiplatelet monotherapy percentage (47.4%) versus 80-84 and 85-89 years (32.8% and 46.3%), and only 18.8% of patients 90 years and over were receiving OACs.

As shown in Fig. 4 and Table3, age, sex, clinical departments where patients were discharged from, years of hospitalization, use of antiplatelets, CHA2DS2-VASC score, CCI, and dementia were associated with prescription of OACs in primary and secondary prevention. Significant differences in years of hospitalization and HAS-BLED scores were found between the anticoagulation and nonanticoagulation groups in primary prevention.

Table 3

Comparison of the prescription of anticoagulants in primary prevention and secondary prevention of stroke

Characteristics	Primary prevention		Secondary prevention			
	Total N=3165 Characteristics of the sample (%)	Prevalence within subgroup (%)		Total N=317 Characteristics of the sample (%)/Mean(\pm SD)	Prevalence within subgroup (%)	
		No Anti. N=359	Anti. N=140		No Anti. N=218	Anti. N=99
Age, N(%)***###						
80-84	1137(54.1)	724(50.6)	413(61.8)	451(42.3)	253(35.8)	198(55.2)
85-89	701(33.4)	496(34.6)	205(30.7)	382(35.9)	265(37.5)	117(32.6)
90+	262(12.5)	212(14.8)	50(7.5)	232(21.8)	188(26.6)	44(12.3)
Sex, Female, N(%)***###	901(42.9)	574(40.1)	327(49)	440(41.3)	263(37.3)	177(49.3)
Clinical department***###						
Cardiology, N(%)	679(32.3)	335(23.4)	344(51.5)	107(10)	48(6.8)	59(16.4)
Geriatrics, N(%)	619(29.5)	458(32)	161(24.1)	510(47.9)	376(53.3)	134(37.3)
Neurology, N(%)	46(2.2)	30(2.1)	16(2.4)	265(24.9)	139(19.7)	126(35.1)
Others, N(%)	756(36)	609(42.5)	147(22)	183(17.2)	143(20.3)	40(11.1)
Year, N(%)***###						
2016-2017	497(23.7)	397(27.7)	100(15)	225(21.1)	174(24.6)	51(14.2)
2017-2018	567(27)	396(27.7)	171(25.6)	259(24.3)	193(27.3)	66(18.4)
2018-2019	552(26.3)	354(24.7)	198(29.6)	299(28.1)	194(27.5)	105(29.2)
2019-2020	484(23)	285(19.9)	199(29.8)	282(26.5)	145(20.5)	137(38.2)
HAS-BLED Score,N(%)**##						
HAS-BLED Score<3	297(14.1)	197(13.8)	100(15)	11(1)	8(1.1)	3(0.8)
3<=HAS- BLED Score<=4	1386(66)	920(64.2)	466(69.8)	385(36.2)	228(32.3)	157(43.7)

Primary prevention, ***p < 0.001, **p < 0.01, *p < 0.05 for comparison of anticoagulation status (anticoagulation, no anticoagulation) within each variable.

Secondary prevention, ###p < 0.001, ##p < 0.01, #p < 0.05 for comparison of anticoagulation status (anticoagulation, no anticoagulation) within each variable.

	Primary prevention			Secondary prevention		
HAS- BLED Score \geq 5	417(19.9)	315(22)	102(15.3)	669(62.8)	470(66.6)	199(55.4)
Use of APT, Y, N(%)***###	808(38.5)	593(41.4)	215(32.2)	584(54.8)	435(61.6)	149(41.5)
Dementia, Y, N(%)**###	115(5.5)	93(6.5)	22(3.3)	168(15.8)	136(19.3)	32(8.9)
Primary prevention, ***p < 0.001, **p < 0.01, *p < 0.05 for comparison of anticoagulation status (anticoagulation, no anticoagulation) within each variable.						
Secondary prevention, ###p < 0.001, ##p < 0.01, #p < 0.05 for comparison of anticoagulation status (anticoagulation, no anticoagulation) within each variable.						

Discussion

The aims of the study were to understand the status quo of anticoagulation therapy and confirm the factors associated with underprescription of OACs in NVAF inpatients aged 80 years and older. We found that only 64.9% of older patients with AF were prescribed antithrombotic medications, and the prevalence of OACs use was particularly low among patients who were older, prescribed antiplatelets, discharged from nondepartmental cardiology, and suffered from comorbidities. Although OACs use is recommended by clinical guidelines for reducing the risk of stroke among older patients who have AF with high risk (CHA₂DS₂-VASc score \geq 2), our findings suggest that OACs are still severely underprescription.

In the study, only 32.4% of patients \geq 80 years and 19.0% of very elderly patients \geq 90 years with NVAF were prescribed OACs. Although the prevalence is increasing year by year (20.9% in 2017, 28.7% in 2018, 35.6% in 2019 and 43.9% in 2020), this prevalence was lower than that in several previous studies showing that 37.5–58.5% of NVAF elderly patients receive OACs^{4,7,11,12}. The FIELD GARFIELD registry in 2016 reported that 57.7% of AF patients with a high risk of stroke received OACs in China. There are several plausible explanations for this discrepancy. We mainly looked at the oldest old with 85.3 \pm 4.3 years of mean age. Moreover, the risk of ischemic stroke was examined using CHA₂DS₂-VAS_c, and all patients had a higher risk of stroke with a CHA₂DS₂-VAS_c score \geq 2.

We found that the prevalence of OACs use was particularly low among patients who were taking antiplatelets. These results were in line with previous studies^{5,6,11}. Our results showed that 44.0% of elderly patients \geq 80 years with AF were prescribing antiplatelets, and 32.5% of patients were receiving antiplatelet monotherapy. In contrast, we did not find that lower prescription of OACs was associated with atherosclerotic disease. A total of 45.1% of patients without atherosclerotic disease were prescribed antiplatelets, and we strongly suspect that these prescriptions were made to prevent the thromboembolic complications of AF. The underprescription of OACs in the elderly population is partly due to limited clinical evidence, particularly in patients \geq 80 years of age. Although antiplatelets have been important medications to treat or prevent cardiovascular events and are widely utilized in a variety of atherosclerotic diseases to which elderly patients are susceptible, large amounts of evidence indicate that antiplatelets are not effective in preventing ischemic stroke in patients with high risk compared to OACs^{4,13–17}. To date, the largest cohort study involving subjects \geq 90 years was conducted in

Taiwan, which included 15,756 participants¹⁸. As a result, OACs were superior in reducing the risk of ischemic stroke and positive net clinical benefit with no significant difference in safety compared with aspirin in patients with AF \geq 90 years.

Although patients with AF who experienced ischemic stroke are likely to have recurrence, contrary to our expectation, our results found that the utilization of anticoagulants in patients with a stroke history was not superior to that in patients without stroke. Underprescription of OACs in secondary prevention of stroke in octogenarian patients was mainly related to antiplatelet prescription, as was pronounced in patients \geq 85 years. More than 46.7% of patients aged 85 years and older were only prescribed antiplatelets in secondary prevention versus 36.2% in primary prevention, which is in line with community-based contemporary registry data that one-third of AF patients with high stroke risk did not receive OACs but instead were prescribed antiplatelet monotherapy even untreated¹⁹. Indeed, antiplatelets do not significantly reduce ischemic stroke risk and have no impact on mortality²⁰.

In this study, the majority of patients aged \geq 80 years with AF were not discharged from the Department of Cardiology or Neurology and were discharged from the Department of Geriatrics (35.7%) and other departments (29.7%) compared to the Department of Cardiology (24.8%) and Neurology (9.8%). Older patients with AF, accompanied by multiple comorbidities, were likely to be admitted to medical specialties such as the Department of Geriatrics Medicine, Respiratory, nephrology, oncology, and surgical departments rather than the Department of Cardiology or Neurology, in which most physicians have not always been trained in standard anticoagulation therapy for AF. Previous studies and systematic reviews indicated no interaction for age with regard to both the efficacy and safety of OACs, even in patients aged \geq 75 years^{21–24}.

Moreover, frailty is frequent in patients aged 80 years or older and vulnerable to adverse clinical events, including hospitalization, falls, and mortality. Frail patients often show age-related hepatic and renal function decline with comorbidities and concomitant medications^{25,26}. Therefore, these challenges are projected to be hurdles to physicians prescribing OACs in older populations²⁷, even though warfarin and NOACs were confirmed to be superior to aspirin and no antithrombotic treatment for the prevention of ischemic stroke in AF patients \geq 65 years, even in patients over the age of 90 years¹⁸. Fears of fall-related intracerebral hemorrhage are also common reasons for not commencing or discontinuing OACs for elderly AF patients. Practically, a clinical decision model has indicated that patients taking warfarin would need to fall 295 times to outweigh the benefit of anticoagulation therapy by the risk of intracerebral hemorrhage²⁸. NOACs are not only superior to warfarin with respect to major bleeding risk but are also more convenient to use in older AF patients^{29,30}. Despite recommendations of guidelines or consent, the proportion of NOACs prescribed in our older AF population taking OACs was only 61.6% (42.4% for warfarin, 30.3% for dabigatran, 31.3% for rivaroxaban, and 4% changed their OACs) due to higher cost. The proportion of NOACs prescribed in our older AF population taking OACs was increasing year by year (13.2% in 2017, 51.0% in 2018, 73.6% in 2019, 80.3% in 2020), which should be the main reason why the use of anticoagulants was increasing year by year.

We acknowledged several limitations. First, except for geriatricians, most physicians in other departments did not implement comprehensive geriatric assessment (CGA) for older patients in their clinical practice in China. Consequently, many geriatric data, which would impact the prescription of anticoagulants, such as frailty, activity of daily living (ADLs), nutrition, and cognition, were not collected from electronic databases. We indirectly

obtained information on geriatric problems using alternative indicators such as age, diagnosis of dementia, and comorbidities. Second, whether commencing anticoagulation therapy in patients with AF is associated with risk of stroke, physicians' perception, and patients' preferences, unfortunately, patients' attitudes toward anticoagulation for AF were not available in some cases due to lack of medical records. Finally, our study was conducted in a teaching hospital, and therefore, the results may not represent other hospitals in different regions.

Conclusions

This study demonstrated that the prevalence of underprescription OACs in very elderly inpatients with NVAF is high and associated with age, prescription of antiplatelets, department where patients are discharged from, comorbidities, physician's perception of anticoagulant treatment rather than coronary heart disease (CHD), hypertension, history of stroke, and cognitive status. Further research is needed to confirm and modify the other factors related to nonadherence to guideline-directed anticoagulation therapy in very elderly NVAF patients.

Abbreviations

NVAF: Nonvalvular atrial fibrillation; **AF:** atrial fibrillation; **DOACs/NOACs:** direct and nonvitamin K antagonist oral anticoagulants; **CHD:** coronary heart disease; **INR:** international normalized ratio; **CCI:** Charlson comorbidity index; **TIA:** transient ischemic attack; **OACs:** oral anticoagulants; **LMWH:** lower molecular weight heparins

Declarations

Ethics approval and consent to participate

The current research was approved by the Ethical Review Committee of West China Hospital of Sichuan University with the committee's reference number 2015(150).

Consent for publication

Not applicable

Availability of data and material

The data that support the findings of this research are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Competing interests

No conflict of interest exists in the submission of this manuscript, and the manuscript has been approved by all authors for publication.

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Authors' Contributions

Xin Xia and Ning Ge designed the study and wrote the paper. Taiping Lin, Chongqing Mi and Yanyu Chen take part in the interpretation of data. Xin Xia, Ning Ge and Chenkai Wu were responsible for data analysis and interpretation. Lishuang Wang, Jirong Yue, Zhonghua Yang, Zaibo Liao and Chenkai Wu reviewed and edited the manuscript. All authors have read and approved the manuscript.

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Figures

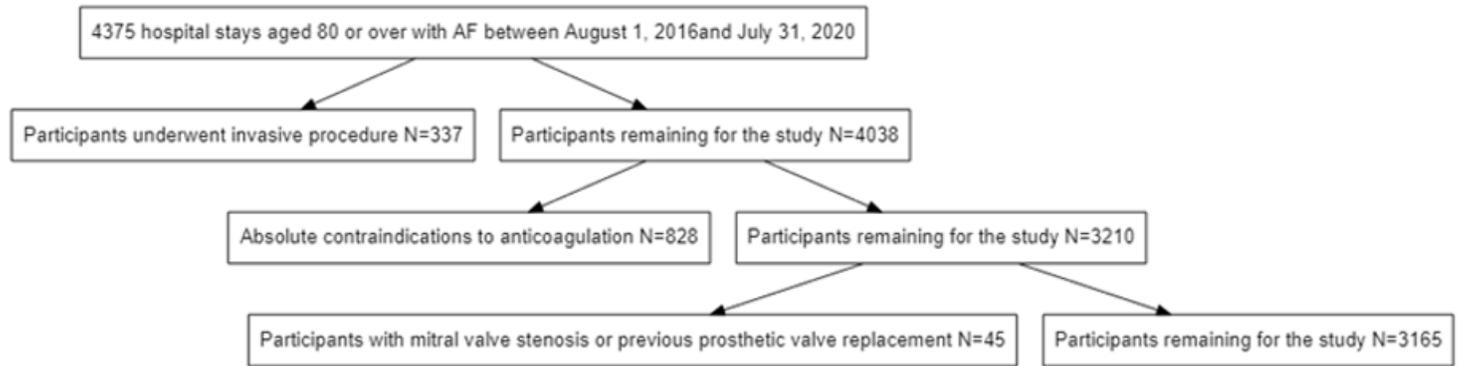


Figure 1

Flow diagram of selection of analytic sample

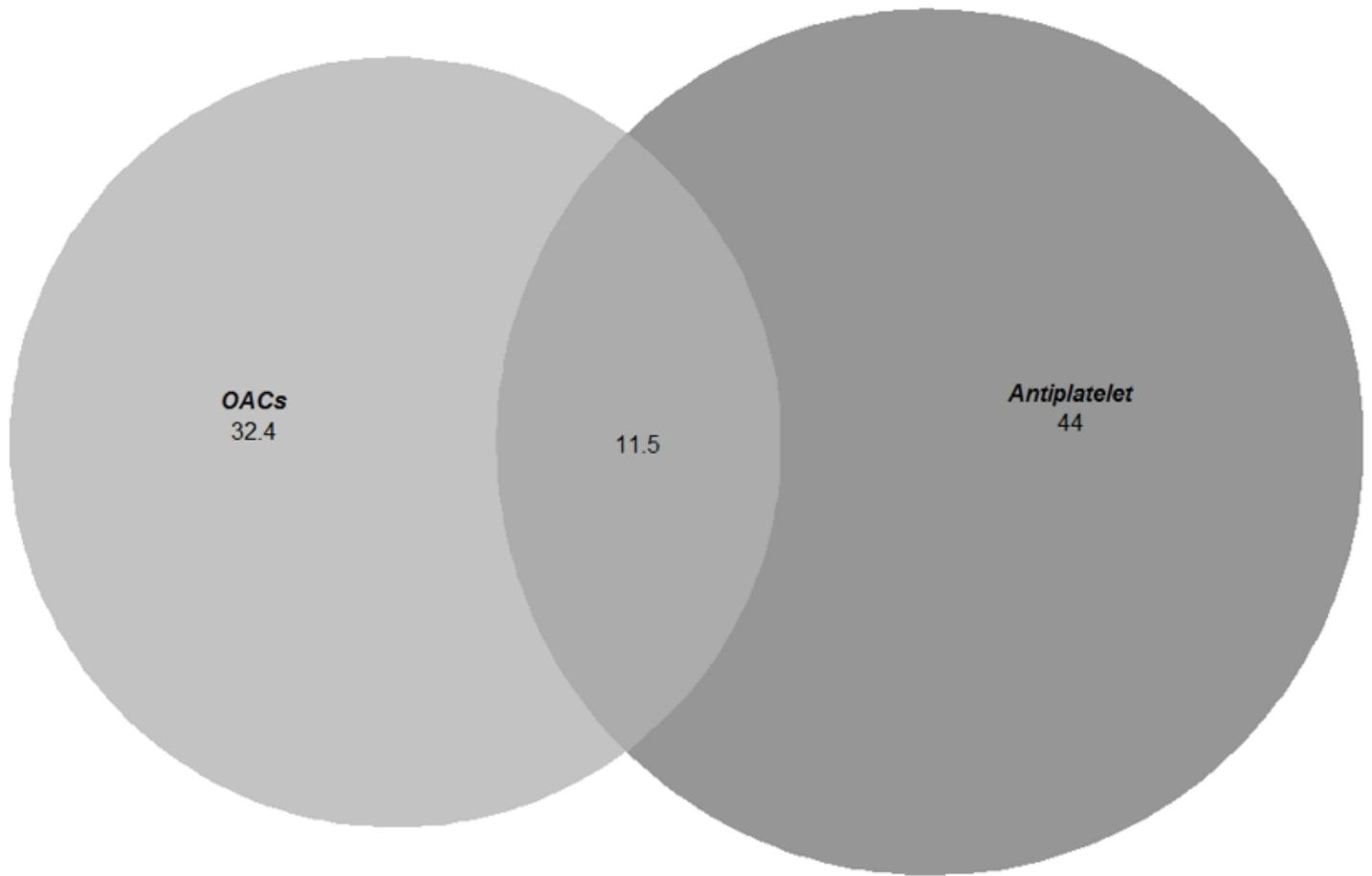


Figure 2

Venn diagram of antithrombotic therapy in patients aged 80 and older with NVAF



Figure 3

Antithrombotic therapy in non-stroke and previous stroke according to age

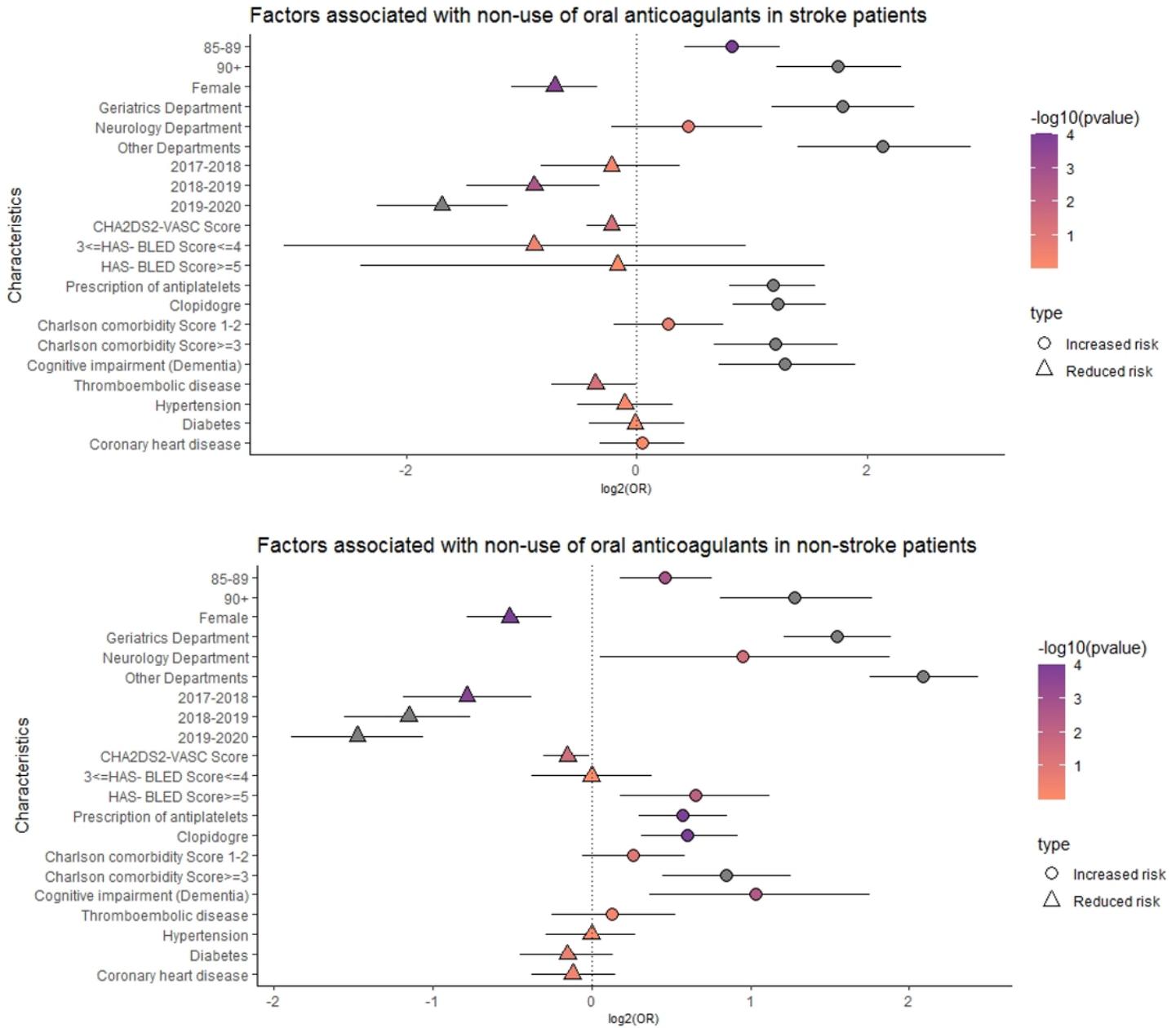


Figure 4

Factors associated with non-use of oral anticoagulants in non-stroke and previous stroke