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Oral anti-coagulants use in Chinese hospitalized patients with atrial fibrillation

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Abstract

Background: Oral anti-coagulants (OAC) are the intervention for the prevention of stroke, which consistently improve clinical outcomes and survival among patients with atrial fibrillation (AF). The main purpose of this study is to identify problems in OAC utilization among hospitalized patients with AF in China.

Methods: Using data from the Improving Care for Cardiovascular Disease in China-Atrial Fibrillation (CCC-AF) registry, guideline-recommended OAC use in eligible patients was assessed.

Results: A total of 52,530 patients with non-valvular AF were enrolled from February 2015 to December 2019, of whom 38,203 were at a high risk of stroke, 9717 were at a moderate risk, and 4610 were at a low risk. On admission, only 20.0% (6075/30,420) of patients with a diagnosed AF and a high risk of stroke were taking OAC. The use of pre-hospital OAC on admission was associated with a lower risk of new-onset ischemic stroke/transient ischemic attack among the diagnosed AF population (adjusted odds ratio: 0.54, 95% confidence interval: 0.43–0.68; *P* <0.001). At discharge, the prescription rate of OAC was 45.2% (16,757/37,087) in eligible patients with high stroke risk and 60.7% (2778/4578) in eligible patients with low stroke risk. OAC utilization in patients with high stroke risk on admission or at discharge both increased largely over time (all *P* <0.001). Multivariate analysis showed that OAC utilization at discharge was positively associated with in-hospital rhythm control strategies, including catheter ablation (adjusted odds ratio [OR] 11.63, 95% confidence interval [CI] 10.04–13.47; *P* <0.001), electronic cardioversion (adjusted OR 2.41, 95% CI 1.65–3.51; *P* <0.001), and anti-arrhythmic drug use (adjusted OR 1.45, 95% CI 1.38–1.53; *P* <0.001).

Conclusions: In hospitals participated in the CCC-AF project, >70% of AF patients were at a high risk of stroke. Although poor performance on guideline-recommended OAC use was found in this study, over time the CCC-AF project has made progress in stroke prevention in the Chinese AF population.

Registration: ClinicalTrials.gov, NCT02309398.

Keywords: Atrial fibrillation; Oral anti-coagulants; OAC; Stroke prevention; Contraindication

Introduction

As the most prevalent arrhythmia worldwide, atrial fibrillation (AF) contributes substantially to morbidity and healthcare burden. According to the most recent study conducted by Chinese AF Epidemiology Study, the prevalence of AF among Chinese individuals older than 45 years was 1.8%, and the number of people with AF is estimated to be approximately 8 million, which is perhaps an underestimate, because more than one-third of AF patients are unaware of their conditions and those with paroxysmal or asymptomatic manifestation may be missed or underdiagnosed.[1]

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While AF can impair health in a number of ways, including decreasing quality of life, and increasing risks of heart failure (HF), dementia, stroke and death,[1–6] oral anticoagulants (OAC) are the only intervention for the prevention of stroke which consistently improve clinical outcomes and survival.[4,7–9] The non-vitamin K antagonist oral anticoagulants (NOAC) therapy offers improved safety and efficacy, as demonstrated in randomized trials involving over 71,000 participants.[10–13] Thus, OAC use is a Class I recommendation in AF patients with high stroke risk in the American College of Cardiology (ACC)/American Heart Association (AHA) guideline, as well as the European Society of Cardiology (ESC) and Asia-Pacific Heart Rhythm Society guidelines.[14–16]

In China, prior studies have shown that OAC has been underused for stroke prevention in AF.[17,18] Over the past decade, the Chinese Society of Cardiology (CSC) has made great efforts to improve stroke prevention among the AF population. Although prior studies have expanded our understanding of clinical practice of AF in China, they are limited by a lack of hospital representation and the lack of quality improvement components.[18–22] In collaboration with the AHA, the CSC launched a series of projects with the objective to improve the quality of care in several cardiovascular diseases.[23,24] In February 2015, the AHA and CSC launched the Improving Care for Cardiovascular Disease in China-Atrial Fibrillation (CCC-AF) project, which focused on improving the quality of AF care in China.[23]

The purpose of this study is to evaluate the guideline-recommended OAC use for stroke prevention, the temporal trends of OAC use, and the variations of OAC use across the participating hospitals in the CCC-AF registry. Second, we assessed the relationship between pre-hospital OAC use and in-hospital outcomes. Finally, we examined related factors and documented contraindications to determine the underlying mechanism behind AF patients not taking OAC.

Methods

Data sources

The CCC-AF project is a nationwide quality improvement registry program. The goal of CCC-AF is to improve cardiovascular health and outcomes in patients with AF by optimizing adherence to guideline recommendations for the treatment and management of AF. Study inclusion of AF was based on electrocardiogram (ECG) results, which are recorded by a 12-lead ECG, a 24 h Holter ECG, or other cardiac rhythm monitors. Patients with valvular AF and AF secondary to reversible conditions were excluded from the study.

The details of the design and methodology of the CCC-AF project have been published previously.[23] Institutional review board approval was granted for this research with an informed consent by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (No. 2014018). This study was registered with ClinicalTrials.gov (NCT02309398). Clinical data elements were collected in accordance with ACC/AHA recommendations and were reported via a web data collection platform (Oracle Clinical Remote Data Capture, Oracle Corporation, Redwood City, California, USA) by trained data abstractors at participating hospitals. Face-to-face training sessions, standardized online reporting with automatic checks for invalid values, on-site quality control, and data completeness monitoring were adopted to ensure the accuracy and completeness of data.

Study population

Between February 2015 and December 2019, a total of 61,136 admissions for AF from 236 hospitals were enrolled in the CCC-AF project. We excluded 8347 patients with a prior diagnosis of valvular AF and 259 patients with a moderate to severe mitral stenosis on cardiac ultrasound. Finally, 52,530 patients with non-valvular AF were included in the present study [Supplementary Figure 1, http://links.lww.com/CM9/B788]. High coverage of medical insurance in this study was defined as patients with urban employees-basic insurance, urban residents-basic insurance, or free medical care. Moderate coverage of medical insurance was defined as patients with new rural cooperative insurance or commercial insurance. Low coverage of medical insurance was defined as patients with self-paying or patients with medical financial assistance.

Risk stratification

The CHA_2DS_2-VASc score and HAS-BLED score were calculated as described previously.[11,18,25] The CHA_2DS_2-VASc score was calculated for each patient by assigning one point for any of an age between 65 and 74 years, a history of hypertension, diabetes mellitus (DM), congestive cardiac failure, vascular disease (coronary artery disease [CAD] or peripheral artery disease [PAD]), and female sex; and two points for a history of stroke/transient ischemic attacks (TIA)/thromboembolism or an age of ≥75 years.[26–28]

AF patients with CHA_2DS_2-VASc score ≥2 in men or ≥3 in women were classified as patients with high stroke risk, whereas those with CHA_2DS_2-VASc score of one point in men or two points in women were classified as moderate stroke risk, and those with CHA_2DS_2-VASc score of zero points in men or one point in women were classified as low stroke risk.

Quality improvement

Four quality improvement tools were developed and applied to improve the hospital-level guideline adherence for patients with AF in daily clinical practice: (1) monthly hospital quality reports; (2) annual hospital recognition; (3) training sessions; and (4) online educational materials. Hospitals were provided performance data from the patient management tool regarding stroke prevention, rate control, and maintenance of sinus rhythm every quarter. Strict contraindications in this study were defined as allergy, recent operations, active bleeding, and severe hepatic or renal comorbidities. Overall contraindications to OAC included the presence of any contraindication.

Definition of in-hospital outcomes

The CCC-AF project routinely collected all-cause deaths and ischemic stroke or TIA data as a part of core in-hospital outcomes. A new-onset ischemic stroke or TIA is one that occurs between hospital admission and discharge. Strict contraindications are defined as allergy, recent operations, active bleeding, and severe hepatic or renal comorbidities.[25]

Statistical analysis

Descriptive statistics were used to summarize the clinical characteristics of the non-valvular AF population stratified by CHA_2DS_2-VASc score. Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]) and compared using Student's *t*-test or Mann–Whitney *U* test. Categorical variables were expressed as frequencies and percentages (%) and compared using the χ^2 test. The time trend of prescription rate at discharge or utilization rate before admission of OAC was tested using the Cochran–Armitage test.

Associations between pre-hospital OAC use and in-hospital outcomes were determined by binary logistic regression, and adjusted for age, sex, hospital levels, AF types, medical insurance, medical history of smoking, drinking, hypertension, DM, stroke or TIA, PAD, HF, CAD, previous bleeding, chronic obstructive pulmonary disease (COPD), chronic renal disease, prior treatment including catheter ablation, surgical ablation, antiarrhythmic drugs (AADs) use, electronic cardioversion, and prior concomitance with antiplatelet, as well as in-hospital OAC use and catheter ablation, surgical ablation, AADs use, and electronic cardioversion. Logistic multivariate regression analysis was also used to identify factors associated with OAC use at hospital discharge. In addition to the variables described above, the variables incorporated within this model included the use of antiplatelets at discharge. All analyses were two-tailed, and *P* values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS version 24 (SPSS Inc., Chicago, IL, USA).

Results

We enrolled 52,530 patients with non-valvular AF, with a mean age of 69.2 ± 12.0 years; a total of 29,597 (56.3%) were male; the median CHA_2DS_2-VASc score was 3.0 (IQR, 2.0–4.0); the median HAS-BLED score was 1.0 (IQR, 1.0–2.0); there were 20.7% (n = 10,887) of newly diagnosed AF and 40.7% (21,386) of paroxysmal AF. Based on CHA_2DS_2-VASc score, 38,203 (72.7%) patients had a high stroke risk, 9717 (18.5%) had a moderate stroke risk, and 4610 (8.8%) had a low stroke risk. There were substantial differences among these three groups in sociodemographic characteristics, medication history, AF types, and baseline treatments [Supplementary Table 1, http://links.lww.com/CM9/B788].

OAC utilization before admission in patients with high stroke risk

The characteristics of patients with high stroke risk taking OAC before admission are shown in Supplementary Table 2, http://links.lww.com/CM9/B788. Before admission, 6075/30,420 (20.0%) patients with a high risk of stroke and a previous diagnosis of AF were taking OAC.

After admission, 2.0% (616/30,420) of patients suffered a newly diagnosed ischemic stroke or TIA, including 85/6075 patients (1.4%) receiving OAC before admission and 531 patients (531/24,345, 2.2%) who were not. There were 179/30,420 (0.6%) in-hospital deaths, including 22/6075 (0.4%) patients taking OAC before admission and 157/24,345 (0.6%) not taking OAC before admission. Univariate and multivariate analysis showed that OAC usage before hospitalization was related with a decreased risk of all-cause mortality (adjusted odds ratio [aOR]: 0.60, 95% CI: 0.38–0.93; *P* = 0.024) and in-hospital ischemic stroke/TIA (aOR: 0.54, 95% CI: 0.43–0.68; *P* <0.001). On sensitivity analysis, when excluding AF patients with strict contraindications (n = 922), multivariate analysis showed that OAC usage before this hospitalization was still related with a substantial reduction in in-hospital ischemic stroke/TIA (aOR: 0.53, 95% CI: 0.42–0.67; *P* <0.001) [Supplementary Table 3, http://links.lww.com/CM9/B788].

OAC prescription in patients at discharge

At discharge, the prescription rate of OAC was 64.0% (16,757/26,190) in eligible patients (no documented contraindications) with high stroke risk and 72.3% (2778/3842) with low stroke risk. However, when excluding patients with strict contraindications, the prescription rate of OAC was 45.2% (16,757/37,087) in eligible patients with high stroke risk and 60.7% (2778/4578) with low risk of stroke. Patient characteristics in high risk and low risk groups according to OAC use at discharge are shown in Table 1 and Supplementary Table 4, http://links.lww.com/CM9/B788, respectively.

OAC prescriptions over time

To assess the trends of OAC prescription during the course of the study, the annual rates of OAC prescription in eligible patients at discharge were assessed. In 2015, the OAC prescribing rate at discharge, that is, only 35.1% (2513/7151) was found in patients with high stroke risk. Over the course of the project, the rate of OAC prescription at discharge increased, reaching 50.1% (3784/7547) in 2019 [Figure 1]. OAC utilization in patients with high stroke risk on admission increased from 12.4% (802/6467) in 2015 to 29.3% (1563/5330) in 2019. The rate of OAC prescription in AF patients with low risk of stroke increased from 53.2% (501/941) in 2015 to 65.8% (521/792) in 2019 [Supplementary Figure 2, http://links.lww.com/CM9/B788].

The details of specific NOAC are included in Supplementary Table 5, http://links.lww.com/CM9/B788. In 2015, in the group of high stroke risk, warfarin use at discharge was 27.9% (1997/7151) and NOAC use at discharge was 6.2% (446/7151). Dabigatran and rivaroxaban constituted the vast majority of NOAC use. Over time, there was a significant increase in NOAC prescriptions and a significant decrease in warfarin prescriptions at discharge, as seen in Figure 1.

Table 1: Clinical characteristics of OAC use at discharge in AF patients with high risk of stroke and without strict contraindications to OAC.

Characteristics	At discharge (n = 37,087)		Statistics	P values
	Non-OAC medication (n = 20,330)	OAC medication (n = 16,757)		
Age (years)			1219.000*	<0.001
<65	2135 (10.5)	2935 (17.5)		
65–74	6256 (30.8)	6984 (41.7)		
≥75	11,939 (58.7)	6838 (40.8)		
Male	10,583 (52.1)	8980 (53.6)	8.666*	0.003
Han ethnicity	19,929 (98.0)	16,349 (97.6)	9.202*	0.002
Tertiary hospitals	15,701 (77.2)	15,098 (90.1)	1080.422*	<0.001
Medical insurance			670.560*	<0.001
High coverage	12,963 (63.8)	11,216 (66.9)		
Moderate coverage	4738 (23.3)	2326 (13.9)		
Low coverage	2629 (12.9)	3215 (19.2)		
Hospital stay (days)	9.0 (6.0–12.0)	8.0 (8.0–12.0)	46.644†	<0.001
Drinking	1887 (9.3)	1962 (11.7)	58.157*	<0.001
Smoking	3663 (18.0)	3384 (20.2)	28.252*	<0.001
Medical history				
Hypertension	13,123 (64.5)	11,479 (68.5)	64.269*	<0.001
DM	4379 (21.5)	4022 (24.0)	31.786*	<0.001
CAD	8063 (39.7)	4353 (26.0)	772.280*	<0.001
Stroke or TIA	3601 (17.7)	3273 (19.5)	20.138*	<0.001
PAD	360 (1.8)	435 (2.6)	29.815*	<0.001
HF	3477 (17.1)	1960 (11.7)	214.588*	<0.001
Major bleeding	387 (1.9)	237 (1.4)	13.292*	<0.001
COPD	1365 (6.7)	747 (4.5)	87.082*	<0.001
BMI (kg/m^2)	24.0 ± 4.0	24.8 ± 3.9	0.091†	0.762
Blood pressure (mmHg)				
SBP	133.4 ± 22.3	133.4 ± 20.2	126.441†	<0.001
DBP	80.1 ± 14.6	80.5 ± 13.8	29.429†	<0.001
eGFR (mL·min^{-1}·1.73 m^{-2})	85.8 ± 49.3	88.8 ± 48.0	12.539†	<0.001
Left atrial diameter (mm)	42.4 ± 8.1	42.7 ± 7.6	45.480†	<0.001
LVEF (%)	55.3 ± 12.2	57.2 ± 11.5	106.774†	<0.001
Total cholesterol (mmol/L)	4.1 ± 2.2	4.0 ± 1.6	30.505†	<0.001
LDL-C (mmol/L)	2.3 ± 0.9	2.26 ± 0.9	10.039†	0.002
CHA_2DS_2-VASc score	4.0 (3.0–5.0)	3.0 (3.0–4.0)	1.295†	0.255
HAS-BLED risk score	1.0 (1.0–2.0)	1.0 (1.0–2.0)	9.546†	<0.001
AF type			745.960*	<0.001
First diagnosed	4450 (21.9)	3095 (18.5)		
Paroxysmal	7061 (34.7)	6718 (40.1)		
Persistent	4544 (22.4)	4933 (29.4)		
Long-standing persistent/permanent	4275 (21.0)	2011 (12.0)		
Sinus rhythm	3528 (17.4)	3312 (19.8)	35.505*	<0.001
Baseline treatment				
Prior concomitance with antiplatelet	2183 (10.7)	1105 (6.6)	195.195*	<0.001
Prior treatment with anticoagulant	1139 (5.6)	5147 (30.7)	4115.401*	<0.001
Prior AADs use	1000 (4.9)	1813 (10.8)	456.248*	<0.001
Prior catheter ablation	243 (1.2)	781 (4.7)	410.881*	<0.001
Prior cardioversion	154 (0.8)	264 (1.6)	55.150*	<0.001
Prior surgical ablation	35 (0.2)	45 (0.3)	3.965*	0.046
In-hospital treatment				
Rhythm control strategies	3159 (15.5)	6163 (36.8)	2202.214*	<0.001
AADs use	3047 (15.0)	4908 (29.3)	1115.093*	<0.001
Surgical ablation	6 (<0.1)	6 (<0.1)	0.112*	0.737
Catheter ablation	209 (1.0)	3968 (23.7)	4715.866*	<0.001
Cardioversion	42 (0.2)	303 (1.8)	255.673*	<0.001
Antiplatelet at discharge	14,051 (69.1)	2229 (13.3)	11618.703*	<0.001

Data are expressed as n (%), mean ± standard deviation, or median (interquartile range). * χ^2 value. † F value. AADs: Antiarrhythmic drugs; AF: Atrial fibrillation; BMI: Body mass index; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; DBP: Diastolic blood pressure; DM: Diabetes mellitus; eGFR: Estimated glomerular filtration rate; HF: Heart failure; LDL-C: Low-density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; OAC: Oral anticoagulation; PAD: Peripheral arterial disease; SBP: Systolic blood pressure; TIA: Transient ischemic attack.

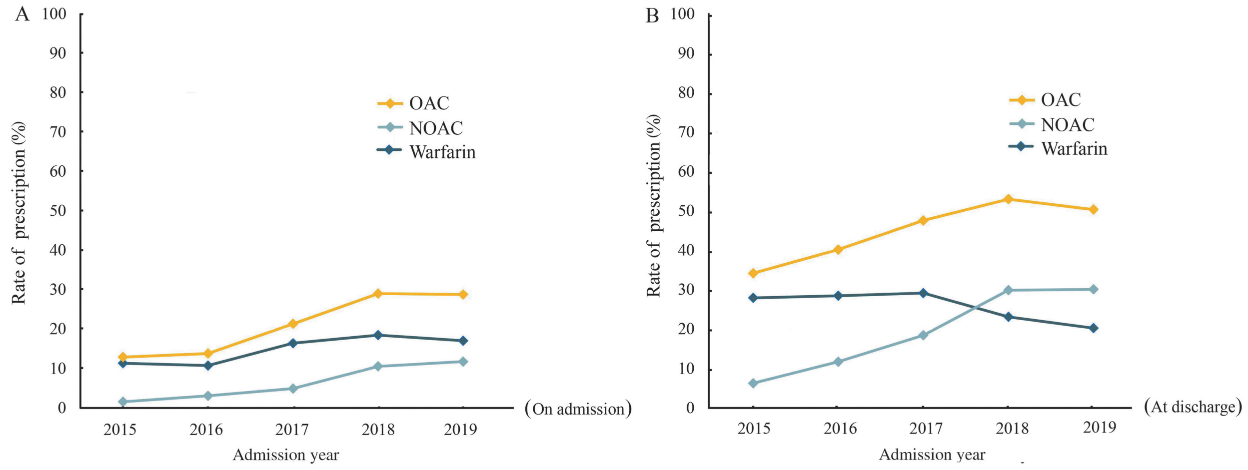

Figure 1: The trend of OAC utilization rate before admission and at discharge in eligible AF patients with high risk of stroke. The trend of pre-hospital OAC utilization rate before admission (A) and OAC prescription rate at discharge (B) in eligible patients with high risk of stroke. AF: Atrial fibrillation; NOAC: Non-vitamin K antagonist oral anticoagulants; OAC: Oral anti-coagulants.

Variation in OAC prescription at discharge among hospitals

To assess the degree to which OAC prescription at discharge differed among hospitals, hospitals with at least 50 AF patients were included. Across the 187 sites, the OAC prescription rate at discharge in patients with high stroke risk was 46.5% (IQR, 22.0%–64.8%) in tertiary hospitals (n = 132) and 23.0% (IQR, 12.0%–47.0%) in secondary hospitals (n = 55).

Across the 163 sites, the OAC prescription rate at discharge in patients with low risk of stroke was 50.0% (IQR, 25.0%–69.0%) in tertiary hospitals (n = 123) and 21.0% (IQR, 0–50.0%) in secondary hospitals (n = 40) [Supplementary Figure 3, http://links.lww.com/CM9/B788].

OAC prescription at discharge in special populations

Rates of OAC prescription in special populations with high stroke risk are shown in Supplementary Figure 4, http://links.lww.com/CM9/B788. In general, the rates of OAC prescription at discharge were low and less than 50% for all subgroups of patients, with the exception of those who received rhythm control and those who underwent catheter ablation (OAC prescription rates were 66.1% and 95.0%, respectively). Overall, males, patients with DM, and those with ischemic stroke/TIA were more likely to be prescribed OACs (all P <0.01). OAC prescriptions were lowest among patients aged ≥75 years, and those with HF, estimated glomerular filtration rate (eGFR) <60 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$, and newly diagnosed AF (P <0.001 for all).

Factors associated with OAC use at discharge

Among AF patients with high risk of stroke, in-hospital catheter ablation, electronic cardioversion, AADs use, persistent AF, tertiary hospital or a medical history of PAD, previous stroke/TIA, hypertension, or DM was associated with significantly higher odds of OAC prescription at discharge [Table 2]. Conversely, age ≥75 years, a medical history of HF, long-standing or permanent AF, or concomitance with antiplatelets at discharge were associated with lower OAC prescriptions at discharge (all P <0.001). Among AF patients with low risk of stroke, in-hospital catheter ablation, AADs use, persistent AF, and tertiary hospital were associated with significantly higher odds of OAC prescription (all P <0.001) [Supplementary Table 6, http://links.lww.com/CM9/B788]. Conversely, the phenomenon of concomitant antiplatelets at discharge was associated with lower OAC prescription (P <0.001).

Contraindications to OAC in patients with high stoke risk

Among patients with high risk of stroke who did not take OAC at discharge, 5.2% (1116/21,446) had a strict contraindication to OAC. In contrast, 55.9% (11,993/21,446 of the patients had some or any documented contraindication at discharge). The three most common documented contraindications were patient refusal (30.7%, 4319/14,086), unable to adhere/monitor (19.1%, 2696/14,086), and physician preference (15.8%, 2223/14,086). The proportion of patients unable to adhere/monitor decreased over time from 29.8% (573/1921) in 2015 to 13.5% (563/4185) in 2019. In 2019, among the total population of patients characterized by an absence of monitoring/adherence, the proportions with patient refusals and physician preference listed as their only reason for contraindication were, respectively, 25.7% (1017/3953) and 21.9% (866/3953) [Supplementary Table 7, http://links.lww.com/CM9/B788].

Discussion

In an analysis of over 53,000 patients with non-valvular AF in the CCC-AF project, our principal findings are as follows: First, patients at high risk of stroke in this Chinese AF population were 72.7% (38,203/52,530). Second, the

Table 2: Multivariate analysis of factors associated with OAC use at discharge in AF patients with high risk of stroke and without strict contraindications to OAC.

Variables	Adjusted OR (95% CI)	*P* values
Age		
<65 years	Reference	
65–74 years	0.94 (0.86–1.02)	0.151
≥75 years	0.59 (0.54–0.64)	<0.001
Ethnicity		
Non-Han	Reference	
Han	1.23 (1.03–1.47)	0.026
Hospital level		
Secondary hospital	Reference	
Tertiary hospital	1.54 (1.43–1.66)	<0.001
AF type		
Newly diagnosed	Reference	
Paroxysmal	0.98 (0.91–1.05)	0.503
Persistent	1.30 (1.20–1.41)	<0.001
Long-standing persistent/ permanent	0.79 (0.73–0.87)	<0.001
Medical history*		
Hypertension	1.22 (1.16–1.29)	<0.001
DM	1.15 (1.07–1.22)	<0.001
Stroke or TIA	1.24 (1.16–1.33)	<0.001
PAD	1.74 (1.45–2.08)	<0.001
HF	0.84 (0.78–0.90)	<0.001
Previous bleeding	0.62 (0.51–0.75)	<0.001
In-hospital treatment†		
Catheter ablation	11.63 (10.04–13.47)	<0.001
Electronic cardioversion	2.41 (1.65–3.51)	<0.001
AADs use	1.45 (1.38–1.53)	<0.001
Antiplatelet use at discharge	0.08 (0.08–0.09)	<0.001

*The reference group for medical history of hypertension, DM, stroke or TIA, PAD, HF, and previous bleeding comprised patients without a medical history of hypertension, DM, stroke or TIA, PAD, HF, and previous bleeding. †The reference group for in-hospital treatment of catheter ablation or electronic cardioversion comprised patients without an in-hospital treatment of catheter ablation or electronic cardioversion. Variables in multivariate analysis included age, sex, hospital levels, AF types, medical insurance, smoking, drinking, medical history of hypertension, DM, stroke or TIA, PAD, HF, CAD, previous bleeding, COPD, chronic renal disease, prior treatment including catheter ablation, surgical ablation, AADs use, electronic cardioversion, prior concomitance with antiplatelet use, in-hospital OAC use and in-hospital catheter ablation, surgical ablation, AADs use, electronic cardioversion, and antiplatelet use at discharge. AADs: Antiarrhythmic drugs; AF: Atrial fibrillation; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; DM: Diabetes mellitus; HF: Heart failure; OAC: Oral anticoagulation; OR: Odds ratio; PAD: Peripheral arterial disease; TIA: Transient ischemic attack.

OAC prescribing rate on admission or at discharge both increased over time, although poor performance on guideline adherence to OAC was evident. Third, OAC use was independently associated with in-hospital catheter ablation, electronic cardioversion, or AADs use. Finally, analysis of documented contraindications showed that patients and physicians needed to be targeted for stroke prevention.

Using the data from CCC-AF project, the largest and most extensive AF registry in China to date, we found that the proportion of hospitalized AF patients with high risk of stroke in the Chinese AF population at discharge was 72.7%. This proportion was comparable to the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation Treatment (ORBIT-AF) registry and the Get with the Guidelines–Atrial Fibrillation (GWTG-AF) registry, in which 72% of 10,094 AF patients in the ORBIT-AF study and 86.7% of 38,358 patients in GWTG-AFIB registry were at a high risk (≥2).[29,30]

OAC treatment was previously underutilized worldwide,[31] but this changed recently. In the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Pilot Survey, 80.5% of European AF patients with CHA_2DS_2-VASc scores ≥1 received OAC therapy.[32] In the GWTG-AFIB registry, more than 95% of patients with CHA_2DS_2-VASc scores >2 received OAC.[19] Overall, the use of OAC in the Chinese AF population remains relatively low.[15,19,27] In the China National Stroke Registry II, between 2012 and 2013, only 19.4% of acute ischemic stroke patients were taking warfarin at discharge.[33] In the Chinese Atrial Fibrillation Registry study, 36.5% of 11,496 non-valvular AF patients with CHA_2DS_2-VASc scores >2 reported the use of OACs.[18] More recently, in the Optimal Thromboprophylaxis in Elderly Chinese Patients with Atrial Fibrillation (ChiOTEAF) registry, which was conducted between October 2014 and December 2018, the overall use of OAC was low, at approximately 38% of the entire cohort at 1-year follow-up.[22]

Interestingly, in this study, we found a relatively lower proportion (45.2%) of OAC prescriptions at discharge in patients with high risk of stroke but a relatively higher rate (60.7%) of OAC prescriptions in patients with low risk of stroke. The latter finding was also reported in the EORP-AF Pilot General Registry.[34] In the present study, one possible explanation would be that a large proportion of patients, especially patients with low risk of stroke, underwent catheter ablation and cardioversion during hospitalization and thus improved OAC prescription at discharge; second, AF patients with low risk of stroke had fewer co-morbidities, thus encouraging clinicians to be less concerned about OAC-related complications. Actually, the risk of stroke/thrombo-embolism is low (<1%) in the low-risk population and overtreating with OAC in AF patients with low risk of stroke was associated with increased risk of adverse outcomes, particularly with increased bleeding.[35–37] Guidelines clearly state that AF patients at "low risk of stroke" should not be offered OAC therapy. Either inadequate treatment or overtreatment in adherence to guidelines are associated with poor outcomes.[32,38] Thus, more attention should, in future studies, be focused on the issue of both under- and over-treatment with OAC.

Furthermore, consistent with previous studies,[18] the OAC prescription rates for AF patients varied widely among hospitals in China. For example, the OAC prescription rate for patients at risk for high stroke is as low as 3% in some tertiary hospitals and as high as 98% in some other tertiary hospitals. These findings highlighted areas for improvement in current stroke prevention in China.

Although these data collectively indicate a poor guideline adherence in stroke prevention, the CCC-AF project has made progress in the treatment for stroke prevention among the Chinese AF population. First, compared to the data reported in previous Chinese studies,[18,22,33] the OAC prescribing rate in our study increased largely, reaching 45.2% after excluding only strict contraindications, even 64.0% after excluding documented contraindications. Considering the large size of the AF population in China, even a small increase in the OAC prescribing rate would translate into a major benefit in stroke prevention. Second, with the continued intervention, we can see a significant increase in OAC prescription rates over time, either at discharge or admission. Third, a substantial association was observed between pre-hospital OAC usage and in-hospital new-onset ischemic stroke or TIA, despite the fact that only 20.0% of patients with a high risk of stroke had OAC on admission. Finally, in analysis among special populations, high guideline recommended OAC utilization was achievable, as high as 95% in patients who underwent catheter ablation, representing an important part of the quality improvement in the CCC-AF project.

In the multivariate analysis, we found that OAC use was more likely to be prescribed in patients underwent rhythm control strategy, such as catheter ablation, electronic cardioversion, or AADs use. Two explanations may account for this finding: patients under rhythm control strategies in the hospital are more likely to be followed up for rhythm status and outcome events, thus inadvertently increasing the use of OAC for stroke prevention; and the physicians administering rhythm control strategy for patients are more likely to be cardiologists or even arrhythmia specialists and thus more focused on stroke prevention.

Previous research revealed the possible reasons for the poor OAC utilization in China: unable to adhere to OAC, a large number of patients attending outpatient clinics limits the time organizing education and monitoring of anticoagulation in patients with atrial fibrillation, and patients' financial status.[8,18,36,39,40] However, in analysis of documented contraindications in our study, the rates of non-adherence to OAC decreased significantly over time, possibly owing to the circumstance that the increased NOACs usage improved the adherence to OAC.[8] Considering the high prescribing OAC rate in low risk of stroke patients, it was unreasonable to attribute the poor guideline adherence to the economic factors and heavy outpatient workload. More importantly, documented contraindications were common but subjective. For patients who reported contraindications, the benefits of receiving OAC treatment outweigh the potential harms.[41] Indeed, strict contraindications accounted for only 5.3% of those not taking OAC in the high risk of stroke population, compared with 55.3% of documented contraindications in our study, suggesting substantial room for future improvement in stroke prevention. More specifically, physician preference and patient refusal accounted for the high proportions of patients who did not take OAC. Clearly, physicians and patients are two primary target populations for improving stroke prevention in the future.

Our study had some potential limitations. First, participation in the study was voluntary, which may lead to selection bias. Consequently, the results of this study may not present characteristics of hospitals that did not participate in this study. However, hospitals in the CCC-AF project were recruited by geographic and economic regions and represented the diversity of AF care in hospitals across China. Second, since clinical information was abstracted from inpatient records, the quality of documentation had a potential impact on the present study. Third, although we did adjust for many of the significant factors and use sensitivity analysis to explore the "true" association, residual confounding effects may exist.

In conclusion, in hospitals participating in the CCC-AF quality improvement program, >70% of AF patients were at high risk of stroke. Although poor performance on guideline adherence to OAC use was found in this study, the CCC-AF project made substantial progress in the use of stroke prevention therapies in the Chinese AF population.

Acknowledgements

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Conflicts of interest

The CCC-AF project is a collaborative project of the American Heart Association and the Chinese Society of Cardiology. The American Heart Association received funding from Pfizer through an independent grant for learning and change and AstraZeneca as a quality improvement initiative. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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Corrigendum

Corrigendum: Role of glutamine in the mediation of E-cadherin, p120-catenin and inflammation in ventilator-induced lung injury

Following the original article's publication,[1] the authors informed us of the following errors. The third panel (c) in Figure 2 and the sham panel in Figure 7 are incorrect. The corrected Figures are shown below. The errors do not affect the results and conclusions of the article. The authors sincerely apologize for the errors.

Reference

1. Qiu JL, Song BL, Wang YJ, Zhang FT, Wang YL. Role of glutamine in the mediation of E-cadherin, p120-catenin and inflammation in ventilator-induced lung injury. Chin Med J 2018;131:804-812. doi: 10.4103/0366-6999.228230.

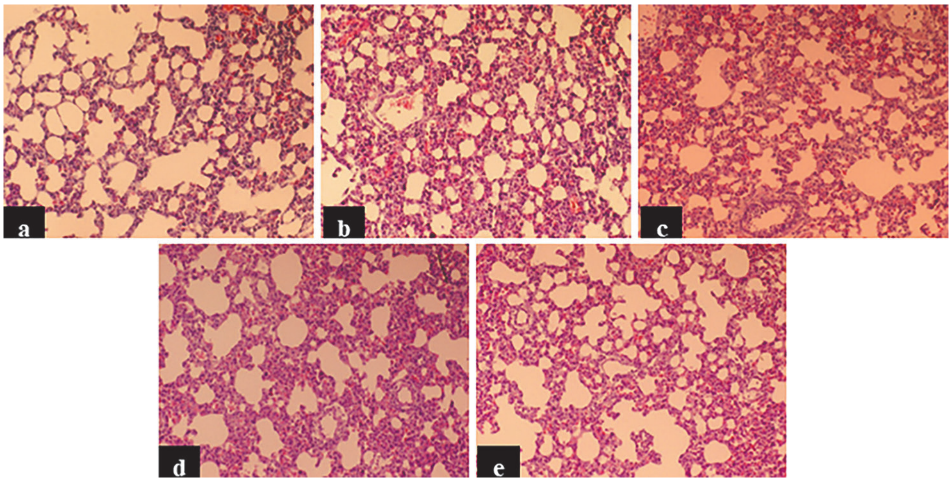

Figure 2:

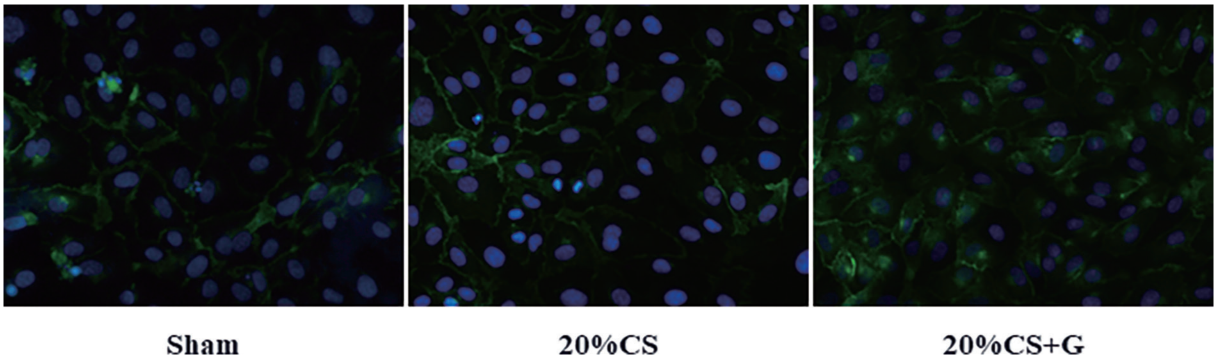

Figure 7: