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Long-Term Persistence with Newly-Initiated Warfarin or Non-VKA Oral Anticoagulant (NOAC) in Patients with Non-Valvular Atrial Fibrillation: Insights from the Prospective China-AF Registry

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Background: Oral anticoagulants (OACs) such as warfarin and non-VKA oral anticoagulants (NOACs) have been recommended for patients with atrial fibrillation (AF) who are at risk for stroke. Whether NOACs have a higher persistence than warfarin is still unclear. This is especially true in China.

Material/Methods: Data from a large hospital-based cohort in China (China-AF Registry) from 2011 to 2017 were used for this study. Non-valvular AF patients with newly initiated OACs were included. A time-to-event approach was used to analyze patient persistence. The survival distributions of persistence were compared using the log-rank test. A multivariable Cox regression model was used to explore predictors of warfarin and NOACs non-persistence.

Results: Patients with newly initiated warfarin (n=4845) or NOACs (n=854) were included in this study. Persistence rates at 1, 2, and 3 years were 93.2%, 89.4%, and 87.2% in the warfarin group and 88.8%, 84.3%, and 81.3% in the NOAC group respectively. Non-persistence was significantly higher with NOACs than with warfarin. On multivariate analysis, age <75 years old, outpatient clinic visits, asymptomatic AF, paroxysmal AF, duration of AF <3 years, history of peptic ulcer, and no previous TIA, stroke or thromboembolism were strong predictors of warfarin non-persistence, while in the NOACs group, age <75 years old, outpatient clinic visits, lower education status and no history of congestive heart failure were predictors.

Conclusions: Treatment persistence of NOACs was lower than that of warfarin among Chinese patients with AF. Patients with characteristics of non-persistence predictors need special attention to maintain their therapy.

MeSH Keywords: Anticoagulants • Atrial Fibrillation • Medication Adherence

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Background

Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide and is an important risk factor for ischemic stroke, and it is associated with high mortality and morbidity, and considerable medical costs [1]. Therefore, stroke prevention is central to the management of AF. Oral anticoagulants (OACs) decrease the risk of thromboembolic events and mortality in AF patients and are recommended for all AF patients at risk of stroke [2].

Optimal stroke prevention with OACs in AF patients depends on medication adherence, defined as the accurate intake of medications based on the dose, frequency, and schedule prescribed [3]. Medication persistence to OACs, defined as the duration of time from the initiation to discontinuation of therapy, is also widely adopted metrics to evaluate medical therapy [4]. Non-persistence to OACs is a major obstacle to stroke prevention in AF [5–7].

The OACs include vitamin K antagonists (VKAs) such as warfarin, and non-VKA oral anticoagulants (NOACs) such as dabigatran, rivaroxaban, apixaban, and edoxaban. The most commonly used NOACs in China are dabigatran and rivaroxaban. Before NOACs were introduced, VKA warfarin was the standard anticoagulant therapy for patients with AF [8–10]. NOACs have been shown to be non-inferior to warfarin in terms of efficacy in stroke prevention, with a lower risk of major bleeding, with even better efficacy and safety in Asians compared to non-Asians [11]. NOACs also have the advantage of not needing routine monitoring and dose-adjustment, due to limited food-drug and drug-drug interactions. While some studies have shown that patients taking NOACs generally have higher persistence than patients taking VKAs [12], other studies have shown the opposite [13,14]. No treatment persistence data exist in Chinese AF populations.

The purpose of this study was to investigate and compare therapeutic persistence of warfarin and NOACs and explore factors associated with non-persistence to warfarin and NOACs therapy in Chinese AF patients, using data of a large, prospective hospital-based registry cohort, the China AF Registry.

Material and Methods

Study population and data collection

The China-AF Registry enrolled AF patients in routine clinical practice from 31 tertiary and non-tertiary hospitals in Beijing [15]. Eligible patients were recruited from outpatient clinics and in-hospital wards and all patients signed informed consent to participate. From August 2011 to December 2017,

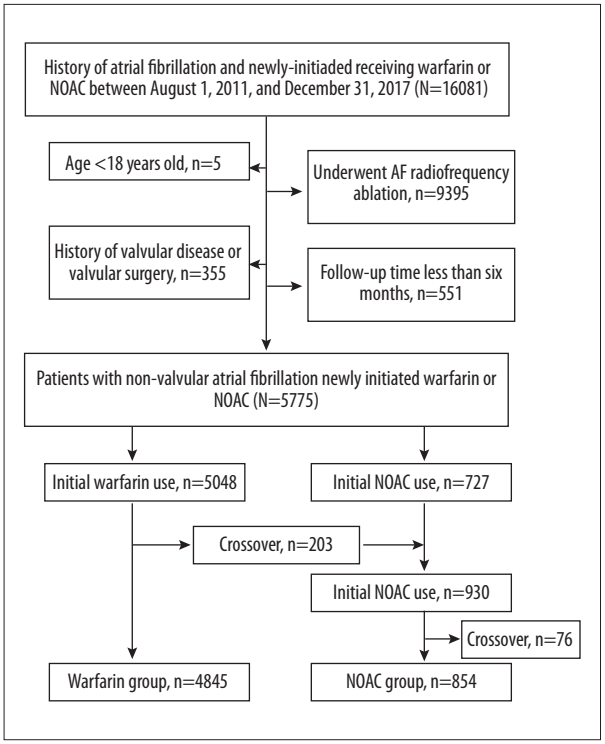

Figure 1. Patients selection flowchart.

a total of 19 515 AF patients were recruited. Information on baseline characteristics included age, gender, body mass index (BMI), smoking status, alcohol consumption, education status, health insurance coverage, AF type, history of congestive heart failure, hypertension, diabetes, previous stroke/transient ischemic attack (TIA)/thromboembolism, prior bleeding events, peptic ulcer, use of antiplatelet drugs, CHA_2DS_2-VASc score, and duration of AF were recorded upon patient enrolment.

The CHA_2DS_2-VASc score [16] was calculated by assigning 1 point for age between 65 and 74 years, a history of hypertension, diabetes, congestive heart failure, vascular disease, and female sex and 2 points for a history of stroke/TIA/thromboembolism and age ≥75 years. All definitions were consistent with the American College of Cardiology/American Heart Association recommendations for establishing an AF database [17].

A flowchart of patient-selection for the current analysis is shown in Figure 1. New initiation was defined as no OACs usage at the last time of follow-up while reported to be on the OAC therapy at the index follow-up. Exclusion criteria were as follows: age <18 years; follow-up time <6 months; with valvular AF (presence of mitral stenosis or mechanical valve implantation); and those undergoing AF radiofrequency ablation.

Patients were categorized into a warfarin group and a NOACs group depending on the initial OACs. Patients who initiated warfarin and then switched to NOACs during follow-up were

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allocated into the NOACs group and the initiation time was calculated from the time of switching. Patients who initiated NOAC and switched to warfarin during follow-up were excluded from the analysis as the number of these patients was small and therefore the impact would be minimal. Finally, 5699 patients (4845 in the warfarin group and 854 in the NOACs group) were included.

Each patient was followed through outpatient interview or telephone interview by trained nurse practitioners every 6 months after enrollment during a follow-up period of 3 years as NOACs were available in China 3 years ago. At follow-up intervals, medical conditions, serious adverse events (including bleeding complications), adverse drug reactions, and the date of discontinuation of warfarin or NOACs were recorded. All data were entered into an electronic data collection platform.

Ethics

The project has been reviewed by the Beijing Anzhen Hospital Ethics Committee (No: D11110700300000) on June 10, 2011.

Definitions

Therapy persistence was defined as the duration of time from initiation to discontinuation of therapy. Initiation of therapy was defined as the index date for the first dose of the drug. Discontinuation was determined by self-reported cessation of warfarin or NOAC therapy during follow-up. Non-persistence was the cumulative incidence, which was evaluated by a Kaplan-Meier time-to-event analysis for each medication separately [9,18].

Meta-analysis

A meta-analysis was performed to compare the persistence rate between NOACs and warfarin. Systematic searches were conducted in Medline, Embase, and Cochrane using terms such as warfarin, dabigatran, rivaroxaban, apixaban, non-VKA oral anticoagulants, non-valvular atrial fibrillation, and persistence. Research studies containing persistence rate data of both NOACs and warfarin were included. Target study designs included randomized clinical trials, prospective cohorts, and retrospective analysis. Studies in which time of follow-up was <6 months and group participants <200 were excluded.

Quality of the data was analyzed. Data of persistence rates and the total number of participants were extracted for meta-analysis. To minimize heterogeneity of different studies, the time point of follow-up at about 1 year in each study was selected for data extracted. Heterogeneity between studies was assessed using I-squared and the *P*-value of the Cochrane Q test. Random effects model was used according to the heterogeneity between studies. Analyses were conducted using Revman 5.3. Meta-analysis results are presented as Relative Risk (RR) with its 95% confidence interval (CI).

Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD), and categorical variables were presented as raw numbers and percentages. A time-to-event approach was used to analyze patient persistence to warfarin or NOACs respectively. The survival distributions of persistence between the warfarin group and the NOACs group were compared using the log-rank test. Cox proportional hazards regression models were carried out to determine the association between OAC categories (warfarin or NOAC) and non-persistence, with adjustment for age, gender, education status, type of AF, comorbid diseases, and medications (all covariates with $P<0.2$ in the univariate models). For the analysis of predictors of warfarin and NOACs non-persistence, Cox proportional hazards regression was conducted. Variables that showed significant association on univariate analysis and of clinical importance were adjusted using multivariate Cox regression. These factors included age, gender, BMI, education status, health insurance coverage, outpatient clinic visit within 6 months before the last follow-up, paroxysmal or persistent AF, duration of AF< or ≥3 years, as well as those with or without previous TIA, stroke or thromboembolism, congestive heart failure, hypertension, diabetes, prior bleeding, peptic ulcer, or use of antiplatelet drugs. Multiple imputation methods were used to calculate the missing covariate data in Cox proportional hazard regression analysis.

All *P*-values tests were 2-tailed and *P*-values <0.05 was considered statistically significant. All analyses were conducted using SAS statistical software version 9.4 (SAS Institute Inc, Cary, NC, USA).

Results

Patients characteristics

The mean age of the 4845 patients in the warfarin group was 67.9±10.2, similar to that of the 854 patients in the NOACs group (68.3±11.4). Compared to patients in the NOACs group, patients in the warfarin group were less likely to be male (56.7% versus 60.9%), older than 75 years of age (29.1% versus 34.8%), have paroxysmal AF (44.7% versus 51.8%), have a high level of education (29.4% versus 49.3%), while a higher proportion of patients had congestive heart failure (19.1% versus 11.9%) and CHA_2DS_2-VASc score ≥2 (85.8% versus 83.0%) (Table 1).

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Table 1. Baseline characteristics.

	All N = 5699	Warfarin N = 4845	NOAC N = 854
Male, n/N (%)	3265/5699 (57.3)	2745/4845 (56.7)	520/854 (60.9)
Age, years	67.9±10.4	67.9±10.2	68.3±11.4
age ≥75 years, n/N (%)	1706/5699 (29.9)	1409/4845 (29.1)	297/854 (34.8)
BMI, kg/m^2	25.6±3.7	25.6±3.7	25.6±3.8
Drinking, n/N (%)	974/5641 (17.3)	829/4804 (17.3)	145/837 (17.3)
Smoking, n/N (%)	752/5615 (13.3)	654/4807 (13.6)	98/838 (11.7)
Completed high school, n/N (%)	1680/5170 (32.5)	1286/4371 (29.4)	394/799 (49.3)
All health insurance covered, n/N (%)	657/5634 (11.7)	541/4829 (11.2)	116/805 (14.4)
Paroxysmal AF, n/N (%)	2604/5691 (45.8)	2164/4841 (44.7)	440/850 (51.8)
Congestive heart failure, n/N (%)	1028/5699 (18.0)	926/4845 (19.1)	102/854 (11.9)
Hypertension, n/N (%)	4228/5697 (74.2)	3599/4845 (74.3)	629/852 (73.8)
Diabetes, n/N (%)	1498/5698 (26.3)	1287/4845 (26.6)	211/853 (24.7)
Stroke/TIA/Thromboembolism, n/N (%)	1266/5694 (22.2)	1096/4842 (22.6)	170/852 (20.0)
Major bleeding, n/N (%)	310/5693 (5.5)	249/4842 (4.1)	61/851 (7.2)
CHA_2DS_2-VASc risk score ≥2, n/N (%)	4637/5431 (85.4)	3972/4630 (85.8)	665/801 (83.0)
Symptomatic AF, n/N (%)	2105/5699 (36.9)	1794/4845 (37.0)	311/854 (36.4)
Peptic ulcer, n/N (%)	179/5699 (3.1)	130/4845 (2.7)	49/854 (5.7)
Duration of AF, years	4.5±6.5	4.6±6.6	3.9±5.9
Use of antiplatelet drugs, n/N (%)	3498/5699 (61.4)	2947/4845 (60.8)	551/854 (64.5)
Number of drugs used	1.9±1.4	1.9±1.5	1.8±1.4

AF – indicates atrial fibrillation; SD – standard deviation; BMI – body mass index; TIA – transient ischemic attack.

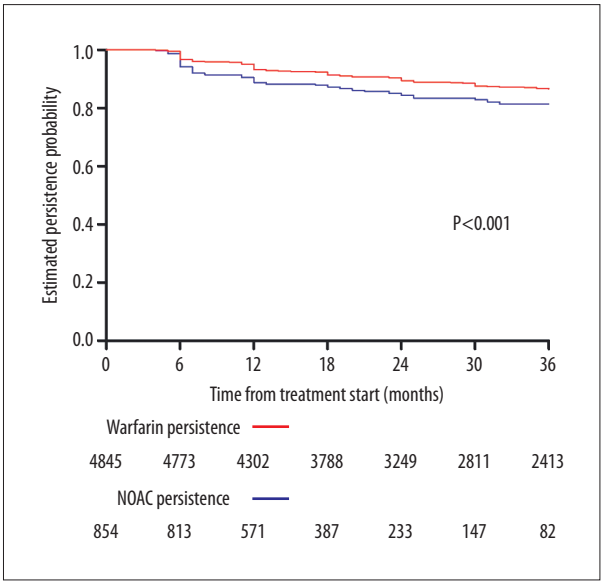

Figure 2. Therapy persistence with warfarin and NOAC: Kaplan-Meier curve of time to treatment discontinuation over 3 years. The persistence rates at 1, 2, and 3 years were 93.2%, 89.4%, and 87.2% in the warfarin group and 88.8%, 84.3%, and 81.3% in the NOAC group, respectively. Warfarin persistence was significantly higher than that of NOAC using the log-lank test (*P*<0.001).

Treatment persistence and persistence rates

Persistence rates at 1, 2, and 3 years were 93.2%, 89.4%, and 87.2% in the warfarin group and 88.8%, 84.3%, and 81.3% in the NOACs group respectively (Figure 2). The treatment persistence was significantly higher for warfarin than for NOACs (*P*<0.001). Patients in the NOACs group were more likely to be non-persistent than those in the warfarin group [hazard ratio (HR) for NOACs, 1.63; 95%CI: 1.31–2.02; *P*<0.001].

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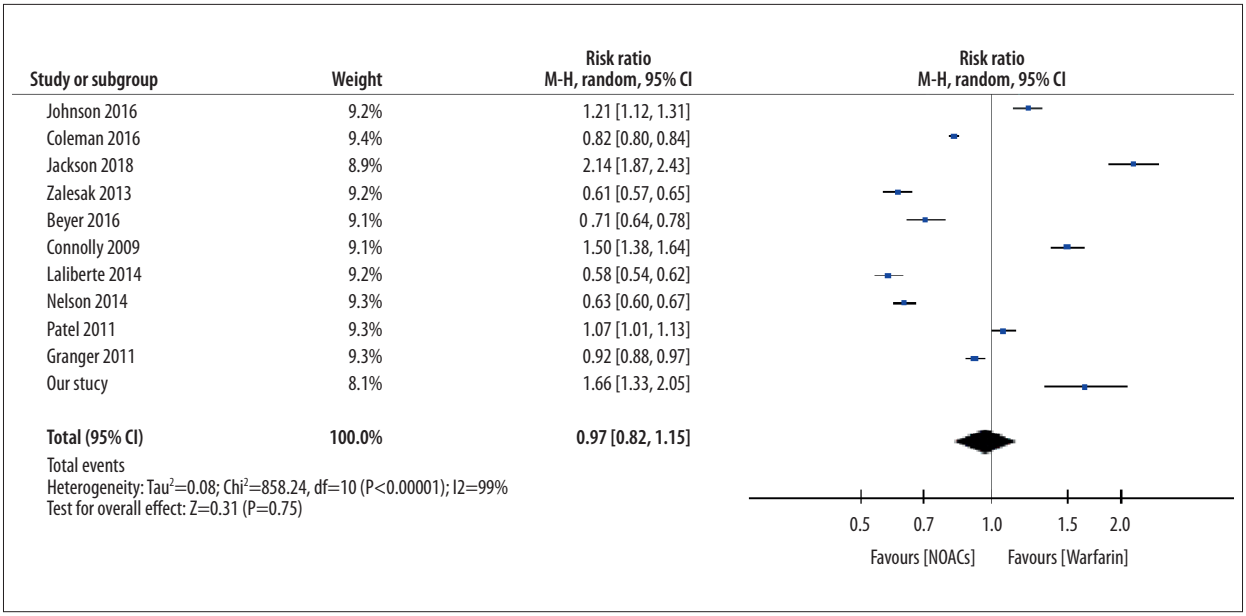

Figure 3. Meta-analysis results of non-persistence risk for NOACs versus warfarin.

Of the 105 patients who discontinued NOACs, 14 patients (13.3%) stopped because of bleeding complications. Of the 538 patients who discontinued warfarin, 50 patients (9.29%) stopped because of bleeding complications. The proportions of patients who stopped OACs due to bleeding events were not different between the 2 groups (*P*=0.206).

Meta-analysis of non-persistence risk of NOACs compared with warfarin

To summarize and review the literature about persistence comparison between NOACs and warfarin, we sought to conduct a meta-analysis. A total of 11 studies were included finally [9,13,19–26]. The outcomes showed that there was no significant difference of non-persistence risk between NOACs and warfarin (RR: 0.97, 95%CI: 0.82–1.15) (Figure 3).

Predictors of treatment non-persistence

Factors associated with higher risk of warfarin non-persistence include outpatient clinic visit within 6 months before OACs termination [HR 3.78 (3.16–4.52)], paroxysmal AF [HR 2.37 (1.67–3.37)], duration of AF less than 3 years [HR 1.27 (1.07–1.52)], and history of peptic ulcer [HR 1.65 (1.09–2.51)]. Patients older than 75 years of age [HR 0.53 (0.35–0.79)], symptomatic AF [HR 0.81 (0.67–0.97)], previous TIA, stroke or thromboembolism [HR 0.67 (0.53–0.84)] were associated with lower risk of non-persistence (Table 2).

In the NOACs group, patients with higher risk of non-persistence were associated with factors including outpatient clinic visit within 6 months before OACs termination [HR 3.93 (2.49–6.19)] and lower education status [HR 1.56 (1.03–2.38)] while patients older than 75 years of age [HR 0.55 (0.34–0.88)] and history of congestive heart failure [HR 0.46 (0.22–0.96)] were associated with lower risk of non-persistence (Table 2).

Factors such as education status and no history of congestive heart failure were associated with non-persistence only in the NOACs group. While factors such as paroxysmal AF, asymptomatic AF, duration of AF less than 3 years, history of peptic ulcer, and no previous TIA, stroke or thromboembolism were associated with warfarin non-persistence, they had no significant difference with regard to NOACs persistence.

Discussion

To the best of our knowledge, this study is the first to investigate long-term persistence and factors associated with discontinuation in newly-initiated OAC patients with non-valvular AF in China. The most notable finding of our study was that the OAC treatment persistence was significantly higher for warfarin than for NOACs in China, which is generally counter-intuitive to our perceptions, based on data in non-Asian cohorts. Previous studies had proposed the need for structured educational programs to improve the persistence of OAC [27]. Our study suggests that warfarin and NOACs may have different risk factors for treatment non-persistence, and therefore, different strategies need to be developed to address different issues affecting their treatment persistence.

Medical non-persistence is associated with adverse outcomes, and this will result in more healthcare costs [3]. Non-persistence

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Table 2. Main predictors of warfarin and NOAC non-persistence.

	Warfarin			NOAC		
	N = 538	HR (95% CI)	P	N = 105	HR (95% CI)	P
Age class						
<75 years	390/3436 (11.35)	Ref.	0.002	78/557 (14.00)	Ref.	0.014
≥75 years	148/1409 (10.50)	0.53 (0.35–0.79)		27/297 (9.09)	0.55 (0.34–0.88)	
Sex						
Male	286/2745 (10.42)	Ref.	0.343	65/520 (12.50)	Ref.	0.295
Female	252/2100 (12.00)	1.09 (0.91–1.30)		40/334 (11.98)	0.80 (0.53–1.22)	
BMI, kg/m^2						
<28	389/3548 (10.96)	Ref.	0.361	84/653 (12.86)	Ref.	0.413
≥28	124/1005 (12.34)	1.10 (0.89–1.36)		20/177 (11.30)	0.81 (0.49–1.34)	
Education status						
High	146/1286 (11.35)	Ref.	0.806	42/394 (10.66)	Ref.	0.034
Low	344/3085 (11.15)	0.97 (0.79–1.19)		59/405 (14.57)	1.56 (1.03–2.38)	
Health insurance coverage						
Partially or none	479/4288 (11.17)	0.93 (0.70–1.23)	0.594	84/689 (12.19)	Ref.	0.393
All covered	58/541(10.72)	Ref.		15/116 (12.93)	1.29 (0.72–2.33)	
Outpatient clinic visit*						
Yes	241/1009 (23.88)	3.78 (3.16–4.52)	<0.001	34/130 (26.15)	3.93 (2.49–6.19)	<0.001
No	297/3836 (7.74)	Ref.		71/724 (9.81)	Ref.	
Type of AF						
Paroxysmal AF	273/2164 (12.62)	2.37 (1.67–3.37)	<0.001	60/440 (13.64)	1.21 (0.81–1.80)	0.360
Persistent or Permanent AF	264/2677 (9.86)	Ref.		44/410 (10.73)	Ref.	
Categorization of AF						
Symptomatic	209/1794 (11.65)	0.81 (0.67–0.97)	0.022	43/310 (13.87)	1.04 (0.68–1.58)	0.858
Asymptomatic	329/3051 (10.78)	Ref.		62/544 (11.40)	Ref.	
Duration of AF <3 years						
Yes	335/2790 (12.01)	1.27 (1.07–1.52)	0.008	73/555 (13.15)	1.38 (0.90–2.11)	0.144
No	203/2055 (9.88)	Ref.		32/299 (10.70)	Ref.	
Previous TIA/stroke/thromboembolism						
Yes	91/1096 (8.30)	0.67 (0.53–0.84)	0.001	18/170 (10.59)	0.85 (0.50–1.44)	0.536
No	446/3746 (11.91)	Ref.		87/682 (12.76)	Ref.	
Congestive heart failure						
Yes	91/926 (9.83)	0.83 (0.66–1.04)	0.112	8/102 (7.84)	0.46 (0.22–0.96)	0.038
No	447/3919 (11.41)	Ref.		97/752 (12.90)	Ref.	
Either hypertension or diabetes						
Yes	432/3827 (11.29)	0.70 (0.46–1.08)	0.107	78/664 (11.75)	0.87 (0.54–1.40)	0.564
No	106/1018 (10.41)	Ref.		27/189 (14.28)	Ref.	

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Table 2 continued. Main predictors of warfarin and NOAC non-persistence.

	Warfarin			NOAC		
	N = 538	HR (95% CI)	P	N = 105	HR (95% CI)	P
Prior bleeding						
Yes	28/249 (11.24)	1.04 (0.71–1.52)	0.853	11/61 (18.03)	1.55 (0.81–2.97)	0.186
No	509/4593 (11.08)	Ref.		94/790 (11.90)	Ref.	
Peptic ulcer						
Yes	23/130 (17.69)	1.65 (1.09–2.51)	0.019	4/49 (8.16)	0.55 (0.20–1.51)	0.244
No	515/4715 (10.92)	Ref.		101/805(12.54)	Ref.	
Use of antiplatelet drugs						
Yes	349/2947 (11.84)	1.15 (0.96–1.39)	0.124	70/555 (12.61)	0.78 (0.51–1.19)	0.245
No	189/1898 (9.96)	Ref.		35/299 (11.70)	Ref.	
Number of drugs used*						
≥3	214/1642 (13.03)	1.02 (0.84–1.23)	0.859	36/274 (13.14)	0.93 (0.59–1.47)	0.768
<3	324/3203 (10.11)	Ref.		69/580 (11.89)	Ref.	

CI – indicates confidence interval; HR – hazard ratio; BMI – body mass index; TIA – transient ischemic attack. * Within 6 months before following up termination.

of OAC increases the risk of ischemic stroke in AF patients [28]. Indeed, warfarin persistence has been well-documented in previous studies, and the non-persistence rates at 1 year ranged from 22% to 33% [13,29,30]. A previous study described warfarin discontinuation rates at 1 year and 2 years as 44.4% and 57.6% in China [31], which were much higher than rates in the present study; this might be because the population selected included patients who underwent AF radiofrequency ablation and these patients might stop OACs after restoring sinus rhythm.

Other recent studies have described the persistence rates for NOAC at 1 year ranging from 63% to 79% [22,28,32]. In our study, treatment persistence rates were relatively higher than those studies. This could possibly be explained by the differences in terms of patient populations, study designs, and definitions of persistence. Comparing persistence rates across studies is difficult, even those focused on the same OAC.

Persistence comparisons between NOAC and warfarin remain controversial. The majority of previous data published showed that patients taking NOACs had better persistence compared with VKAs [12]. However, other studies showed the opposite results. In the RE-LYs trial, warfarin had higher 2-year persistence rates compared with dabigatran 110 mg (83.4% versus 79.3%) [22]. Observational studies have generally been consistent. For example, a recent study enrolled 7150 American AF patients treated with warfarin [N=6691 (93.6%)] and dabigatran [N=459 (6.4%)] between June 29, 2010 and August 09, 2011, and defined non-persistence as discontinuing dabigatran or warfarin at 6 months or 1 year for any reason, and showed lower persistence of dabigatran versus warfarin at 1 year, with persistence rates 66% versus 82% [13]. In Japan, Shiga et al. retrospectively studied 401 Japanese patients with NVAF who had newly started NOACs and 200 patients with NVAF who had newly started warfarin during the same period; persistence rates of patients prescribed NOACs were consistently lower than those of patients prescribed warfarin at 3, 6, and 12 months (85% versus 93%, 79% versus 88%, and 70% versus 82% respectively) [14].

Our results are therefore in line with these studies, showing a lower persistence for NOACs than for warfarin. The lower persistence rate of NOACs in our study might be explained by the higher incidence of adverse events including dyspepsia and hepatobiliary disorders of NOACs compared with warfarin [22], as well as high price and non-coverage by health insurance of NOACs in China. Indeed, high costs of medications often contribute to non-persistence [33]. Some studies showed a significant difference of non-persistence risk between NOACs and warfarin. However, the meta-analysis did not show a significant difference between them. This might be due to the heterogeneity between studies. Further research studies should be undertaken to delineate the comparison of persistence rate by subgroups.

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We subsequently identified several clinical factors significantly associated with warfarin discontinuation. Patients older than 75 years of age were less likely to discontinue warfarin. Prior studies also found older patients were more likely to be persistence [34–36]. Older patients are at high risk of stroke, and they might contact healthcare professionals more frequently and are supervised more strictly. It was interesting that patients who had been to outpatient clinic within 6 months before OACs termination were more likely to be non-persistence. Outpatient clinic visits were commonly associated with adverse drug reactions. These patients might stop warfarin due to serious side effects such as intracranial hemorrhage and gastrointestinal bleeding [37]. Patients with a history of peptic ulcer also had a lower likelihood of persistence in the warfarin group. Bleeding risk will be higher for those with a history of peptic ulcer when treated by warfarin [38]. This risk worries the patients and doctors which might be reflected by a lower treatment persistence for warfarin.

Other predictors for the persistence of warfarin therapy included symptomatic AF, persistent or permanent AF, duration of AF ≥3 years, history of peptic ulcer, and previous TIA, stroke or thromboembolism. These factors primarily either reflected the severity of the AF or were associated with a higher risk of stroke [39,40]. Clinicians and the patients might thus pay more attention to the anticoagulation therapy and be less likely to discontinue the medication. Furthermore, patients who experienced a previous TIA, stroke or thromboembolism, or who have been suffering AF for a long period might be more likely to take care of their condition and to continue their anticoagulation therapy. However, we did not find these factors associated with NOACs persistence in our study.

Patients older than 75 years of age or who had been to an outpatient clinic within 6 months before OACs termination had similar effects on NOAC persistence and warfarin. Possible explanations might also be similar. Patients with a history of congestive heart failure were associated with higher persistence only for NOACs, possibly because heart failure patients are generally followed by cardiologists, who appreciate the importance of anticoagulation better than other specialists. Low educated status was associated with non-persistence for NOACs but not for warfarin, perhaps reflecting that social economic status and affordability of the medicine is important for therapeutic persistence.

Limitations

This study had several limitations that should be considered. First, the patients in our study primarily came from the Beijing area, an area at a higher economic level than that of other areas. Therefore, the patients might not be representative of the entire Chinese population, especially the rural areas where low-income people resident. Second, discontinuation of OAC was calculated by self-reported time, and we did not consider restarting of OAC usage, which might result in lower persistence. Third, clinical factors such as the liver and renal function and international normalized ratio testing were not incorporated in the study because of incomplete data. Fourth, the reasons for discontinuation remained unclear in a majority of cases.

Conclusions

Treatment persistence of NOACs was lower than that of warfarin amongst Chinese patients with AF. Strategies are needed for better management of OACs therapy.

Conflict of interest

Dr. Ma received honoraria from Bristol-Myers Squibb (BMS), Pfizer, Johnson & Johnson, Boehringer-Ingelheim (BI), and Bayer for giving lectures. Dr. Lip was a consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally. Other authors report no conflicts.

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