



Factors Associated with Anticoagulation Adherence in Chinese Patients with Non-Valvular Atrial Fibrillation

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Purpose: Inadequate medication adherence among patients with non-valvular atrial fibrillation (NVAF) will directly affect the efficacy and safety of anticoagulation therapy, leading to a considerable increase in the risk of ischemic stroke and death. In this study, we aim to investigate medication adherence and identify the influencing factors, including social-demographic, disease-related information and self-efficacy.

Patients and Methods: We recruited 170 patients with NVAF from a tertiary hospital atrial fibrillation outpatient clinics and cardiology ward from June 2020 to September 2020. Patients who had been taking oral anticoagulation medication for at least 3 months were included. And Morisky medication adherence scale (MGL) was used to assess the adherence to anticoagulants, which scores <4 were considered as low adherence.

Results: Fifty (29.4%) NVAF patients had a MGL score <4. Monthly income, types of comorbidities, number of drugs, and self-efficacy were determinants of anticoagulation adherence. Binomial logistic regression showed that patients had been prescribed more drugs (OR: 3.51, $p=0.002$), had high monthly income (OR: 7.87, $p=0.001$), without other diseases (OR: 8.00, $p=0.005$), and with higher self-efficacy (OR: 1.42, $p=0.001$) showed high adherence.

Conclusion: Number of drugs, types of comorbidities, monthly income, and self-efficacy were associated with the adherence of non-vitamin K antagonist oral anticoagulants (NOACs).

Keywords: atrial fibrillation, medication adherence, anticoagulation, non-vitamin K antagonist oral anticoagulants, determinants

Introduction

Atrial fibrillation (AF) includes non-valvular atrial fibrillation (NVAF) and valvular atrial fibrillation (VAF). There is an incidence rate of 77 per 10,000 people among Chinese people over 35 years old. AF significantly increases the risk of stroke by about five times. Appropriate oral anticoagulant (OAC) therapy can positively prevent the stroke.¹⁻³ OAC treatment can prevent most ischemic stroke in AF patients and can extend their survival time.^{4,5} Currently, vitamin K antagonist (VKA) and non-vitamin K antagonist oral anticoagulants (NOACs) are the primary drugs used in the treatment for NVAF. NOACs is an appropriate alternative to prevent ischemic stroke.⁶ The 2016 European Society of Cardiology (ESC) Atrial Fibrillation Management Guidelines have expressed a preference for NOACs over VKA in stroke prevention for AF patients.⁷ World Health Organization

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(WHO) defines adherence as the extent of taking medications as prescribed by health care professionals. However, patients with NVAF usually had low adherence, leading to a significantly increased risk of stroke.^{8,9} Moreover, some studies have found that the factors such as gender, age, educational level, and economic status can affect anticoagulation adherence of NVAF patients,^{9–11} while other factors, such as clinical factors and self-efficacy can also affect medication adherence.¹²

Self-efficacy is an individual's subjective judgement on whether he or she can complete a specific task or achieve a set goal in a particular situation.¹³ Many studies have shown that the level of self-efficacy affects patients' medication adherence. Research by Fang et al showed that the self-efficacy level of AF patients affects their adherence to anticoagulation, the higher self-efficacy, the better anticoagulation adherence.¹²

Through reviewing previous publications, we found that studies on anticoagulation adherence in NVAF patients few focused on self-efficacy, which is an essential factor influencing adherence in other populations. Therefore, we designed a cross-sectional study to investigate medication adherence and explore its independent predictors among patients with NVAF in China.

Study Design

This study was a cross-sectional study conducted in NVAF outpatient clinics and cardiology ward at the RuiJing hospital Shanghai Jiao Tong University School of Medicine, China. Inclusion criteria were as follows: (a) aged more than 18 years, (b) diagnosed with NVAF, (c) had been taking oral anticoagulation medication for at least 3 months, (d) currently taking NOACs for NVAF treatment. Patients diagnosed with cognitive impairment, valvular atrial fibrillation, and hard to understand the content of questionnaires were excluded. All included patients were given informed consent and signed an informed consent form. The patients were asked to fill out three questionnaires, included social-demographic information, self-efficacy scale and Morisky adherence scale. Furthermore, disease-related information were collected from medical records.

Measurements

The social-demographic and disease-related information contains 17 variables, including age, gender, marital status, education level, monthly income (less than 367€, 367–612€, above 612€), residence (town and country), employment

status (employed and unemployed) and insurance type (urban employee/resident basic medical insurance, new rural cooperative medical insurance), atrial fibrillation type, EHRA symptom classification, duration of NVAF, duration of medication, radiofrequency ablation surgery in the past, adverse events, number of drugs, types of complications, and CHA₂DS₂-VASc score. Self-efficacy in the medical therapy were evaluated by the Self-Efficacy for Appropriate Medication Use Scale,¹⁴ compiled by Risser et al.¹⁵ This scale includes one dimension, 13 items. Each item used a 3-point Likert scale and ranging from 1 - 3, which 1 is not confident, 2 is relatively confident, and 3 is very confident. Higher scores indicate a higher level of self-efficacy in medication adherence. The total score ranged from 13 to 39 points. We used Morisky medication adherence scale (MGL) to evaluate medication adherence. For four items, if the patient's choice is "yes," it is counted as 0 point, and the option is "no" counted as 1 point, the highest point is 4 points. Based on the scores, we divided the patient's adherence into two levels: below 4 points were defined as low adherence, and 4 were high adherence.¹⁶ A total of 170 patients were included. The detailed flow chart is shown in Figure 1.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Clinical Trial Ethics Committee of the RuiJing Hospital Shanghai Jiao Tong University School of Medicine. (No.2019227). The attributes, benefits, uses and disadvantageous effects of the study were explained to all participants and informed consent was also obtained. Patients have the right to refuse to fill in questions that he/she does not want to answer. In order to protect the

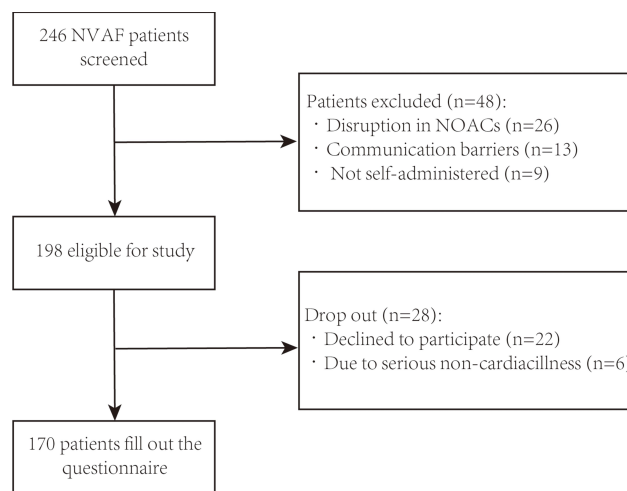


Figure 1 Sample selection flowchart.

privacy of patients, we use numbers to code these questionnaires.

Statistical Analysis

We used IBM SPSS20.0 for data entry and analysis. Mean, standard deviation (SD), frequency and percentage were used for descriptive statistics. For the two group comparisons (low adherence vs high adherence), we used the chi-square test for categorical variables, and the Student's *t*-tests or Wilcoxon rank sum test for continuous data. Multivariate analysis was performed by binomial logistic regression, which $P < 0.05$ was considered statistically significant.

Results

Medication Adherence According to Morisky Medication Adherence Scale (MGL)

Adherence to anticoagulation therapy, according to the MGL, 50 (29.4%) patients were defined as low adherers, 120 (70.6%) were defined as high adherers. Main reason for poor adherence was forgetting to take the medicine (21.20%), followed by stopping taking the medicine when they feel better (9.40%). The third reason was they stop taking the medicine when they feel worse (7.60%), and finally, sometimes they were careless to taking the medicine (7.10%), which are shown in Table 1.

Sociodemographic and Clinical Disease Characteristics of Chinese NVAf Patient

The sociodemographic and clinical characteristics of the participants are shown in Table 2. Among the 170

Table 1 Anticoagulation Adherence According to Morisky Medication Adherence Scale (MGL)

MGL Questions	Scoring	(%)
1. Do you ever forget to take your medicine?	No 1 Yes 0	78.80 21.20
2. Are you careless at times about taking your medicine?	No 1 Yes 0	92.90 7.10
3. Do you sometimes stop taking your medicine when you feel better?	No 1 Yes 0	90.60 9.40
4. Sometimes, if you feel worse when you take medicine, do you stop taking it?	No 1 Yes 0	92.40 7.60

participants, 99 (58.2%) were male, 71 (41.8%) were female, and 158 (92.9%) lived in the town. 89 were taking three or more drugs. 71 (41.8%) had undergone radio-frequency catheter ablation (RFCA), and 91 (53.5%) had more than one complication. 129 (75.9%) were diagnosed with paroxysmal atrial fibrillation, 41 (24.1%) were persistent atrial fibrillation. 138 (81.2%) had the CHA₂DS₂-VaSc score more than 2. Monthly income, number of drugs and types of complications were significantly difference between two groups while others were not, which are shown in Table 3.

Results of Logistic Regression

Logistic regression showed that high adherence was associated with higher self-efficacy (OR=1.42; 95% CI=1.15–1.74, $p=0.001$). As shown in Table 4, patients who take three or more drugs were more adherent to anticoagulation therapy than those less than three (OR=3.51; 95% CI=1.57–8.01 $p=0.002$). And patients whose monthly income is more than 612€ showed better adherence than patients with a monthly payment less than 612€ (OR=7.87, 95% CI=2.68–23.11 $p=0.001$). The adherence of patients without other diseases is better than patients with more than 3 diseases (OR=8.00, 95% CI= [1.90–33.71]). Still, there is no difference of adherence between patients with one or two diseases and those with more than three diseases.

Discussion

In our study, patients' medication adherence was evaluated by MGL and we found that almost 30% of Chinese NVAf patients had low adherence, which was similar to the adherence rate in other countries (21.1% to 26.2%).^{17,18} Adherence was suboptimal in this study population. Compared with the results of other Chinese study, there were also specific differences,¹⁹ resulted from the different evaluation tools and the included populations. We found that the poor adherence of NVAf patients, in a large extent, is due to forgetting to take medication. E-health is an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies.²⁰ Approaches such as e-health, including remote medication adherence monitoring system, short message service, medication reminder application (APP), were proven to be effortable at improving patient adherence.^{21,22} Therefore, we can try to make use of

Table 2 Sociodemographic and Clinical Characteristics of Patients (n=170)

Age		69.52±9.14
Gender, n(%)		
Male	99	58.2
Female	71	41.8
Residence		
Town	158	92.9
Country	12	7.1
Education level		
Elementary school and lower	16	9.4
Junior high school	53	31.2
High school or technical secondary school	45	26.5
College degree and above	56	32.9
Marital status		
Unmarried/Divorced/Widowed	26	15.3
Married	144	84.7
Employment status		
Employed	15	8.8
Unemployed/Retired	155	91.2
Monthly income		
<612€	23	13.5
≥612€	147	86.5
Insurance type		
Urban employee/Resident basic medical insurance	154	90.6
New Rural Cooperative Medical Insurance	16	9.4
Duration of atrial fibrillation		
<1 year	50	29.4
1~3 years	60	35.3
>3 years	60	35.3
Duration of anticoagulation therapy		
<1 year	116	68.2
1~3 years	48	28.2
>3 years	6	3.6
Number of drugs		
0~2	81	47.6
≥3	89	52.4
EHRA classification		
I	49	28.8
II	97	57.1
III and IV	24	14.1
RFCA in the past		
Yes	71	41.8
No	99	58.2

(Continued)

Table 2 (Continued).

Age		69.52±9.14
Bleeding		
Yes	45	26.5
No	125	73.5
Types of complications		
0	79	46.5
1~2	77	45.3
≥3	14	8.2
Types of atrial fibrillation		
Paroxysmal atrial fibrillation	129	75.9
Persistent atrial fibrillation	41	24.1
CHA ₂ DS ₂ -VaSc score		
<2	32	18.8
≥2	138	81.2

these reminder techniques to help patients improve adherence. Surprisingly, we found that the rate of non-adherence of NOACs was lower than the warfarin.²³ One possible explanation was that the NOACs could make the blood concentration stable, do not require frequent blood tests, was much more convenient. Therefore, for physicians, if NVAf patients had low adherence to warfarin, they can consider prescribing NOACs for the patient according to their condition. For patients' factors, previous studies had shown that being younger age, male, employed predicted of low adherence in NVAf patients.^{24,25} But our investigation found no correlation between age, gender, employment and adherence. One possible explanation was the sample size is small or the economic and cultural background differences between China and other countries. Besides, in our study, the educational level did not seem to affect adherence. And there was no relationship between marital status, residence, or insurance type, but monthly income, which was found to be related to adherence, and patients who had a higher monthly income showed better adherence. One possible explanation was the high price of NOACs. People with higher monthly payments can afford the cost of the drug and are more inclined to insist on taking the medication. And clinicians should help patients get more social support, such as the help of social charity organizations, to reduce their financial burden. Also, the remarkable discovery was patients

Table 3 Characteristics of the Patients According to Anticoagulation Adherence

	Low Adherence (n/%)	High Adherence (n/%)	P-value
Patients	50(29.4)	120(70.6)	
Age	68.36±6.97	70.00±9.89	0.175
Gender			0.609
Male	31(62.0)	68(56.7)	
Female	19(38.0)	52(43.3)	
Residence			0.195
Town	44(88.0)	114(95.0)	
Country	6(12.0)	6(5.0)	
Education level			0.281
Elementary school and lower	7(14.0)	9(7.5)	
Junior high school	18(36.0)	35(29.1)	
High school or technical secondary school	13(26.0)	32(26.7)	
College degree and above	12(24.0)	44(36.7)	
Marital status			0.441
Unmarried/Divorced/Widowed	6(12.0)	20(16.7)	
Married	44(88.0)	100(83.3)	
Employment status			0.807
Employed	4(8.0)	11(9.2)	
Unemployed/Retired	46(92.0)	109(90.8)	
Monthly income			0.001
<612€	14(28.0)	9(7.5)	
≥612€	36(82.0)	111(92.5)	
Insurance type			0.301
Urban employee/Resident basic medical insurance	7(14.0)	9(7.5)	
New Rural Cooperative Medical Insurance	43(86.0)	111(92.5)	
Duration of atrial fibrillation			0.892
<1 year	14(28.0)	36(30.0)	
1~3 years	17(34.0)	43(35.8)	
>3 years	19(38.0)	41(34.2)	
Duration of anticoagulation therapy			0.515
<1 year	37(74.0)	79(65.8)	
1~3 years	12(24.0)	36(30.0)	
>3 years	1(2.0)	5(4.2)	
Number of drugs			0.006
0~2	32(64.0)	49(40.8)	
≥3	18(36.0)	71(59.2)	
EHRA classification			0.261
I	Low adherence 10(20.0)	High adherence 39(32.5)	

(Continued)

Table 3 (Continued).

	Low Adherence (n/%)	High Adherence (n/%)	P-value
II III and IV	32(64.0) 8(16.0)	65(54.2) 16(13.3)	
RFCA in the past			0.968
Yes	21(42.0)	50(41.7)	
No	29(58.0)	70(58.3)	
Bleeding			0.151
Yes	17(34.0)	28(23.3)	
No	33(66.0)	92(76.7)	
Types of complication			0.047
0	16(32.0)	63(52.5)	
1~2	29(58.0)	48(40.0)	
≥3	5(10.0)	9(7.5)	
Types of atrial fibrillation			0.418
Paroxysmal atrial fibrillation	40(80.0)	89(74.2)	
Persistent atrial fibrillation	10(20.0)	31(25.8)	
CHA ₂ DS ₂ -VaSc score			0.859
<2	9(18.0)	23(19.2)	
≥2	41(82.0)	97(80.8)	
Self-efficacy score (Mean±SD)	32.13±1.50	36.48±3.83	<0.001

with higher self-efficacy scores show better adherence, which had been reported in NVAf patients.²⁶ Self-efficacy reflects one's confidence in accomplishing things; thus, high self-efficacy of patients has the confidence to take medicine on time, under the condition of uncertainty and difficulty to insist on taking medicine. A previous study showed that the effectiveness of the self-efficacy enhancement program could effectively improve medication adherence in patients with acute myocardial infarction.²⁷ Therefore, physicians can design relevant interventions to improve the self-efficacy of patients and further improve the adherence of patients with oral anticoagulants. For treatment-related factors, our study found that the adherence of patients taking more than 3 drugs is higher than that of less than 3, which is consistent with Bennis's research.²⁸ This may be explained by that patients taking more than one medication may remember that they need to take anticoagulants while taking other drugs. Clinicians and nurses should increase the frequency of assessing patients' adherence, as the guidelines

Table 4 Logistic Regression: Factors Influencing NOACs Adherence

Variables	Low Adherence	High Adherence	Odds Ratio (95% CI)	P-value
Monthly income, n (%)				
<612€	14 (73.9)	9 (27.1)	1	-
≥612€	36 (24.5)	111 (75.5)	7.87[2.68–23.11]	0.001
Number of drugs, n (%)				
0–2	32(39.5)	49(60.5)	1	-
≥3	18(18.2)	71(81.8)	3.51[1.57–8.01]	0.002
Types of complication n (%)				
0	16(20.3)	63(79.7)	8.00[1.90–33.71]	0.005
1–2	29(37.7)	48(62.3)	2.33[0.63–8.64]	0.207
≥3	5(35.7)	9(64.3)	1	-
Self-efficacy score	32.13±1.50	36.48±3.83	1.42[1.15–1.74]	0.001

recommended that adherence be evaluated on each visit.⁷ In our study, we also found that patients who had more diseases combined had low adherence, which may be related to the poor physical condition. Choosing the variable of self-efficacy is an advantage of this study. In contrast, previous studies have mostly considered the influence of demographic-related factors and disease-related factors on adherence. Furthermore, our study focused on NOACs adherence in NVAF patients in Shanghai, the southeast coastal city of China, which can reflect the adherence status of economically developed regions to a certain extent. This study also had certain limitations. This study only included patients from one tertiary hospital, which resulted in limited sample representation. There may be a selection bias in the research results. The research is a cross-sectional survey, it is difficult to obtain the causal relationship between variables. Therefore, the results of this research need to be further confirmed by future multi-center, longitudinal study and large-sample studies, or we could use the instrumental variables to prove the causality relationship in medication adherence.^{29,30} In summary, the adherence level of NOACs in patients with NVAF in Shanghai is suboptimal. Monthly income, number of drugs, types of complications, and self-efficacy are associated with adherence.

Highlights

- Poor oral anticoagulants in patients with non-valvular atrial fibrillation increase the risk of stroke and bleeding.

- Adherence was suboptimal in patients with NVAF; the proportion of non-adherent patients is about 30%.
- Monthly income, number of drugs, type of comorbidities, and self-efficacy are associated with NOACs adherence.

Abbreviations

NVAF, non-valvular atrial fibrillation; NOACs, non-vitamin K oral anticoagulants; RFCA, radiofrequency catheter ablation.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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