

BMJ Open Anticoagulation adherence and its associated factors in patients with atrial fibrillation: a cross-sectional study

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ABSTRACT

Objective To investigate anticoagulant adherence and its associated factors, including demographics, clinical variables, atrial fibrillation (AF) severity, knowledge, satisfaction with services, perceived barriers, perceived benefits, symptom severity and self-efficacy in patients with AF.

Design This is a cross-sectional study.

Participants and setting A convenient sample of patients with AF were recruited from cardiology clinics of two teaching hospitals in Taiwan.

Measures Data were collected using the study questionnaires, including the AF-related symptom subscale of the AF Severity Scale, the Knowledge of Warfarin Anticoagulation Treatment Scale, the Satisfaction Scale about Service and Warfarin Treatment, the perceived benefits subscale of the Beliefs about Anticoagulation Survey, the Concerns about Anticoagulation Therapy Scale, The Self-efficacy for Appropriate Medication Use Scale and the short-form Adherence to Refills and Medications Scale.

Results A total of 151 patients with AF participated in the study; 53 treated with warfarin and 98 treated with novel oral anticoagulants (NOACs). The difference in adherence to warfarin (mean=8.6; SD=1.6) and NOACs (mean=8.9; SD=2.0) was statistically insignificant. Multiple linear regression analysis showed that perceived barriers ($\beta=0.18$, $p=0.017$) and self-efficacy ($\beta=-0.48$, $p<0.001$) were significant predictors of anticoagulation adherence. For every 1-unit increase in the perceived barriers, there will be a 0.18-unit increase in the adherence to anticoagulation therapy. For every 1-unit increase in the self-efficacy, there will be a 0.48-unit decrease in the adherence to anticoagulation therapy. Perceived barriers and self-efficacy collectively explained 34.0% of the variance in adherence to anticoagulation therapy ($F_{(2,149)}=38.11$, $p<0.001$).

Conclusion We found no better adherence to NOACs compared with warfarin. Patients with greater self-efficacy and perceived fewer barriers showed better adherence to anticoagulation therapy.

INTRODUCTION

Atrial fibrillation (AF) is the most common type of arrhythmia.^{1–3} AF associated haemodynamic changes and thrombosis increases risks of heart failure, stroke and sudden death.⁴ In Taiwan, patients with AF are

Strengths and limitations of this study

- This is one of the few studies that compared medication adherence between patients taking warfarin and novel oral anticoagulants.
- The cross-sectional nature of the study precluded an assessment of medication adherence change over time and did not permit us to determine causal relationships among the study variables.
- A self-report questionnaire was used to measure medication adherence, which was subject to recall and social desirability biases.

fivefold more likely to have a stroke than the general population, whereas one in five patients with stroke has AF.⁵ Moreover, 46.2% of patients with AF have an ischaemic stroke within 3 years of diagnosis.⁶ Anticoagulation treatment is the most important measure for preventing stroke in patients with AF.^{1–3} However, inadequate anticoagulation use is a global problem.^{7,8} In Taiwan, while 90% of patients with AF meet the criteria for anticoagulation treatment, only 28.28% use it.⁹ Correlation studies on AF and stroke show that 185 570 cases of stroke occur each year in patients with AF with no antiplatelet or oral anticoagulation treatment.¹⁰

Vitamin K antagonists (VKAs) such as warfarin and novel oral anticoagulants (NOACs) are the two main types of anticoagulants currently used for patients with AF.^{1–3} While using warfarin, the international normalised ratio (INR) must be closely monitored as warfarin tends to interact with other drugs or foods, and it is difficult to maintain the percentage of time in the therapeutic range.^{1–3} NOACs should be used if INR is difficult to maintain in the desired therapeutic range while using warfarin.² Lin *et al*¹¹ found that it is difficult to choose an optimal dose of warfarin in Asian populations because of substantial variation in the individual response to warfarin and the narrow

therapeutic range. Chiang *et al*¹ also found that warfarin significantly increases the risk of intracranial haemorrhage and recommended NOACs as the preferred treatment in Asian populations with AF. However, warfarin is still the most common and widely used anticoagulant for patients with AF in Taiwan.¹¹

Good anticoagulant adherence ensures medication safety and effective prevention of stroke. Low adherence is associated with higher mortality and morbidity of cardiovascular diseases.¹² Knowing factors that affect anticoagulant adherence will help identify the populations at risk for non-adherence and allow for the development of appropriate measures to improve medication adherence. Previous studies showed that low adherence was related to (1) concerns about adverse drug reactions¹³; (2) inadequate knowledge of AF associated risks for stroke¹³; (3) unawareness of the importance of medication adherence¹³; (4) symptom severity¹³; (5) fear of regular blood tests¹³; (6) inability to attend frequent clinical visits¹⁴; (7) undergoing invasive treatments or procedures¹³ and (8) comorbidities.¹⁴ However, most of these studies were conducted in Western Caucasian populations and in patients taking warfarin. Whether patients from different cultural backgrounds share similar factors deserve further investigations. Additionally, few studies have investigated the differences in medication adherence for taking NOACs versus warfarin in patients with AF, and they have yielded inconsistent results. Yao *et al*¹⁵ conducted a retrospective cohort analysis to investigate adherence to oral anticoagulants in patients with AF, wherein the proportion of days covered (PDC) $\geq 80\%$ indicated good adherence. The overall PDC was 47.5% for NOACs (dabigatran, rivaroxaban and apixaban) and 38.7% for warfarin ($p < 0.001$), indicating better adherence to NOACs than to warfarin. Choi *et al*¹⁶ analysed 364 AF cases (warfarin: $n = 204$, dabigatran: $n = 160$) and assessed medication adherence with missed doses per month. The data showed that an average of 0.65 dabigatran tablets and an average of 0.63 warfarin tablets were missed per month ($p = 0.916$). The results from the above studies show that medication adherence varies with each NOACs, which is not always superior to that of warfarin.

Therefore, the purposes of this study were to (1) compare the differences in adherence between patients treated with warfarin and NOACs; (2) explore factors influencing anticoagulant adherence in patients with AF, including demographics, clinical variables (disease duration, stroke risk assessment, bleeding risk assessment, anticoagulation therapies and adverse reactions), AF severity, anticoagulation treatment knowledge, satisfaction with services, beliefs about anticoagulation treatment and self-efficacy for appropriate medication and (3) investigate the important predictors of anticoagulant adherence in patients with AF.

METHODS

Study design

This is a cross-sectional study. Data were collected with self-reported questionnaires.

Participants and setting

Patients with AF who met the following eligibility criteria were recruited from cardiology outpatient clinics of two teaching hospitals in Taipei, Taiwan. The inclusion criteria were (1) ≥ 20 years of age; (2) fluent in Mandarin or Taiwanese; (3) diagnosed with AF and (4) treated with warfarin or NOACs for anticoagulation. The exclusion criteria were (1) diagnosed with psychological diseases; (2) diagnosed with uncontrolled hypertension; (3) diagnosed with the New York Heart Association grade VI heart failure; (4) implanted with a cardiac pacemaker; (5) had a cardiac surgery in the past 3 months and (6) hospitalised for AF in the past 3 months. The desired sample size was estimated by using the G power V.3.1 software. In consideration of the number of potential predictors ($n = 17$) in this study, a sample size of 146 would have 80% power to detect a medium effect size of $f^2 = 0.15$ with a 0.05 level of significance using a multiple linear regression fixed model. The use of NOACs or warfarin was treated as a single variable for the sample size calculation.

Patient and public involvement

The development of the research hypothesis was informed by working closely with patients with AF. However, patients and the public were not involved in the recruitment process and conduct of the study. An abstract of the study results will be mailed to the study participants.

Data collection

The investigator administered the study questionnaire after obtaining informed consent from each subject. The data collection took place in the waiting areas outside the outpatient clinics during the patients' visits to the clinics. For subjects who were unable to read the questionnaire due to vision or other problems, the investigator read each question to help them complete the questionnaire.

Variables and measurements

Sociodemographics were provided by the subjects, including age, sex, education level, marital status and employment status. Data on clinical variables were extracted from the participants' medical records, including disease duration, $\text{CHA}_2\text{DS}_2\text{-VASc}$ score for stroke risk assessment, HAS-BLED score for bleeding risk assessment and anticoagulation therapies (name of the medication and dosing frequency). The subjects were also asked to report anticoagulant-related adverse reactions, including bleeding events, hypersensitivity, gastrointestinal reactions, dizziness, headache, fainting, limb pain and oedema.

The AF related symptom subscale of the AF Severity Scale (AFSS)¹⁷ was used to measure symptom severity. The seven-item subscale covers seven AF-related symptoms. For each item, the subjects indicated how often

within the last month they experienced the symptom on a 6-point Likert scale (from 0—I have not had this symptom in the past 4 weeks to 5—a great deal). The total score of the seven items represents the scale score, with a possible range of 0 to 35. Higher scores indicate higher levels of symptom severity. The scale has shown an acceptable level of reliability and validity in past studies involving patients with AF.¹⁸ This English scale was translated into Chinese through the following steps: Chinese translation, synthesis, back translation, expert committee review and pilot testing.¹⁹ Its Content Validity Index (CVI) was greater than 0.9, indicating good expert validity.¹⁹ In this study, Cronbach's α value was 0.80. A high Cronbach's α coefficient (eg, >0.8) indicates good internal consistency reliability.²⁰

The Chinese version of Knowledge of Warfarin Anticoagulation Treatment Scale²¹ was used to measure warfarin treatment knowledge. The 11-item scale covers four areas of warfarin treatment knowledge: administration (eg, dose, colour and route of administration), interaction with foods, interaction with other drugs and side effects. There are five choices for each item, and only one of the choices is correct (scored 1). The total score of the 11 items represents the scale score, with a possible range of 0–11. Higher scores indicate higher levels of understanding of warfarin treatment. The scale was also modified to measure NOACs treatment knowledge. The item 1 (regarding anticoagulant dosage) in the original scale was revised into two items, one for dosage and one for the name of the medication in the NOACs knowledge scale. The item 2 (regarding INR) in the original scale was deleted. The item 4 (regarding how to make up the missing dose) was revised into two items, one for missing a dose in taking NOACs once a day and one for missing a dose in taking NOACs twice a day. The total score of the 13 items represents NOACs treatment knowledge. The potential scores range from 0 to 12, with higher scores indicating higher levels of understanding of NOACs treatment. To facilitate analysis and comparison, the score of each scale was converted to a scale of 0 to 100 (actual score/possible maximum score \times 100). The knowledge of warfarin anticoagulation treatment scale has shown good psychometric properties in a previous study involving patients treated with anticoagulants.²¹ In the current study, Kuder-Richardson Formula 20 (KR-20) was 0.68 for warfarin treatment knowledge and 0.63 for NOACs treatment knowledge. The KR-20 is a measure of internal consistency reliability for dichotomous scale items.

The Chinese version of Satisfaction Scale about Service and Warfarin Treatment (SSWT)¹⁹ was used to measure subjects' satisfaction with services and anticoagulation treatment provided by the healthcare team. The original scale includes seven positive statements about the services and warfarin treatment. In the current study, the term warfarin was replaced with anticoagulants. The item 5 (regarding INR monitoring) in the original scale was deleted as it only applies to patients treated with warfarin. Therefore, there were only six items used in the current

study. For each item, the subjects indicated their levels of agreement on a 5-point Likert scale (from 0—strongly disagree to 4—strongly agree). The total score of the six items represents the scale score, with a possible range of 0–24. Higher scores indicate higher levels of satisfaction about service and warfarin treatment. The scale has shown good psychometric properties in a previous study involving patients treated with anticoagulants.²¹ In this study, Cronbach's α was 0.87.

The perceived benefits subscale of the Beliefs about Anticoagulation Survey (BAAS)²² was used to measure subjects' perceived benefits associated with taking anticoagulants. The subscale covers five potential benefits of taking anticoagulation, including lessening the risk of having a stroke, lowering the chance of being hospitalised, feeling healthier, improving quality of life and worrying less about the disease. For each item, the subjects indicated their levels of agreement on a 5-point Likert scale (from 1—strongly disagree to 5—strongly agree). The potential scores range from 5 to 25, with higher scores indicating higher levels of perceived benefits associated with taking anticoagulation. The scale has shown reasonable psychometric properties in a previous study involving patients treated with anticoagulation.²² The scale was translated into Chinese by our research team following the same steps as described prior. Its CVI was 1.0 and Cronbach's α was 0.84.

The Chinese version of the Concerns about Anticoagulation Therapy Scale¹⁹ was used to measure perceived barriers regarding anticoagulation treatment. The scale lists 10 potential concerns, including drug interactions, forgetting to take anticoagulants, side effects, hospital visits, diet interactions, activity restrictions, impact on work, not helpful and difficulty of following instructions.

Table 1 Descriptive data of study variables (n=151)

| Variables | Mean | SD | Range |
|--|------|------|--------|
| Age | 72.0 | 8.6 | 55–93 |
| Disease duration (month) | 74.0 | 61.1 | 2–389 |
| Symptom severity | 6.8 | 5.4 | 0–22 |
| Anticoagulation treatment knowledge | 35.9 | 19.3 | 0–92 |
| Warfarin (n=53) | 33.5 | 20.6 | 0–90.9 |
| NOACs (n=98) | 38.4 | 19.1 | 0–91.7 |
| Satisfaction with services and anticoagulation treatment | 19.1 | 3.2 | 7–24 |
| Perceived benefits of anticoagulation treatment | 20.1 | 2.5 | 13–25 |
| Perceived barriers to anticoagulation treatment | 1.1 | 1.3 | 0–6 |
| Self-efficacy for anticoagulant use | 32.9 | 6.1 | 18–39 |
| Anticoagulation adherence | 8.8 | 1.9 | 7–15 |

NOACs, novel oral anticoagulants.

Table 2 Sample characteristics and comparisons of self-efficacy and anticoagulation adherence among different characteristics of patients with atrial fibrillation (n=151)

| Variables | N | Self-efficacy | | | Adherence | | |
|--|-----|---------------|-------|---------|-----------|-------|---------|
| | | M±SD | F/t | P value | M±SD | F/t | P value |
| Gender | | | -1.56 | 0.121 | | 1.50 | 0.135 |
| Female | 56 | 31.9±6.8 | | | 9.1±2.1 | | |
| Male | 95 | 33.5±5.6 | | | 8.7±1.7 | | |
| Educational level | | | 0.17 | 0.915 | | 0.37 | 0.779 |
| Primary school and below | 51 | 32.9±6.2 | | | 8.8±1.9 | | |
| Middle school | 21 | 33.5±7.1 | | | 8.8±2.2 | | |
| High school | 33 | 33.1±5.8 | | | 8.6±1.9 | | |
| College and above | 46 | 32.4±5.7 | | | 9.0±1.7 | | |
| Marital status | | | 1.18 | 0.238 | | -0.52 | 0.604 |
| Married | 125 | 32.6±5.9 | | | 8.9±1.9 | | |
| Single, divorced or widowed | 26 | 34.2±6.9 | | | 8.7±2.0 | | |
| Employment status | | | 0.54 | 0.584 | | 0.73 | 0.482 |
| Full time, part-time | 29 | 32.9±6.5 | | | 9.2±2.0 | | |
| Retired | 107 | 33.1±5.7 | | | 8.7±1.8 | | |
| Unemployed | 15 | 31.3±7.6 | | | 8.7±2.0 | | |
| CHA ₂ DS ₂ -VAS _C | | | 0.18 | 0.86 | | -0.82 | 0.416 |
| Low-middle risk | 9 | 33.2±6.1 | | | 8.3±1.6 | | |
| High risk | 142 | 32.9±6.1 | | | 8.9±1.9 | | |
| HAS-BLED | | | 0.92 | 0.360 | | -0.86 | 0.392 |
| Low risk | 60 | 33.4±6.0 | | | 8.7±1.8 | | |
| High risk | 91 | 32.5±6.14 | | | 8.9±1.9 | | |
| Anticoagulants | | | 1.37 | 0.172 | | -0.99 | 0.324 |
| Warfarin | 53 | 33.8±4.9 | | | 8.6±1.6 | | |
| NOACs | 98 | 32.4±6.6 | | | 8.9±2.0 | | |
| Dosing frequency | | | 0.08 | 0.922 | | 0.45 | 0.641 |
| Once a day | 135 | 32.9±6.0 | | | 8.8±1.9 | | |
| Twice a day | 11 | 33.5±6.9 | | | 9.3±1.6 | | |
| Once every 2 days | 5 | 32.2±7.1 | | | 8.4±1.4 | | |
| Number of adverse reactions | | | 1.18 | 0.320 | | -2.15 | 0.096 |
| None | 77 | 33.4±5.7 | | | 8.7±1.8 | | |
| One | 51 | 33.0±6.3 | | | 8.8±1.7 | | |
| Two | 14 | 30.9±6.7 | | | 8.7±1.9 | | |
| Three and more | 9 | 30.4±7.0 | | | 10.3±2.5 | | |

F, the value of one-way analysis of variables; NOACs, novel oral anticoagulants; t, the value of dependent t-test.

The subjects were asked to indicate all concerns that apply to them. Each concern was scored 1. The potential scores range from 0 to 10, with higher scores indicating more concerns. The scale has shown acceptable psychometric properties in a previous study involving patients treated with anticoagulants.²²

The Self-efficacy for Appropriate Medication Use scale (SEAMS)²³ was used to measure self-efficacy for appropriate anticoagulant use. The 13-item scale covers two dimensions of self-efficacy: for taking medications under

difficult circumstances and for taking medications under uncertain or changing circumstances. For each item, the subjects indicated their level of confidence about taking medications correctly under a specific circumstance on a three-point response scale (1—not confident, 2—somewhat confident, and 3—very confident). The potential scores range from 13 to 39, with high scores indicating higher levels of self-efficacy for appropriate anticoagulant use. The SEAMS has shown good psychometric properties for patients with coronary heart disease and other

Table 3 Person product-moment correlation coefficients among study variables (n=151)

| Variables | Age | Disease duration | Symptom severity | Knowledge | Satisfaction | Perceived benefits | Perceived barriers | Self-efficacy | Adherence |
|--------------------|---------|------------------|------------------|-----------|--------------|--------------------|--------------------|---------------|-----------|
| Age | 1 | | | | | | | | |
| Disease duration | 0.11 | 1 | | | | | | | |
| Symptom severity | -0.21** | -0.16* | 1 | | | | | | |
| Knowledge | -0.15 | -0.01 | 0.02 | 1 | | | | | |
| Satisfaction | -0.05 | -0.01 | -0.03 | 0.26** | 1 | | | | |
| Perceived benefits | -0.00 | 0.03 | -0.08 | 0.13 | 0.39*** | 1 | | | |
| Perceived barriers | -0.03 | -0.12 | 0.29*** | -0.05 | -0.09 | -0.17* | 1 | | |
| Self-efficacy | 0.05 | 0.06 | -0.23** | 0.06 | 0.29*** | 0.31*** | -0.45*** | 1 | |
| Adherence | -0.02 | 0.06 | 0.09 | -0.05 | -0.05 | -0.10 | 0.40*** | -0.56*** | 1 |

*P<0.05; **P<0.01; ***P<0.001.

comorbid conditions.²³ The scale was translated into Chinese by our research team with a CVI 1.0 and Cronbach's α 0.93.

The short-form Adherence to Refills and Medications Scale (ARMS)²⁴ was used to measure adherence to anticoagulation treatment. There are seven items on the scale. Subjects were asked to indicate how often they actually miss taking their anticoagulants in each item on a 4-point Likert scale (1—none of the time to 4—all of the time). The total score of the seven items represents the scale score, with a possible range of 7–28. A higher score indicates worse adherence to anticoagulation treatment. The scale has shown good psychometric properties for patients with coronary heart diseases (n=435).²⁴ The scale correlated strongly both with the Morisky adherence scale²⁵ (Spearman's rho=-0.598, p<0.01) and the cumulative medication gap²⁶ during the previous 6 months (Spearman's rho=0.339, p<0.01).²⁴ Patients with low ARMS scores were significantly more likely to have controlled blood pressure (81.3% vs 73.2%, p<0.05). The scale also had good internal consistency (Cronbach's α =0.814) and test-retest reliability (Spearman's rho=0.693, p<0.001).²⁴ In this study, Cronbach's α was 0.70.

Statistical methods

Data were analysed using the Statistical Package for Social Sciences V.20.0 (SPSS). Descriptive analyses were used to describe study variables. Independent t-tests and one-way analysis of variance were performed to analyse the differences in anticoagulation adherence scores among different categorical study variables. Pearson product-moment correlations were performed to analyse the correlations among the continuous variables. Due to a large number of potential explanatory variables, stepwise linear regression was chosen for statistical model selection. All study variables were entered as dependent variables into stepwise linear regression models to find significant influencing factors of anticoagulant adherence. These included demographics (age, gender, educational level, marital status and employment status), clinical variables (disease duration, CHA₂DS₂-VASc score, HAS-BLED score, anticoagulants, dosing frequency and adverse reactions), symptom severity, anticoagulation treatment knowledge, satisfaction with services, perceived benefits, perceived barriers and self-efficacy for appropriate anticoagulant use. Categorical variables were dummy coded prior to analysis. The probability-of-F-to-enter ≤ 0.05 was used as the criterion for entering a variable into the model; the probability-of-F-to-remove ≥ 0.10 was used as the criterion for removing a variable from the model. Standardised residual plots and collinearity statistics of variance inflation factor were used to examine the normality and independent assumptions of the regression. There was no violation in both assumptions.

RESULTS

One of the researchers approached 156 eligible patients; 6 of them declined to participate. This left 151 eligible

Table 4 Results of stepwise regressions on self-efficacy and anticoagulation adherence in patients with atrial fibrillation (n=151)

| Model | Dependent variables | Independent variables | β | t | R ² | Adjusted R ² | F | VIF |
|-------|---------------------|-----------------------|---------|---------|----------------|-------------------------|---------|------|
| 1 | | | | | 0.29 | 0.28 | 20.00** | |
| | Self-efficacy | Perceived barriers | -0.41 | -5.74** | | | | 1.03 |
| | | Satisfaction | 0.19 | 2.50* | | | | 1.18 |
| | | Perceived benefits | 0.17 | 2.20* | | | | 1.21 |
| 2 | | | | | 0.34 | 0.33 | 38.11** | |
| | Adherence | Self-efficacy | -0.48 | -6.40** | | | | 1.25 |
| | | Perceived barriers | 0.18 | 2.42* | | | | 1.25 |

*P<0.05; **P<0.001. Adjusted R² a modified version of R² for the number of predictors in a model.

patients to take part in the study. All of them completed the study questionnaires, and their data were included in the final analysis. Every subject filled out all the questionnaires except the knowledge scale. Fifty-three (35.1 %) subjects receiving warfarin answered The Knowledge of Warfarin Anticoagulation Treatment Scale; 98 (64.9%) subjects receiving NOACs filled out The Knowledge of NOACs Treatment Scale.

These subjects were recruited from clinics associated with two hospitals, with 93 and 58 subjects from each hospital, respectively. There was no significant difference in demographics or values of study variables between subjects recruited from the different hospitals (data not shown). The average age of the subjects was 72.0 (SD=8.6) (table 1). There were 95 men and 56 women in the study. The majority of the subjects were married (n=125) and retired (n=107) (table 2). Subjects were diagnosed with an AF for 74.0 months (SD=61.1) on average (table 1). Of the 151 subjects, 98 received NOACs and 53 received warfarin. Most subjects (n=77) did not experience anticoagulation-related side effects (table 2).

The subjects reported an average score of 8.8 (SD=1.9) on ARMS. The average score on the symptom subscale of the AFSS was 6.8 (SD=5.4). Shortness of breath during physical activity was the most common symptom experienced by these subjects. The subjects had a mean score of 35.9 (SD=19.3) on the anticoagulation treatment knowledge scale. Most subjects miss more than half of the treatment-related questions, with most mistakes made in

drug–food interactions, INR values, the timing of taking anticoagulants and how to prevent bleeding risks. They reported a mean score of 19.1 (SD=3.2) on the SSWT. Their average score on the perceived benefits subscale of the BAAS was 20.1 (SD=2.5). They reported an average score of 1.1 (SD=1.3) on the concerns about anticoagulation therapy scale. The top three concerns indicated by the subjects were: (1) side effects (n=53); (2) drug interactions (n=44) and (3) forgetting to take anticoagulants (n=33). The subjects had a mean score of 32.9 (SD=6.1) on the SEAMS.

The difference in medication adherence between warfarin (mean=8.6; SD=1.6) and NOACs (mean=8.9; SD=2.0) was statistically insignificant. There was also no significant difference both in anticoagulant adherence and self-efficacy among subjects with different demographics and clinical variables (CHA₂DS₂-VASc score, HAS-BLED score, anticoagulants, dosing frequency and adverse reactions) (table 2). Results of Pearson correlation analyses showed that anticoagulation adherence was significantly associated with perceived barriers to (r=0.40, p<0.001) and self-efficacy for appropriate anticoagulant use (r=-0.56, p<0.001). Other study variables (age, disease duration, symptom severity, knowledge, satisfaction and perceived benefits) were not significantly associated with anticoagulation adherence (table 3). The self-efficacy for anticoagulant use was significantly associated with symptom severity (r=-0.23, p=0.02), satisfaction (r=0.29, p<0.001), perceived benefits (r=0.31, p<0.001) and perceived barriers (r=-0.45, p<0.001). Age, disease duration and knowledge were not related to self-efficacy.

Results of stepwise linear regression analyses showed that perceived barriers (β =0.18, p=0.017) and self-efficacy (β =-0.48, p<0.001) were significant predictors of adherence to anticoagulation therapy. For every 1-unit increase in the perceived barriers score, there will be a 0.18-unit increase in the adherence to anticoagulation therapy score. In addition, for every 1-unit increase in the self-efficacy score, there will be a 0.48-unit decrease in the adherence to anticoagulation therapy score. Perceived barriers and self-efficacy collectively explained 34.0% of the variance in adherence to anticoagulation therapy

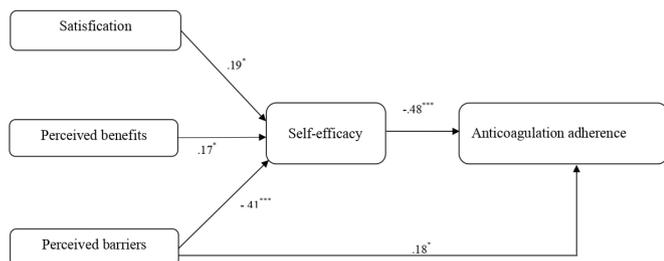


Figure 1 Relationships among symptom severity, satisfaction, perceived benefits and perceived barriers in self-efficacy and adherence to anticoagulation therapy. *P<0.05; ***P<0.001.

($F_{(2,149)}=38.1, p<0.001$) (see table 4). Other variables were excluded from the model. As for self-efficacy, the satisfaction with services, perceived benefits and perceived barriers were the significant predictors. These three variables together explained 29.0% of the variance in self-efficacy for anticoagulant use ($F_{(3,148)}=20.0, p<0.001$) (see table 4). Figure 1 presents the relationships among perceived benefits, perceived barriers, self-efficacy and adherence to anticoagulation therapy with their respective standardised regression coefficients (β).

DISCUSSION

This is one of the few studies that compared differences in medication adherence between warfarin and NOACs among patients with AF. We found no better adherence to NOACs compared with warfarin. It is difficult to compare our findings with other studies because most studies included only patients treated with warfarin²⁷ and used different adherence measures.²⁷ Nevertheless, our study subjects reported relatively good adherence to anticoagulant therapy with an average score of 8.8 (SD=1.9) out of the possible range 7–28 in ARMS, compared with 32.3% of non-adherent to warfarin therapy in a cross-sectional survey of 288 patients with AF.²⁷

Perceived barriers and self-efficacy were found to be significant predictors of medication adherence. Consistent with findings in previous studies of other populations,^{28 29} patients with greater self-efficacy and perceived fewer barriers reported better adherence to anticoagulation therapy. When considering the pharmacokinetics of these anticoagulants, the effect of the adherence on clinical outcomes may be different. It may be better to show their results separately. Therefore, we further analysed warfarin and NOACs users separately and found that the independent predictors of perceived barriers and self-efficacy for adherence were persistent. Concerns about side effects, drug interactions and forgetting to take anticoagulants were the top barriers to appropriate anticoagulant use.²⁷ Symptom severity, satisfaction, perceived benefits and perceived barriers were significant predictors of self-efficacy for appropriate anticoagulant use. Patients with severer symptoms, lower satisfaction, perceived less benefit and perceived greater barriers reported lower self-efficacy for appropriate anticoagulant use. Addressing AF-related symptoms, satisfaction with services, perceived benefits and barriers of taking anticoagulants may help increase self-efficacy and lead to enhanced anticoagulation adherence.

Different from findings in previous studies,^{25 26} we found that medication adherence was not significantly related to anticoagulation treatment knowledge. This may be because most of these studies were conducted in different countries and only focused on patients treated with warfarin. Although our subjects showed poor understanding of anticoagulation treatment, they reported good adherence to anticoagulation treatment. This may be partially explained by the Taiwanese culture of obedience

to a physician's orders. The treatment knowledge scores were low in both warfarin and NOACs treatment groups, indicating the need for strengthening anticoagulation treatment patient education. Special attention should be paid to treatment-related issues, such as drug–food interactions, INR values, the timing of taking anticoagulants and how to prevent bleeding risks. These are areas that most of our subjects answered incorrectly.

This study had several limitations. First, the subjects were recruited from cardiology clinics of two teaching hospitals and may vary from those seen in other clinical settings. Thus, the results may not be generalisable outside this sample. Second, the cross-sectional nature of the study precluded an assessment of medication adherence change over time and did not permit us to determine causal relationships among the study variables. Third, a self-report questionnaire was used to measure medication adherence, which was subject to recall and social desirability biases. Finally, the influences of anticoagulation adherence on patients' treatment outcomes were not examined. Replication of the findings with longitudinal study design, objective measures of medication adherence and clinical outcome measures are warranted. Nevertheless, the study results showed no better adherence to NOACs compared with warfarin and present evidence for the importance of perceived barriers and self-efficacy on the adherence to anticoagulation therapy in patients with AF. Strategies to address perceived barriers and self-efficacy may be more likely to be translated to other population groups, as the influence of these factors on medication adherence has also been reported in studies with other populations.^{28 29}

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REFERENCES

- Chiang CE, TJ W, Ueng KC, *et al*. Guidelines of the Taiwan heart rhythm Society and the Taiwan Society of cardiology for the management of atrial fibrillation. *J Formos Med Assoc* 2016;2016:893–952.
- January CT, Wann LS, Alpert JS, *et al*. AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of cardiology/American heart association Task force on practice guidelines and the heart rhythm Society. *J Am Coll Cardiol* 2014;2014:e1–76.
- Kirchhof P, Benussi S, Kotecha D, *et al*. Esc guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *EP Europace* 2016;2016:1609–78.
- Kishore A, Vail A, Majid A, *et al*. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. *Stroke* 2014;45:520–6.
- Taiwan Heart Rhythm Society. The current situation cur and complications of atrial fibrillation in Taiwan, 2015. Available: <http://thrs.org.tw/people/content.asp?id=10> [Accessed 1 May 2017].
- Yu H-C, Tsai Y-F, Chen M-C, *et al*. Underuse of antithrombotic therapy caused high incidence of ischemic stroke in patients with atrial fibrillation. *Int J Stroke* 2012;7:112–7.
- Gamra H, Murin J, Chiang C-E, *et al*. Use of antithrombotics in atrial fibrillation in Africa, Europe, Asia and South America: insights from the International RealiseAF survey. *Arch Cardiovasc Dis* 2014;107:77–87.
- Mozaffarian D, Benjamin EJ, Go AS, *et al*. Heart disease and stroke statistics-2016 update: a report from the American heart association. *Circulation* 2016;133:e38–60.
- Hsieh FI, Lien LM, Chen ST, *et al*. Get with the Guidelines-Stroke performance indicators: surveillance of stroke care in the Taiwan stroke Registry: get with the Guidelines-Stroke in Taiwan. *Circulation* 2010;122:1116–23.
- Chao T-F, Liu C-J, Wang K-L, *et al*. Using the CHA2DS2-VASc Score for Refining Stroke Risk Stratification in 'Low-Risk' Asian Patients With Atrial Fibrillation. *J Am Coll Cardiol* 2014;64:1658–65.
- Lin SY, Chen YW, Kang HC, *et al*. Warfarin dosing algorithm: specific Inr goal for Asian population. *Formosa J Clin Pharm* 2015;23:189–202.
- Shore S, Carey EP, Turakhia MP, *et al*. Adherence to dabigatran therapy and longitudinal patient outcomes: insights from the Veterans health administration. *Am Heart J* 2014;167:810–7.
- Brown TM, Siu K, Walker D, *et al*. Development of a conceptual model of adherence to oral anticoagulants to reduce risk of stroke in patients with atrial fibrillation. *JMCP* 2012;18:351–62.
- O'Brien EC, Simon DN, Allen LA, *et al*. Reasons for warfarin discontinuation in the outcomes Registry for better informed treatment of atrial fibrillation (ORBIT-AF). *Am Heart J* 2014;168:487–94.
- Yao X, Abraham NS, Alexander GC, *et al*. Effect of adherence to oral anticoagulants on risk of stroke and major bleeding among patients with atrial fibrillation. *J Am Heart Assoc* 2016;5:1–13.
- Choi JC, Dibonaventura MD, Kopenhafer L, *et al*. Survey of the use of warfarin and the newer anticoagulant dabigatran in patients with atrial fibrillation. *Patient Prefer Adherence* 2014;8:167–77.
- Maglio C, Sra J, Paquette M, *et al*. Measuring quality of life and symptom severity in patients with atrial fibrillation. *Pacing Clin Electrophysiol* 1998;21.
- Dorian P, Burk C, Mullin CM, *et al*. Interpreting changes in quality of life in atrial fibrillation: how much change is meaningful? *Am Heart J* 2013;166:381–7.
- Waltz CF, Strickland O, Lenz ER. *Measurement in Nursing and Health Research*. New York, NY: Springer Publishing Company, 2010.
- DeVellis RF. *Scale development: theory and applications*. Los Angeles, CA: Sage, 2012: 109–10.
- Wang Y, Kong MC, Lee LH, *et al*. Knowledge, satisfaction, and concerns regarding warfarin therapy and their association with warfarin adherence and anticoagulation control. *Thromb Res* 2014;133:550–4.
- Orensky IA, Holdford DA. Predictors of noncompliance with warfarin therapy in an outpatient anticoagulation clinic. *Pharmacotherapy* 2005;25:1801–8.
- Risser J, Jacobson TA, Kripalani S. Development and psychometric evaluation of the self-efficacy for appropriate medication use scale (SEAMS) in low-literacy patients with chronic disease. *J Nurs Meas* 2007;15:203–19.
- Kripalani S, Risser J, Gatti ME, *et al*. Development and evaluation of the adherence to Refills and medications scale (arms) among low-literacy patients with chronic disease. *Value Health* 2009;12:118–23.
- Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67–74.
- Gazmararian J, Kripalani S, Miller MJ, *et al*. Factors associated with medication refill adherence in cardiovascular-related diseases: a focus on health literacy. *J GenIntern Med* 2006;21:1215–21.
- Zhao S, Zhao H, Wang X, *et al*. Factors influencing medication knowledge and beliefs on warfarin adherence among patients with atrial fibrillation in China. *Patient Prefer Adherence* 2017;11:213–20.
- Di Minno A, Spadarella G, Tufano A, *et al*. Ensuring medication adherence with direct oral anticoagulant drugs: lessons from adherence with vitamin K antagonists (VKAs). *Thromb Res* 2014;133:699–704.
- Mishra SI, Gioia D, Childress S, *et al*. Adherence to medication regimens among low-income patients with multiple comorbid chronic conditions. *Health Soc Work* 2011;36:249–58.