Rate of anticoagulant use, and factors associated with not prescribing anticoagulant in older Thai adults with non-valvular atrial fibrillation: A multicenter registry

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Abstract

Objectives To investigate the rate of anticoagulant use, the reasons for not prescribing anticoagulant, and the factors associated with non-prescription of anticoagulant in older Thai adults with non-valvular atrial fibrillation. Methods A multicenter registry of patients with non-valvular atrial fibrillation was conducted during 2014 to 2017 in Thailand. Demographic, medical history, antithrombotic medication, non-antithrombotic medication, and laboratory data were collected and analyzed. Data were compared between the older adult (≥ 65 years) and younger adult (< 65 years) groups. The reasons why anticoagulant was not prescribed were collected, and predictive factors were identified. Results A total of 3218 patients (1873 males) with an average age of 67.3 ± 11.3 years were included. Almost two-thirds (61.0%) of patients were in the older adult group. Anticoagulant was prescribed in 2422 patients (75.3%): 81.4% in the older adult group and 65.7% in the younger adult group. The three main reasons for not prescribing anticoagulant were already taking antiplatelets, patient refusal, and bleeding risk. These reasons were more common in older adults as compared to younger adults. Multivariate analysis revealed current use of antiplatelets to be the most important factor that predict the non-prescription of anticoagulant in older population. Conclusions The prevalence of anticoagulant prescription among older Thai adults with atrial fibrillation is 81.4%. Taking antiplatelet drugs was found to be the strongest reason that predicts the non-prescription of anticoagulant in this patient population. A guideline should be developed to optimize the use of anticoagulant and antiplatelet in older adults.

Keywords: Anticoagulant use; Multicenter registry; Non-valvular atrial fibrillation; Older Thai adults

1 Introduction

Many previous studies reported the efficacy of anticoagulation therapy for stroke prevention in patients with non-valvular atrial fibrillation that also have one or more risk factors for stroke. The CHA2DS2-VASc scoring system has been recommended as a tool to assess stroke risk. Practice guidelines recommend the use of anticoagulants in atrial fibrillation patients with a CHA2DS2-VASc score of 1 or more. Patients aged older than 75 years and patients with history of ischemic stroke or transient ischemic attack (TIA) are given a CHA2DS2-VASc score of 2 due to a stronger risk of developing stroke, whereas patients with risk factors like heart failure, diabetes, hypertension, or age 65–74 years are given a CHA2DS2-VASc score of 1. Although the risk of ischemic stroke is high in older adult population, and a significant proportion of these individuals should be prescribed anticoagulation therapy, many of them...
do not receive anticoagulant.[7–10] There are many reasons why anticoagulant is not prescribed, including fear of fall and bleeding risk.[7,11–13] Other studies reported that anticoagulant should not be withheld due to these reasons since the benefit of anticoagulant should outweigh the risk of treatment.[14,15] As a result, the debate continues regarding whether or not to prescribe anticoagulant in older adults with atrial fibrillation.

Accordingly, the aims of this study were to investigate the rate of anticoagulant use, the reasons for not prescribing anticoagulant, and the factors independently associated with not prescribing anticoagulant in older Thai adults with non-valvular atrial fibrillation.

2 Methods

2.1 Study population

A multicenter registry was conducted to enroll patients aged older than 18 years with non-valvular atrial fibrillation receiving treatment at 1 of 24 hospitals located across Thailand during the 2014 to 2017 study period. Details relating to the inclusion criteria, exclusion criteria, and study protocol were previously published.[16] The data collected in this study included clinical information, CHA2DS2-VASc score, HAS-BLED score, medications, and laboratory data (including international normalized ratio [INR]). Details of antithrombotic treatment were recorded. The reasons why anticoagulant was not prescribed were collected and analyzed, and factors that predict non-prescription of anticoagulant were identified. The protocol for this study was approved by the Institutional Review Board of each participating hospital, and all participating patients provided written informed consent.

A study nurse from each participating hospital collected and then entered the data into a web-based system. Data entry and data quality were monitored and verified by the central data management team. To further ensure the quality of the data, random site monitoring was performed, with approximately 70% of study sites being audited during the study period.

Patients were classified into either the older adult (≥ 65 years) group or the younger adult (< 65 years) group. Risk of ischemic stroke was classified into 3 groups according to CHA2DS2-VASc score, as follows: low risk = CHA2DS2-VASc score of 0; intermediate risk = CHA2DS2-VASc score of 1; and, high risk = CHA2DS2-VASc score of 2 or more. Risk of bleeding was classified into three groups according to HAS-BLED score, as follows: low risk = HAS-BLED score of 0; intermediate risk = HAS-BLED score of 1 to 2; and, high risk = HAS-BLED score of 3 or more.

2.2 Statistical analysis

SPSS Statistics version 22 (SPSS, Inc., Chicago, IL, USA) was used for all data analyses. Descriptive statistics were used to summarize demographic and clinical data. Normality of the continuous data has been tested by one-sample Komolgorov-Smirnov test. Data are presented as mean ± SD for continuous data with normal distribution, and number and percentage for categorical data. Student’s t-test was used to compare continuous data, and chi-square test was used to compare categorical data. Data were compared between the older adult (≥ 65 years) group and the younger adult (< 65 years) group. Univariate and multivariate logistic regression analyses were performed to identify factors significantly associated with the non-prescription of anticoagulant in older adults with atrial fibrillation. Diagnostic test of the multivariable regression model was evaluated by the C-statistics of the receiving operating characteristic curve. A P-value less than 0.05 was considered to be statistically significant.

3 Results

There was a total of 3218 patients enrolled, the average age was 67.3 ± 11.3 years, 1873 (58.2%) were male, and 1963 (61.0%) were aged ≥ 65 years (older adult group). Baseline demographic and clinical characteristics and antithrombotic medication use of the study population, are shown in Table 1. Older adult patients were more likely to be female, and were more likely to have a longer duration of atrial fibrillation, permanent type of atrial fibrillation, history of coronary artery disease (CAD), history of stroke or transient ischemic attack (TIA), hypertension, history of bleeding, greater CHA2DS2-VASc score, greater HAS-BLED score, devices, and greater use of anticoagulants—all compared to younger adult patients.

There were 796 (24.7%) patients who were not prescribed anticoagulant, including 365 (18.6%) patients in the older adult group and 431 (34.3%) patients in the younger adult group. The reasons for not prescribing anticoagulant in older adults are shown in Table 2. The common reasons for not prescribing anticoagulant in older adults were current use of antiplatelets, patient decision, bleeding risk, physician decision, fall risk, and compliance concern.

The overall rate of anticoagulant use was 75.3%; however, anticoagulant use was significantly higher among older adults than among younger adults (81.4% vs. 65.7%, respectively; P < 0.001). Figure 1 demonstrates that the rate of anticoagulant use increased when age group increased from < 65, 65–75, and ≥ 75 years, respectively. When we compared anticoagulant use between the older and younger
Table 1. Baseline demographic and clinical characteristics of the study population, and antithrombotic medications taken by the study population.

| Variables                            | All (n = 3,218) | Older adults (n = 1,963) | Younger adults (n = 1,255) | P-value |
|--------------------------------------|----------------|--------------------------|---------------------------|---------|
| Age, yrs                             | 67.3 ± 11.3    | 74.6 ± 6.5               | 56.0 ± 7.3                | < 0.001 |
| Male gender                          | 1873 (58.2%)   | 1053 (53.7%)             | 820 (65.3%)               | < 0.001 |
| Time after diagnosis of atrial fibrillation, yrs | 3.4 ± 3.4     | 3.81 ± 4.8               | 2.9 ± 3.5                 | < 0.001 |
| Atrial fibrillation                  |                |                          |                           | 0.018   |
| Paroxysmal                           | 1075 (33.4%)   | 619 (31.5%)              | 456 (36.3%)               |         |
| Persistent                           | 623 (19.4%)    | 376 (19.2)               | 247 (19.7%)               |         |
| Permanent                            | 1520 (47.2%)   | 968 (49.3%)              | 552 (44.0%)               |         |
| History of heart failure             | 875 (15.7%)    | 517 (26.3%)              | 358 (28.5%)               | 0.174   |
| History of coronary artery disease   | 505 (15.7%)    | 353 (18.0%)              | 152 (12.1%)               | < 0.001 |
| History of PCI                       | 232 (7.2%)     | 165 (8.4%)               | 67 (5.3%)                 | < 0.001 |
| History of ACS                       | 256 (8.0%)     | 185 (9.4%)               | 70 (5.6%)                 | < 0.001 |
| Devices                              | 330 (10.3%)    | 256 (13.0%)              | 74 (5.9%)                 | < 0.001 |
| History of TIA/ischemic stroke       | 555 (17.2%)    | 378 (19.3%)              | 177 (14.1%)               | < 0.001 |
| Hypertension                         | 2183 (67.8%)   | 1480 (75.4%)             | 703 (56.0%)               | < 0.001 |
| Diabetes mellitus                    | 777 (24.1%)    | 487 (24.8%)              | 290 (23.1)                | 0.271   |
| History of bleeding                  | 308 (9.6%)     | 218 (11.1%)              | 90 (7.2%)                 | < 0.001 |
| CHA2DS2-VASc score                   |                |                          |                           | < 0.001 |
| 0                                    | 207 (6.4%)     | 0 (0%)                   | 207 (16.5%)               |         |
| 1                                    | 419 (13.0%)    | 53 (2.7%)                | 366 (29.2%)               |         |
| ≥ 2                                  | 2592 (80.6%)   | 1910 (97.3)              | 682 (54.3%)               |         |
| HAS-BLED score                       |                |                          |                           | < 0.001 |
| 0                                    | 458 (14.2%)    | 6 (0.3%)                 | 452 (36.0%)               |         |
| 1–2                                  | 1190 (37.0)    | 1501 (76.5%)             | 756 (60.2%)               |         |
| ≥ 3                                  | 1570 (48.8%)   | 456 (23.2%)              | 47 (3.7%)                 |         |
| Antithrombotic medications           |                |                          |                           |         |
| Antiplatelets                        | 854 (26.5%)    | 502 (25.6%)              | 352 (28.0%)               | 0.121   |
| Aspirin alone                        | 657 (20.4%)    | 356 (18.1%)              | 301 (24.0%)               | < 0.001 |
| P2Y12 inhibitors alone               | 97 (3.0%)      | 71 (3.6%)                | 26 (3.1%)                 | < 0.001 |
| Aspirin plus P2Y12 inhibitors        | 94 (2.9%)      | 69 (3.5%)                | 25 (2.0%)                 | < 0.001 |
| Anticoagulants                       | 2422 (75.3%)   | 1,598 (81.4%)            | 824 (65.7%)               | < 0.001 |
| Warfarin                             | 2202 (68.5%)   | 1,460 (74.4%)            | 742 (59.1%)               | < 0.001 |
| NOACs                                | 220 (6.8%)     | 138 (7.0%)               | 82 (6.5%)                 | 0.586   |
| Anticoagulant plus 1 antiplatelet    | 255 (7.9%)     | 169 (8.6%)               | 86 (6.9%)                 | 0.041   |
| Anticoagulant plus 2 antiplatelets   | 39 (1.2%)      | 29 (1.5%)                | 10 (0.8%)                 | 0.041   |

Data are presented as mean ± SD or n (%). ACS: acute coronary syndrome; NOACs: non-vitamin K antagonist oral anticoagulants; PCI: percutaneous coronary intervention; TIA: transient ischemic attack.

Table 2. Reasons given for not prescribing anticoagulants (i.e., warfarin or NOACs).

| Reasons                          | All (n = 796) | Older adults (n = 365) | Younger adults (n = 431) | P-value |
|---------------------------------|--------------|-----------------------|--------------------------|---------|
| Already taking antiplatelet drugs | 211 (26.5%)  | 131 (35.9%)           | 80 (18.6%)               | < 0.001 |
| Patient preference              | 166 (20.9%)  | 117 (32.1%)           | 49 (11.4%)               | < 0.001 |
| Bleeding risk                   | 81 (10.2%)   | 67 (18.4%)            | 14 (3.2%)                | < 0.001 |
| Physician preference            | 83 (10.4%)   | 47 (12.9%)            | 36 (8.4%)                | 0.037   |
| Alcohol abuse                   | 1 (0.1%)     | 0                     | 1 (0.2%)                 | 0.357   |
| Fall risk                       | 21 (2.6%)    | 20 (5.5%)             | 1 (0.2%)                 | < 0.001 |
| Warfarin compliance concern     | 14 (1.8%)    | 11 (78.6%)            | 3 (21.4%)                | 0.013   |
| Taking medication contraindicated or cautioned for use with warfarin | 7 (0.9%) | 2 (0.5%) | 5 (1.4%) | 0.173 |
| Allergy                         | 0            | 0                     | 0                        |         |
| Low stroke risk                 | 318 (39.9%)  | 36 (9.9%)             | 282 (65.4%)              | < 0.001 |

Data are presented as n (%). NOACs: non-vitamin K antagonist oral anticoagulants.
adult groups relative to CHA2DS2-VASc score, no significant difference was observed between groups for either a CHA2DS2-VASc score of 1 or a CHA2DS2-VASc score of 2 or more (Figure 2A). The rate of anticoagulant use increased as the HAS-BLED score increased, which was consistent with the trend observed for the CHA2DS2-VASc score. The anticoagulant rate was not significantly different for those at high risk for bleeding compared between the older adult and younger adult groups (Figure 2B).

Table 3 shows comparisons of clinical information between older adult patients taking and not taking anticoagulant. Patients not prescribed anticoagulant were more likely to have paroxysmal atrial fibrillation, history of coronary artery disease, ischemic stroke or TIA, and current use of antiplatelets. Table 4 demonstrates univariate and multivariate analysis for factors associated with non-prescription of anticoagulant. Multivariate logistic regression analysis revealed that permanent atrial fibrillation ($P = 0.002$), history of coronary artery disease ($P < 0.001$), history of ischemic stroke/TIA ($P < 0.001$), and hypertension ($P = 0.049$), to be independent predictors that reduce the rate of non-prescription of anticoagulant whereas current use of antiplatelets ($P < 0.001$) were independent predictor that increase the rate of non-prescription of anticoagulant in older adults with non-valvular atrial fibrillation. Of those, current use of antiplatelets was identified as the strongest predictor (odds ratio [OR]: 58.682; 95% confidence interval [CI]: 40.5–85.0) (Table 4). The multivariable regression model has been developed and tested. The C-statistics of the model was 0.898 (0.877–0.920). Among the 502 older adult patients who used antiplatelets, only 60 patients (12.0%) had a history of percutaneous coronary intervention (PCI) or acute coronary syndrome (ACS) within 1 year and 482 patients (96.0%) had CHA2DS2-VASc score of 2 or more.

The reasons that the odds ratio of history of CAD in the prediction of non-prescription of anticoagulant from univariate analysis is in different direction from odds ratio from multivariate analysis is due to the interaction between history of CAD and antiplatelet on the rate of non-prescription of anticoagulant (interaction test < 0.001). Table 5 clearly demonstrate this interaction. Antiplatelet use markedly increased the rate of non-prescription of anticoagulant. When CAD patients did not use antiplatelet, the rate of non-prescription of anticoagulant is only 2.8%. Therefore, the odds ratio of univariate analysis of history of CAD for non-prescription of anticoagulant in Table 4 is > 1 (driven by the effect of antiplatelet), but < 1 in multivariate analysis. This explanation is also true for HAS-BLED score in Table 4. But for stroke/TIA, the odds ratio is <1 in univariate and multivariate analysis due to the rate of using antiplatelet in patients with stroke/TIA is less than those without stroke/TIA.

4 Discussion

The results of this multicenter study in patients with
Table 3. Characteristics of older adults compared between those taking and not taking anticoagulant.

| Characteristics                        | Older adults taking OAC (n = 1598) | Older adults not taking OAC (n = 365) | P-value |
|----------------------------------------|------------------------------------|--------------------------------------|---------|
| Age, yrs                               | 74.5 ± 6.4                         | 74.7 ± 7.0                           | 0.584   |
| Male gender                            | 857 (53.7%)                        | 196 (53.7%)                          | 1.000   |
| Time after diagnosis of atrial fibrillation, yrs | 3.9 ± 4.8                          | 3.5 ± 4.9                           | 0.240   |
| Type of atrial fibrillation            |                                    |                                      |         |
| Paroxysmal                             | 466 (29.2%)                        | 153 (41.9%)                          | < 0.001 |
| Persistent                             | 294 (18.4%)                        | 82 (22.5%)                           |         |
| Permanent                              | 838 (52.4%)                        | 130 (35.6%)                          |         |
| History of heart failure               | 413 (25.8%)                        | 104 (28.5%)                          | 0.300   |
| History of coronary artery disease     | 264 (16.5%)                        | 89 (24.4%)                           | < 0.001 |
| Devices                                | 206 (12.9%)                        | 50 (13.7%)                           | 0.730   |
| History of ischemic stroke/TIA         | 342 (21.4%)                        | 36 (9.9%)                            | < 0.001 |
| Hypertension                           | 1,216 (76.1%)                      | 264 (72.3%)                          | 0.132   |
| Diabetes mellitus                      | 398 (24.9%)                        | 89 (24.4%)                           | 0.835   |
| History of bleeding                    | 178 (11.1%)                        | 40 (11.0%)                           | 0.921   |
| Chronic kidney disease                 | 739 (54.7%)                        | 176 (56.4%)                          | 0.575   |
| CHA2DS2-VASc score                     |                                    |                                      |         |
| 1*                                     | 30 (1.9%)                          | 25 (6.3%)                            |         |
| ≥ 2                                    | 1568 (98.1%)                       | 342 (93.7%)                          |         |
| HAS-BLED score                         |                                    |                                      | 0.002   |
| 0–2                                    | 1249 (78.2%)                       | 258 (70.7%)                          |         |
| ≥ 3                                    | 349 (21.8%)                        | 107 (29.3%)                          |         |
| Taking antiplatelets                   | 201 (12.6%)                        | 301 (82.5%)                          | < 0.001 |

Data presented as mean ± SD or n (%). *CHA2DS2-VASc score had a minimum score of 1 in patients older than 65 years. OAC: oral anticoagulant; TIA: transient ischemic attack.

Table 4. Univariate and multivariate analysis for factors significantly associated with non-prescription of anticoagulant in older Thai adults with atrial fibrillation.

| Factors                              | Univariate analysis | P-value | Multivariate analysis | OR (95% CI) | P-value |
|--------------------------------------|---------------------|---------|-----------------------|--------------|---------|
| Male gender                          | 1.001 (0.797–1.258) | 0.990   |                       |              | 0.006   |
| Atrial fibrillation                  |                     | < 0.001 |                       |              |         |
| Paroxysmal                           | Ref                 |         |                       |              |         |
| Persistent                           | 0.839 (0.616–1.142) | 0.264   | 0.831 (0.545–1.269)   | 0.392        |
| Permanent                            | 0.466 (0.358–0.607) | < 0.001 | 0.574 (0.401–0.823)   | 0.003        |
| History of heart failure             | 1.143 (0.887–1.473) | 0.300   |                       |              |         |
| History of CAD                       | 1.629 (1.240–2.141) | < 0.001 | 0.254 (0.171–0.376)   | < 0.001      |
| Devices                              | 1.073 (0.769–1.495) | 0.679   |                       |              |         |
| History of ischemic stroke/TIA       | 0.402 (0.279–0.578) | < 0.001 | 0.585 (0.351–0.974)   | 0.039        |
| Hypertension                         | 0.821 (0.635–1.061) | 0.132   |                       |              |         |
| Diabetes mellitus                    | 0.972 (0.746–1.267) | 0.835   |                       |              |         |
| History of bleeding                  | 0.982 (0.683–1.412) | 0.921   |                       |              |         |
| Chronic kidney disease               | 1.073 (0.838–1.376) | 0.575   |                       |              |         |
| CHA2DS2-VASc score                   |                     |         |                       |              |         |
| 1*                                   | Ref                 |         |                       |              |         |
| ≥ 2                                  | 0.284 (0.163–0.496) | < 0.001 | 0.323 (0.135–0.777)   | 0.012        |
| HAS-BLED score                       |                     |         |                       |              |         |
| 0–2                                  | Ref                 |         |                       |              |         |
| ≥ 3                                  | 1.484 (1.150–1.915) | 0.002   | 0.449 (0.299–0.674)   | < 0.001      |
| Taking antiplatelets                 | 32.688 (24.031–44.463) | < 0.001 | 75.794 (50.446–113.878) | < 0.001   |

*CHA2DS2-VASc score had a minimum score of 1 in patients older than 65 years. CAD: coronary artery disease; Ref: reference; TIA: transient ischemic attack.
Table 5. Additional analysis to determine the interaction between history of CAD and antiplatelet use on the outcome measurement of non-prescription rate of OAC demonstrated by the rate of non-prescription of OAC, and univariate and multivariate logistic regression analysis.

| Groups | Rate of non-prescription of OAC |
|--------|---------------------------------|
| No CAD, no antiplatelet (n = 1317) | 4.6% |
| CAD, no antiplatelet (n = 144) | 2.8% |
| No CAD, antiplatelet (n = 293) | 73.7% |
| CAD, antiplatelet (n = 209) | 40.7% |

Odds ratio, 95% confidence interval, and p-value for univariate analysis of factors predicting non-prescription of OAC

| Groups | Odds ratio, 95% confidence interval, and p-value for univariate analysis of factors predicting non-prescription of OAC |
|--------|-------------------------------------------------------------------------------------------------|
| No CAD, no antiplatelet | Ref |
| CAD, no antiplatelet | 0.599 (0.214–1.672), P = 0.327 |
| No CAD, antiplatelet | 58.769 (40.712–84.834), P < 0.001 |
| CAD, antiplatelet | 14.361 (9.836–20.968), P < 0.001 |

Odds ratio, 95% confidence interval, and p-value of multivariate analysis of factors predicting non-prescription of OAC*

| Groups | Odds ratio, 95% confidence interval, and p-value of multivariate analysis of factors predicting non-prescription of OAC* |
|--------|-------------------------------------------------------------------------------------------------|
| No CAD, no antiplatelet | Ref |
| CAD, no antiplatelet | 0.682 (0.242–1.917), P = 0.468 |
| No CAD, antiplatelet | 83.327 (54.534–127.322), P < 0.001 |
| CAD, antiplatelet | 19.088 (12.394–29.397), P < 0.001 |

*Adjusted for factors with significant p-values (other than history of CAD and antiplatelet) from univariate analysis in Table 4. CAD: coronary artery disease; OAC: oral anticoagulant; Ref: reference.

non-valvular atrial fibrillation revealed a rate of anticoagulant use of 81.4% among older adult patients compared to 65.7% among younger adult patients. The strongest predictor of non-prescription of anticoagulant in older adult patients with non-valvular atrial fibrillation was the current use of antiplatelets.

The overall rate of anticoagulant use in this study was 75.3%, which is higher than the rates reported from many previous studies.[17,18] There are some possible explanations for this disparity among studies. First, this is a relatively recent atrial fibrillation registry, and many updated practice guidelines for the management of patients with atrial fibrillation emphasize the use of anticoagulant for stroke prevention.[19] In addition, most patients in our registry were cared for by cardiologists, and cardiologists are generally more confident in their use of anticoagulants than are internists and general practitioners.[20]

We focused on older adult (≥65 years) population in this study since practice guidelines recommend the use of anticoagulant in this group.[4] If we disregard other risk factors for atrial fibrillation-related stroke, age 65–74 is assigned a CHA2DS2-VASc score of 1, whereas age more than 75 is given a CHA2DS2-VASc score of 2. The rate of ischemic stroke was 3 and 5.5 times higher in the 65–74 and > 75 age groups compared to those aged less than 65 years.[8] Major guidelines recommend the use of anticoagulant in patients with a CHA2DS2-VASc score of 1 or more. Therefore, those with atrial fibrillation and age > 65 years should be on anticoagulant unless there is a specific contraindication. Data from the United Kingdom General Practice Research Database revealed that older adult patients, especially those aged older than 80 years, were usually undertreated with anticoagulant, even after adjusting for bleeding risk.[21] A study from China reported that among patients with atrial fibrillation and age older than 75 years, the rate of anticoagulant use was only 41% in patients with a CHA2DS2-VASc score of 2 or more, and patient medication compliance was found to be poor.[22]

In the present study, the rate of anticoagulant use was 81.4% in older adult population and 65.7% in the younger adult group. These rates are higher than the rates reported in Thai population from earlier study, and they are higher than the rates reported from China.[9,23] However, these rates are lower than the rates reported from many European countries.[24] This difference in rates among studies has some possible explanations. First, practice guidelines are generally more widely adopted in developed countries than they are in developing countries. Many patients and physicians fear bleeding that could result from the use of anticoagulants, especially since Asian population tend to bleed more than Western population.[11] Moreover, many patients have a fear of falling, which may lead to bleeding.[15,26] This may be a misconception since experts
suggest that the benefit of anticoagulant outweighs the risk of bleeding from a fall.\textsuperscript{[14,15]} Most importantly, many physicians and patients believe that the use of an antiplatelet agent can prevent stroke in patients with atrial fibrillation.\textsuperscript{[27]} In fact, the effect of antiplatelets for atrial fibrillation-related stroke prevention is very minimal or none.\textsuperscript{[4]} and this assertion is supported by the results of a randomized clinical study conducted in Asian population.\textsuperscript{[28]}

The results of this study revealed current use of antiplatelets to be one of the major reasons for not prescribing anticoagulant in older adult patients. There is a significant interaction between history of CAD and antiplatelet use on rate of non-prescription of anticoagulants. History of CAD increased risk of non-prescription of anticoagulants due to patients with history of CAD use antiplatelet 59.2\% whereas those without history of CAD use antiplatelet only 18.2\%. When CAD patients use antiplatelet, the rate of non-prescription of anticoagulants is high but the rate of non-prescription of anticoagulants was only 2.8\% when CAD patients do not use antiplatelet. Not only is it a misconception that antiplatelets can prevent stroke in patients with atrial fibrillation, the use of antiplatelets in many patients in our study might be related to other concomitant diseases, such as CAD. Many physicians believe that patients with stable CAD need to be on antiplatelets when they actually need to be on anticoagulant.\textsuperscript{[29]} In fact, many atrial fibrillation and CAD practice guidelines indicate that patients with stable CAD do not need antiplatelets if they need to be on anticoagulant.\textsuperscript{[30–32]} Anticoagulant when combined with antiplatelets can increase the risk of bleeding compared to being on anticoagulant alone, as shown by the United Kingdom General Practice Research Database among 70,760 patients with atrial fibrillation,\textsuperscript{[33]} and from a Danish registry of 82,854 patients with atrial fibrillation that demonstrated an increased risk of bleeding with hazard ratios of 1.8 (warfarin plus aspirin) and 3.1 (warfarin plus clopidogrel) compared to warfarin monotherapy.\textsuperscript{[34]} Using data from a Danish nationwide registry, Lamberts, \textit{et al.}\textsuperscript{[29]} showed that warfarin plus antiplatelet significantly increased the risk of bleeding without additional stroke prevention benefit in patients with atrial fibrillation and stable CAD. The aforementioned misconceptions can lead to fears about prescribing anticoagulant when it is thought that patients need to continue antiplatelets. In this setting, the correct therapy decision is often that antiplatelet therapy should be discontinued, and anticoagulant therapy should be started. The findings of our study support this therapeutic strategy since we found current use of antiplatelets to be the strongest independent predictor of a decision not to prescribe or take anticoagulant (OR: 58.7, 95\% CI: 40.5–85.0; \(P < 0.001\)). A sub-evaluation of older adult patients with CAD that took antiplatelets revealed that only 12\% had a history of PCI or ACS during the past 12 months. Therefore, only a small proportion of patients in our study required concurrent antiplatelet and anticoagulant.

High CHA2DS2-VASC score decrease rate of non-prescription of anticoagulant. Since 482 patients (96.0\%) out of 502 older adult patients who used antiplatelets had CHA2DS2-VASc score of 2 or more, it is unlikely that antiplatelet therapy might be the right indication in patients with low CHA2DS2-VASc score.

This study has some mentionable limitations. First, this study enrolled patients mainly from a tertiary care hospital setting, and this may limit the generalizability of our results to other care settings. Second, the outcome data from this study is not yet completely collected. Third, since the use of antiplatelet is the strongest predictor for non-prescription of anticoagulant, there might be a conflicting result on univariate and multivariate analysis in Table 4 depend on the interaction between each factor and antiplatelet use on the non-prescription rate of anticoagulant. Lastly, since patient and physician preference are part of the reason for non-prescription of anticoagulant in Table 2, the true reasons for non-prescription of anticoagulant in this group are not explored.

In conclusion, anticoagulant was prescribed in 81.4\% of the older adult Thai patients with non-valvular atrial fibrillation, and taking antiplatelet drugs was found to be the most significant reason why anticoagulant was not prescribed in the older adult group. Since the risk of stroke is high among older adults with atrial fibrillation, a strategy to improve guideline attainment for antithrombotic use in this group should be developed and implemented.

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**References**

1. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have non-valvular atrial fibrillation. \textit{Ann Intern Med} 2007; 146: 857–867.

2. Connolly SJ, Pogue J, Eikelboom J, \textit{et al.} Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of international normalized ratio control.
achieved by centers and countries as measured by time in therapeutic range. *Circulation* 2008; 118: 2029–2037.

3 Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137: 263–272.

4 Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016; 37: 2893–2962.

5 Chiang CE, Okumura K, Zhang S, et al. 2017 consensus of the Asia Pacific Heart Rhythm Society on stroke prevention in atrial fibrillation. *J Arrhythm* 2017; 33: 345–367.

6 Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. *Eur Heart J* 2012; 33: 1500-1510.

7 Fang MC, Go AS, Hylek EM, et al. Age and the risk of warfarin-associated hemorrhage: the anticoagulation and risk factors in atrial fibrillation study. *J Am Geriatr Soc* 2006; 54: 1231–1236.

8 Mant J, Hobbs FD, Fletcher K, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet* 2007; 370: 493–503.

9 Gao Q, Fu X, Wei JW, et al. Use of oral anticoagulation among stroke patients with atrial fibrillation in China: the ChinaQUEST (Quality evaluation of stroke care and treatment) registry study. *Int J Stroke* 2013; 8: 150-154.

10 Phrommintikul A, Detmuntarat P, Prasertwityakij N, Wongcharoen W. Prevalence of atrial fibrillation in Thai elderly. *J Geriatr Cardiol* 2016; 13: 270-273.

11 Aribou ZM, Mondry A. Anticoagulation needs in asians with atrial fibrillation: a mythbuster. *Ann Acad Med Singapore* 2014; 43: 275–278.

12 Inoue H, Nozawa T, Okumura K, et al. Attitudes of Japanese cardiologists toward anticoagulation for nonvalvular atrial fibrillation and reasons for its underuse. *Circ J* 2004; 68: 417–421.

13 Lip GY, Kamath S, Jafri M, et al. Ethnic differences in patient perceptions of atrial fibrillation and anticoagulation therapy: the West Birmingham Atrial Fibrillation Project. *Stroke* 2002; 33: 238–242.

14 Donze J, Clair C, Hug B, et al. Risk of falls and major bleeds in patients on oral anticoagulation therapy. *Am J Med* 2012; 125: 773–778.

15 Rao MP, Vinereanu D, Wojdyla DM, et al. Clinical outcomes and history of fall in patients with atrial fibrillation treated with oral anticoagulation: insights from the ARISTOTLE Trial. *Am J Med* 2018; 131: 269–275 e262.

16 Krittayaphong R, Winijkul A, Methavigul K, et al. Risk profiles and pattern of antithrombotic use in patients with non-valvular atrial fibrillation in Thailand: a multicenter study. *BMC Cardiovasc Disord* 2018; 18: 174.

17 Gage BF, Boechler M, Doggette AL, et al. Adverse outcomes and predictors of underuse of antithrombotic therapy in medicare beneficiaries with chronic atrial fibrillation. *Stroke* 2000; 31: 822–827.

18 Waldo AL, Becker RC, Tapson VF, et al. Hospitalized patients with atrial fibrillation and a high risk of stroke are not being provided with adequate anticoagulation. *J Am Coll Cardiol* 2005; 46: 1729–1736.

19 Camm AJ, Accetta G, Ambrosio G, et al. Evolving antithrombotic treatment patterns for patients with newly diagnosed atrial fibrillation. *Heart* 2017; 103: 307–314.

20 Turakhia MP, Hoang DD, Xu X, et al. Differences and trends in stroke prevention anticoagulation in primary care vs cardiology specialty management of new atrial fibrillation: The Retrospective Evaluation and Assessment of Therapies in AF (TREAT-AF) study. *Am Heart J* 2013; 165: 93–101 e101.

21 Scowcroft AC, Lee S, Mant J. Thromboprophylaxis of elderly patients with AF in the UK: an analysis using the General Practice Research Database (GPRD) 2000-2009. *Heart* 2013; 99: 127–132.

22 Yu LJ, Chen S, Xu Y, Zhang ZX. Clinical analysis of antithrombotic treatment and occurrence of stroke in elderly patients with nonvalvular persistent atrial fibrillation. *Clin Cardiol* 2018.

23 Yang X, Li Z, Zhao X, et al. Use of warfarin at discharge among acute ischemic stroke patients with nonvalvular atrial fibrillation in China. *Stroke* 2016; 47: 464–470.

24 Stroke prevention in atrial fibrillation study. Final results. *Circulation* 1991; 84: 527–539.

25 Shen AN, Brar SS, et al. Racial/ethnic differences in the risk of intracranial hemorrhage among patients with atrial fibrillation. *J Am Coll Cardiol* 2007; 50: 309–315.

26 Kakkar AK, Mueller I, Bassand JP, et al. Risk profiles and antithrombotic treatment of patients newly diagnosed with atrial fibrillation at risk of stroke: perspectives from the international, observational, prospective GARFIELD registry. *PLoS One* 2013; 8: e63479.

27 Guo Y, Wang H, Tian Y, et al. Time trends of aspirin and warfarin use on stroke and bleeding events in Chinese patients with new-onset atrial fibrillation. *Chest* 2015; 148: 62–72.

28 Sato H, Ishikawa K, Kitabatake A, et al. Low-dose aspirin for prevention of stroke in low-risk patients with atrial fibrillation: Japan Atrial fibrillation stroke trial. *Stroke* 2006; 37: 447–451.

29 Lamberts M, Olesen JB, Ruwald MH, et al. Bleeding after initiation of multiple antithrombotic drugs, including triple therapy, in atrial fibrillation patients following myocardial infarction and coronary intervention: a nationwide cohort study. *Circulation* 2012; 126: 1185–1193.

30 Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/ AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Prac-
tice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2014; 64: 1929–1949.

31 Task Force M, Montalescot G, Sechtem U, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013; 34: 2949–3003.

32 Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2016; 37: 267–315.

33 Azoulay L, Dell’Aniello S, Simon T, et al. The concurrent use of antithrombotic therapies and the risk of bleeding in patients with atrial fibrillation. Thromb Haemost 2013; 109: 431–439.

34 Hansen ML, Sorensen R, Clausen MT, et al. Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation. Arch Intern Med 2010; 170: 1433–1441.