Stroke risks and patterns of warfarin therapy among atrial fibrillation patients post radiofrequency ablation

A real-world experience

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Abstract

We assessed the thromboembolic risks of atrial fibrillation (AF) patients who had undergone radiofrequency ablation (RFA) using the CHADS2-VASc risk scoring system and further investigated the patterns of warfarin use for thromboprophylaxis according to patient thromboembolic risk scores.

In this study, we analyzed the stroke risks of patients who had undergone RFA for AF at our hospital between March 2014 and June 2016 using the CHADS2, CHADS2-VASc, and Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (>65 years) (HAS-BLED) scoring systems. We retrieved medications, comorbidities, and initial warfarin dosage data. The primary outcome was the percentage of patients initiated with warfarin therapy for stroke prophylaxis in AF who had a CHADS2-VASc score of 0.

Totally, 309 patients were initiated with warfarin therapy for stroke prophylaxis in AF post-RFA. The baseline warfarin dosage was 2.76 ± 0.61 mg. The baseline CHADS2-VASc score was 2.93 ± 1.96 and 40 (12.6%) had a CHADS2-VASc score of 0, 42 (13.9%) had a CHADS2-VASc score ≥1, and 227 (73.5%) had a CHADS2-VASc score ≥2. The baseline CHADS2 score was 2.17 ± 1.55 and 48 (15.5%) had a CHADS2 score of 0, 68 (22.0%) had a CHADS2 score of 1, and 193 (62.5%) had a CHADS2 score ≥2. The baseline HAS-BLED score was 1.25 ± 0.91 and 69 (22.3%) had a HAS-BLED score of 0, 121 (39.2%) had a HAS-BLED score of 1, and 119 (38.5%) had a HAS-BLED score ≥2. Patients aged <65 years or 65 years, male and female patients, patients with or without hypertension, coronary heart disease, or diabetes mellitus, and patients with or without previous stroke/transient ischemic attack differed significantly in stroke risks by CHADS2-VASc, CHADS2, and HAS-BLED scores for stroke risks. Patients with different baseline international normalized ratio differed significantly in CHADS2-VASc scores. Furthermore, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and statins were of statistical significance for stroke risks.

The majority of AF patients post-RFAs was of high stroke risk and received warfarin thromboprophylaxis in accordance with national guidelines. Our findings suggest that low and intermediate stroke risk patients should be evaluated for stroke risks and risk factors so that tailored warfarin thromboprophylaxis therapy can be given and inappropriate use of warfarin in AF patients can be avoided.

Abbreviations: ACCP = The American College of Chest Physicians, ACEI = angiotensin-converting enzyme inhibitors, AF = atrial fibrillation, ARB = angiotensin receptor blockers, INR = international normalized ratio, RFA = radiofrequency ablation.

Keywords: atrial fibrillation, CHADS2-VASc, risk factors, stroke, warfarin

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia and remains a major cause of morbidity and mortality, and it is associated with a 5-fold increase in the risk of stroke.[1–3] Catheter ablation therapy for AF has gained a prominent role in maintenance of sinus rhythm versus antiarrhythmic medication. The 2014 American College of Cardiology/American Heart Association (ACC/AHA)/Heart Rhythm Society guideline has emphasized the use of catheter ablation in selected patients as first-line therapy for paroxysmal AF and also recommended the use of the CHA2DS2-VASc score for risk stratification of stroke.[4]

A crucial part of AF management lies in the appropriate use of thromboprophylaxis, contingent upon proper assessment of stroke and bleeding risks. It remains critical that given anticoagulation-related bleeding complications, truly low-risk AF patients who do not require antithrombotic therapy be not given thromboprophylaxis while truly at-risk patients are
appropriately managed by thromboprophylaxis with oral anticoagulation.

Warfarin, as the oldest oral anticoagulant drug, is still in current use for long-term anticoagulant therapy to effectively reduce ischemic/thromboembolic stroke risk in AF patients,[2,3,5,6] with a 64% decrease in relative risk of stroke and a 26% reduction in all-cause mortality.[7] However, warfarin remains vastly underused in China, with <10% of AF patients initiated with warfarin therapy.[8] Although it has been speculated that clinicians in China may overestimate the bleeding risk of warfarin, and do not fully appreciate the importance and effectiveness of warfarin therapy, thromboprophylaxis in AF patients remains suboptimal in China, with an 8% thromboprophylaxis rate in prestroke patients with AF.[9] An analysis of data from the China National Stroke Registry showed only 15.2% moderate and 16.4% high-risk patients who had a history of AF were on warfarin therapy.[10] Suboptimal thromboprophylaxis has also been reported for populations of other ethnic origins.[11]

Although investigators have reported the overuse of warfarin or non-vitamin K antagonist oral anticoagulants for thromboprophylaxis in truly low-risk AF patients and their underuse in at-risk AF patients,[12,13] few studies have described the patterns of thromboprophylaxis with warfarin or non-vitamin K antagonist oral anticoagulants in patients who have undergone radiofrequency ablation (RFA). In the present study, we assessed the thromboembolic risks of AF patients who had undergone RFA using the CHADS2-VASc risk scoring system and further investigated the patterns of warfarin use for thromboprophylaxis according to patient thromboembolic risk scores. The findings of this study will provide useful insights into thromboprophylaxis in AF patients that can be geared toward thromboembolic risks in a real-world setting.

2. Patients and methods

2.1. Patient selection

In this real-world study, we analyzed the stroke risks of patients who had undergone RFA for AF at our hospital between March 2014 and June 2016. Stroke risks were assessed using the CHADS2, CHADS2-VASc, and HAS-BLED scoring systems. Patients with paroxysmal AF, an unclear medical history, chronic AF, or post-RFA AF/atrial tachycardia were excluded.

The study protocol was approved by the institutional review board of Cardiac Center, Beijing Chaoyang Hospital and patient consent was not required because of the retrospective nature of the study.

2.2. Stroke risk stratification

We retrieved the demographic and baseline data of the study patients, including age, gender, body mass index (BMI), baseline international normalized ratio (INR), medications, comorbidities, and initial warfarin dosage. The CHADS2-VASc scoring system assigns 1 point for a history of chronic heart failure, hypertension, diabetes mellitus, vascular disease, including peripheral artery disease, aortic plaque or previous myocardial infarction, age 65 to 74 years, and female patients, and 2 points for a history of stroke or peripheral arterial embolism and age ≥75 years. As aortic plaque was not assessed, we defined vascular disease as previous myocardial infarction or peripheral artery disease for the purpose of the current analysis. A secondary analysis was performed using the CHADS2 score, which was calculated by assigning 1 point each for a history of congestive heart failure, hypertension, age ≥75 years, and diabetes mellitus and 2 points for a history of stroke or transient ischemic attack. A secondary analysis was also performed using the HAS-BLED score. According to the ACC/AHA and American College of Chest Physician (ACCP) guidelines, AF patients were considered low risk for stroke if the CHADS2-VASc score was 0, intermediate risk if the score was 1, and high if the score was ≥2.[14] AF patients were considered low risk for stroke if the CHADS2 score was zero, intermediate risk if the score was 1, and high risk if the score was ≥2. Furthermore, AF patients were considered low risk for stroke if the HAS-BLED score was 0.

2.3. Study endpoints

The primary outcome was the percentage of patients initiated with warfarin therapy for stroke prophylaxis in AF who had a CHADS2-VASc score of 0. The secondary outcomes were the percentage of patients initiated with warfarin therapy for stroke prophylaxis in AF who had a CHADS2-VASc score of 1 and those who had a CHADS2-VASc score of ≥2.

2.4. Statistical analysis

Categorical data were reported as number and percentage and comparison between groups was done using chi-square test or Fisher exact test. Continuous data were expressed as mean±SD and comparison between groups was done using Student t test for normally distributed data or Wilcoxon 2-sample test for non-normally distributed data. One-way analysis of variance analysis was used for normally distributed data and Kruskal-Wallis test for non-normally distributed data. When multiple group comparison was statistically different, Student-Newman-Keuls test was further performed for comparisons between groups. Statistical analysis software for SAS9.3 (the SAS Institute, Cary, NC) was used and the test was 2 sided and P < .05 was considered statistically significant.

3. Results

3.1. Demographic and baseline characteristics of the study population

Totally, 309 patients were initiated with warfarin therapy for stroke prophylaxis in AF post RFA. The baseline warfarin dosage was 2.76 ± 0.61 mg. The demographic and baseline characteristics of the study population are shown in Table 1. They included 172 (55.7%) men and 137 (44.3%) women and their mean age was 62.9 ± 10.6 years and 150 (48.5%) patients were 65 years or older. Two hundred and six (66.9%) patients had hypertension, 73 (23.6%) had diabetes, and 32 (10.4%) had previous stroke or transient ischemic attack. The baseline INR was 1.2 ± 0.84.

3.2. The study outcomes

The stroke risk scores of CHADS2, CHADS2-VASc, and HAS-BLED are shown in Table 2. The baseline CHADS2-VASc score was 2.93 ± 1.96 for the study population and 40 (12.95%) had a CHADS2-VASc score of 0, 42 (13.6%) had a CHADS2-VASc score of 1, and 227 (73.5%) had a CHADS2-VASc score ≥ 2. In addition, the baseline CHADS2 score was 2.17 ± 1.55 for the study population and 48 (15.5%) had a CHADS2 score of 0, 68 (22.0%) had a CHADS2 score of 1, and 193 (62.5%) had a CHADS2 score ≥ 2. Furthermore, the baseline HAS-BLED score was 1.25 ± 0.91 for the study population and 69 (22.3%) had a
Table 1
Demographic and baseline characteristics of the study population.

| Variables | N (%) |
|-----------|-------|
| No.       | 309   |
| Age, y, mean (SD) | 62.9 (10.6) |
| < 65      | 159 (51.46) |
| ≥ 65      | 140 (46) |
| Female sex | 137 (44.34) |
| Body mass index, kg/cm², mean (SD) | 25.91 (3.32) |
| Comorbidities |         |
| Hypertension | 206 (66.88) |
| Type 2 diabetes | 73 (23.62) |
| Previous stroke or transient ischemic attack | 32 (10.39) |
| Coronary heart disease | 57 (18.51) |
| Cor pulmonale | 4 (1.30) |
| Lung disease | 1 (0.32) |
| Hypothyroidism | 4 (1.30) |
| Baseline INR, mean (SD) | 1.20 (0.84) |

Data are expressed as N (%) unless otherwise indicated. INR = international normalized ratio, SD = standard deviation.

HAS-BLED score of 0, 121 (39.2%) had a HAS-BLED score of 1, and 119 (38.5%) had a HAS-BLED score ≥ 2.

3.3. Patient demographic and baseline variables and stroke risks

We further analyzed the stroke risks of patients who were initiated with warfarin therapy for stroke prophylaxis in AF post-RFA. Patients aged < 65 years or ≥ 65 years, male and female patients, patients with or without hypertension, coronary heart disease, or diabetes mellitus, and patients with or without previous stroke/transient ischemic attack differed significantly in stroke risks by CHADS2-VASC (Table 3). Similar findings were demonstrated using CHADS2 and HAS-BLED scores for stroke risks (Supplementary Tables 1 and 2, http://links.lww.com/MD/B975). Furthermore, patients with different baseline INR differed significantly in CHADS2-VASC scores (Wilcoxon 2-sample test, P = .018), whereas BMI and starting dose of warfarin had no apparent effect on CHADS2-VASC scores (P > .05) (Supplementary Table 3, http://links.lww.com/MD/B975). Similar findings were seen in CHADS2 scores (Supplementary Table 4, http://links.lww.com/MD/B975), whereas no statistically significant difference was observed in baseline INR, BMI, and starting dose of warfarin (Supplementary Table 5, http://links.lww.com/MD/B975).

3.4. Patient medication characteristics and stroke risks

The medication characteristics of the study population are shown Table 4. Most patients (88.07%) took antiarrhythmic drugs and amiodarone was the most common antiarrhythmic drug taken (73.84%). Few patients took aspirin (3.82%) or clopidogrel (2.64%). In addition, 36.2% of the patients took post-RFA angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and 30.9% took post-RFA statins. Furthermore, 42.1% of the patients took beta-blockers.

We further investigated whether medications taken by patients on warfarin prophylaxis impacted on the stroke risks of the study population according to stratification by CHADS2-VASC scores. We found a significant statistical difference in stroke risks between patients who took post RFA ACEI or ARB and those who did not (χ² test, P < .000) and between patients who took post-RFA statins and those who did not (χ² test, P = .008) (Table 5). However, no significant statistical difference was observed in stroke risks between patients who took aspirin, clopidogrel, anti-arrhythmic agents, or beta-blockers and those who did not (Fisher exact test or χ² test, P > .05). Similar findings were demonstrated using CHADS2 scores for stroke risks (Supplementary Table 6, http://links.lww.com/MD/B975). On the contrary, we observed significant statistical difference was observed in stroke risks by the HAS-BLED risk scores between patients who took post-RFA ACEI or ARB, post-RFA statins, aspirin, anti-arrhythmic agents, or beta-blockers and those who did not (P < .05) (Supplementary Table 7, http://links.lww.com/MD/B975).

4. Discussion

Currently, scant data are available on the patterns of thromboprophylaxis with warfarin or non-vitamin K antagonist oral anticoagulants in patients who have undergone RFA. The present study provides useful insights into thromboprophylaxis in AF patients who had undergone RFA. We found that, in the real-world setting, although three quarters of our patients had high stroke risk (CHADS2-VASC score ≥2) and received appropriate warfarin thromboprophylaxis, a significant proportion of our patients who were of low or intermediate stroke risks and received warfarin thromboprophylaxis. Our findings are of practical clinical significance, indicating that stroke risks and risk factors should be better assessed in patients who have undergone RFA to avoid the risk and cost associated with inappropriate use of warfarin and tailored warfarin thromboprophylaxis therapy should be instituted.

AF is one of the most frequently seen arrhythmia and its incidence increases along age. Although catheter ablation therapy for AF has increased in popularity in maintenance of sinus rhythm versus antiarrhythmic medication, few studies have described the patterns of thromboprophylaxis with warfarin in patients who have undergone RFA. In the present study, we analyzed the stroke risks and medication patterns of 309 AF patients who were initiated with warfarin therapy for stroke prophylaxis post-RFA. We found that the majority (73.5%) of our patients had high stroke risk (CHADS2-VASC score ≥2),
whereas a meaningful proportion (26.5%) of the patients had low or intermediate stroke risk (CHADS2-VASC=0 or 1). This is consistent with earlier reports for stroke risks in AF patients.\(^\text{12-17}\) The percentage of patients with low or intermediate stroke risk was higher with the CHADS2 scoring system (37.5%). The ACCP guidelines recommend thromboprophylaxis with warfarin in patients with high stroke risks, whereas patients with low or intermediate stroke risks are not treated with thromboprophy-


taxis with warfarin in the absence of compelling complications. Our study indicated that at least one-quarter of our patients who were of low or intermediate stroke risks received thromboprophylaxis with warfarin.

Low-to-intermediate stroke risk patients with AF pose a therapeutic challenge and require an individualized approach to stroke prevention.\(^\text{13}\) AF patients with intermediate stroke risks may receive thromboprophylaxis with warfarin if they have one compelling risk factor such as hypertension or diabetes. Hypertension was present in 61.9% and diabetes was found in 14.3% of the intermediate risk patients. The thromboprophylaxis rate in AF patients in China was reported to be only 8%.\(^\text{9}\) Data from the China National Stroke Registry showed that only 15.2% of AF patients with intermediate stroke risk received warfarin therapy.\(^\text{12}\) Although these studies indicate that thromboprophylaxis remains suboptimal for AF patients in China, our findings highlight another issue in the management of AF patients that low-to-intermediate stroke risk patients with AF may be unduly provided with warfarin thromboprophylaxis, thus unnecessarily being subjected to the cost, inconvenience, and adverse effects of warfarin therapy. We found that the CHADS2 scoring system yielded a far higher proportion of AF patients with low-to-intermediate stroke risk (37.5% vs. CHADS2-VASC score 26.5%). Close to half (48.53%) of the patients with intermediate stroke risk by the CHADS2 scoring system did not have hypertension and approximately 9 in 10 patients (89.71%) did not have diabetes. If patients were managed according to stroke risk by the CHADS2 scoring system, an even greater proportion of low-to-intermediate stroke risk patients with AF would undergo thromboprophylaxis with warfarin. We further found that age, sex, hypertension, coronary disease, diabetes, and previous stroke were of statistical significance for stroke risks, which are consistent with previous findings.\(^\text{5,13}\) Our findings suggest that the CHADS2-VASC scoring system in combination with risk factor assessment of individual AF patients could offer an effective approach to identity at risk patients for warfarin thromboprophylaxis while excluding those who are not indicated for the therapy.

We further analyzed the medication patterns of the study population. Antiarrhythmic drugs remained the most common medication for the patients, with 86.1% of the population taking antiarrhythmic drugs. We found that ACEIs or ARBs and statins were of statistical significance for stroke risks by the CHADS2-VASC scoring system. Aspirin and beta blockers were also of statistical significance when stroke risks were assessed using the HAS-BLED system. Our findings are similar to those previously reported.\(^\text{12,17}\) The CHADS2-VASC system was first used in Europe, and compared with CHADS2 score system, age (65–74 years), vascular disease and sex were added. The CHADS2-VASC system put more emphasis on risk factors and thus is more useful in prediction of high-risk population.\(^\text{13}\) Despite that CHADS2 score system is easier to use in community clinics, the CHADS2-VASC system is currently being evaluated in clinics in China. Patients post-RFA are classified into a different risk group to rationally manage patient warfarin intake.

### Table 3

Demographic and baseline characteristics and stroke risks of the study population by CHADS2_VASC.

| Variables                      | CHADS2_VASC >1 | CHADS2_VASC =0 | CHADS2_VASC =1 | Total | Missing | Statistical tests | Statistical volume | P     |
|--------------------------------|----------------|----------------|----------------|-------|---------|-------------------|-------------------|-------|
| Age, y                         | 83 (36.56)     | 40 (100.0)     | 36 (85.71)     | 159   | 0       | χ² test           | 77.62             | .000  |
| <65                            | 144 (63.44)    | 0 (0.00)       | 6 (14.29)      | 150   |          |                   |                   |       |
| ≥65                            |                |                |                |       |         |                   |                   |       |
| Sex                           |                |                |                |       |         |                   |                   |       |
| Male                          | 98 (43.17)     | 34 (85.00)     | 40 (95.24)     | 172   | 0       | χ² test           | 54.95             | .000  |
| Female                        | 123 (56.83)    | 6 (15.00)      | 2 (4.76)       | 131   |          |                   |                   |       |
| Hypertension                  |                |                |                |       |         |                   |                   |       |
| No                            | 48 (21.24)     | 38 (95.00)     | 16 (38.10)     | 102   | 1       | χ² test           | 84.02             | .000  |
| Yes                           | 178 (78.76)    | 2 (5.00)       | 26 (61.90)     | 206   |          |                   |                   |       |
| Coronary heart disease        |                |                |                |       |         |                   |                   |       |
| No                            | 174 (76.99)    | 39 (97.50)     | 38 (80.48)     | 251   | 1       | χ² test           | 12.07             | .002  |
| Yes                           | 52 (23.01)     | 1 (2.50)       | 4 (9.52)       | 57    |          |                   |                   |       |
| Diabetes                      |                |                |                |       |         |                   |                   |       |
| No                            | 160 (70.48)    | 40 (100.0)     | 36 (85.71)     | 236   | 0       | χ² test           | 18.76             | .000  |
| Yes                           | 67 (29.52)     | 0 (0.00)       | 6 (14.29)      | 73    |          |                   |                   |       |
| Previous stroke or transient ischemic attack | 14 (5.00) | 0 (0.00) | 4 (9.52) | 18 | 0 | χ² test | 9.86 | .002 |
| No                            | 194 (85.84)    | 40 (100.0)     | 42 (100.0)     | 276   | 1       | Fisher exact test | —                | .000  |
| Yes                           | 32 (14.16)     | 0 (0.00)       | 0 (0.00)       | 32    |          |                   |                   |       |

CHADS2-VASC=rheumatic heart failure or left ventricular dysfunction, hypertension, age ≥75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65–74 and sex category (female).

### Table 4

Medication characteristics of the study population.

| Medications                        | N (%)       |
|-----------------------------------|-------------|
| Post radiofrequency ablation ACEIs or ARBs | 104 (36.24) |
| Post-radiofrequency ablation statins | 94 (30.92)  |
| Aspirin                           | 10 (3.28)   |
| Clopidogrel                       | 8 (2.64)    |
| Antiarrhythmic drugs              |             |
| Amiodarone                        | 223 (73.84) |
| Sotalol                           | 4 (1.32)    |
| Propafenone                       | 39 (12.91)  |
| Beta-blockers                     | 128 (42.11) |
One limitation of the present study is that the study was carried out at a single institution in a tertiary care setting. This real-world setting excluded patients in a secondary or primary care setting; these patients may have different stroke risk profiles and exhibit different patterns of warfarin thromboprophylaxis. In the future, a multi-institution study including different care settings should be carried out to fully assess the thromboembolic risks of AF patients who have undergone RFA and provide risk-appropriate thromboprophylaxis.

5. Conclusions

Our real-world analysis of AF patients post-RFA demonstrated that the majority of AF patients was of high stroke risk and received warfarin thromboprophylaxis in accordance with national guidelines. Low and intermediate stroke risk patients also received warfarin thromboprophylaxis, in the presence of compelling indications in certain patients. Our findings suggest that low and intermediate stroke risk patients should be evaluated for stroke risks and risk factors so that tailored warfarin thromboprophylaxis therapy can be given and inappropriate use of warfarin in AF patients can be avoided.

References

[1] Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139-51.
[2] Fang MC, Go AS, Chang Y, et al. Warfarin discontinuation after starting atorvastatin. J Am Coll Cardiol 2008;52:865-8.
[3] Putnam A, Gu X, Haymart B, et al. The changing characteristics of atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Europace 2008;10:674-83.
[4] Littrell R, Flaker G. Implications for your practice: Important changes in the 2014 guideline for the management of patients with atrial fibrillation. Circulation 2015;132:2102-10.
[5] Nieuwlaat R, Capucci A, Lip GY, et al. Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation. Eur Heart J 2006;27:3018-26.
[6] Rowan SB, Bailey DN, Bublitz CE, et al. Trends in anticoagulation for atrial fibrillation in the U.S.: an analysis of the national ambulatory medical care survey database. J Am Coll Cardiol 2007;49:1563-5.
[7] Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007;146:857-67.
[8] Hu D, Sun Y. Epidemiology, risk factors for stroke, and management of atrial fibrillation in China. J Am Coll Cardiol 2009;52:865-8.
[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;8:150-4.
[10] Wang C, Yang Z, Wang C, et al. Significant underuse of warfarin in patients with nonvalvular atrial fibrillation: results from the China national stroke registry. J Stroke Cerebrovasc Dis 2014;23:1137-43.
[11] Hirano T, Kaneko H, Mishima S, et al. Suboptimal anticoagulant management in Japanese patients with nonvalvular atrial fibrillation receiving warfarin for stroke prevention. J Stroke Cerebrovasc Dis 2017;26:2102-10.
[12] Nieuwlaat R, Capucci A, Lip GY, et al. Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation. Eur Heart J 2006;27:3018-26.
[13] Meilzig A, Zimmermann M, Urban F, et al. Atrial fibrillation management by practice cardiologists: a prospective survey on the adherence to national guidelines in the real world. Europace 2008;10:674-80.
[14] Lai KK, Chan PH, Yiu KH, et al. Roles of the CHADS2 and CHA2DS2-VASc scores in post-myocardial infarction atrial fibrillation: a population-based study. Am J Med 2016;129:843-9.
[15] Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(suppl):546S-928.
Marcucci M, Lip GY, Nieuwlaat R, et al. Stroke and bleeding risk co-distribution in real-world patients with atrial fibrillation: the Euro Heart Survey. Am J Med 2014;127:979–86, e2.

Kornej J, Hindricks G, Kosiuk J, et al. Comparison of CHADS2, R2CHADS2, and CHA2DS2-VASc scores for the prediction of rhythm outcomes after catheter ablation of atrial fibrillation: the Leipzig Heart Center AF Ablation Registry. Circ Arrhythm Electrophysiol 2014;7:281–7.

Mitchell LB, Southern DA, Galbraith D, et al. Prediction of stroke or TIA in patients without atrial fibrillation using CHADS2 and CHA2DS2-VASc scores. Heart 2014;100:1524–30.

Olesen JB, Torp-Pedersen C, Hansen ML, et al. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0–1: a nationwide cohort study. Thromb Haemost 2012;107:1172–9.