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Gac Med Mex. 2016;152:425-30

GACETA MÉDICA DE MÉXICO

ORIGINAL ARTICLE

Characterisation of thromboembolic risk in a Mexican population with non-valvular atrial fibrillation and its effect on anticoagulation (MAYA Study)

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Abstract

Objective: *To evaluate the risk of stroke and bleeding using the CHA_2DS_2-VASc and HAS-BLED scores in Mexican patients with atrial fibrillation and to analyze whether the risk score obtained determined treatment decisions regarding antithrombotic therapy.* **Methods:** *This is an observational, retrospective study in Mexican patients recently diagnosed with atrial fibrillation. The risk of stroke was assessed using the CHA_2DS_2-VASc scores. The bleeding risk was evaluated using the HAS-BLED score. The frequency of use of antithrombotic therapy was calculated according to the results of the score risk assessment.* **Results:** *A total of 350 patients with non-valvular atrial fibrillation were analyzed. A 92.9% of patients had a high risk (score ≥ 2) of stroke according to the CHA_2DS_2-VASc score and only 17.2% were treated with anticoagulants. A high proportion of patients with atrial fibrillation (72.5%) showed both a high risk of stroke and a high risk of bleeding based on HAS-BLED score.* **Conclusions:** *In this group of patients with atrial fibrillation, from Northeast Mexico, there is a remarkably underutilization of anticoagulation despite the high risk of stroke of these patients.* (Gac Med Mex. 2016;152:425-30)

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KEY WORDS: *Atrial Fibrillation. Anticoagulation. Thrombotic Risk. Mexico. CHA2DS2-VASc. HAS-BLED.*

Introduction

In clinical practice, atrial fibrillation (AF) is the most common cardiac arrhythmia, and it affects nearly 1-2% of the general population[1]. The incidence of this condition increases with age and, therefore, a future increase in the incidence of AF is expected owing to progressive ageing of the population. AF is considered to be a high emboligenic-risk arrhythmia. In this sense, non-valvular AF is the most common cause of cardioembolic stroke, and it accounts for 25% of ischemic strokes and 50% of cardioembolic strokes. AF-diagnosed patients' initial management should focus on symptom relief and AF-associated risk assessment. The risk of having a stroke depends on the presence or absence of certain factors. Since the group of patients with AF is highly heterogeneous and has different comorbidities, each patient should be individually assessed in order to establish the risk-benefit balance of

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Date of reception: 14-06-2016
Date of acceptance: 06-07-2016

starting prophylactic treatment with antithrombotic agents. Different international clinical practice guidelines recommend the use of specifically developed scales to stratify the risk for stroke in patients with AF and base treatment decisions on scores obtained with these scales[2,3].

The simplest scheme for stroke risk evaluation in patients with AF is the $CHADS_2$ scale[4]. This scale, extensively used until a few years ago, allowed establishing the need to start treatment with anticoagulant or antiplatelet agents depending on risk factors that were present (heart failure, high blood pressure [HBP], age ≥ 75 years, diabetes mellitus (DM), and scoring 2: previous stroke/transient ischemia attack [TIA]). The CHA_2DS_2-VASc scale was proposed as an alternative risk scheme that substituted $CHADS_2$-based scoring in clinical practice[5]. This scale allows stratifying patients that in the previous $CHADS_2$ scale had low or intermediate risk at high risk, which makes them candidates to receive oral anticoagulation in order to try to reduce the incidence of stroke. The CHA_2DS_2-VASc scale includes 3 additional risk factors: age between 64 and 74 years, female gender and vascular disease (previous myocardial infarction/peripheral artery disease).

Anticoagulant therapy is highly effective in reducing stroke risk in patients with AF[6]. However, in the initial evaluation of patients with AF it is also necessary to assess the potential risk of hemorrhage prior to starting anticoagulation. To assess the risk for hemorrhage in patients with AF, specific scales such as HAS-BLED were developed[7]. From the point of view of this scale, thorough treatment control should be maintained in patients at high risk of hemorrhage in order to prevent the onset of hemorrhagic events.

The purpose of the present study was to assess the risk of stroke based on the CHA_2DS_2-VASc scale in patients with non-valvular AF staged in the Cardiology Department outpatient clinic and to analyze if the risk score had an impact on antithrombotic treatment decisions. On the other hand, hemorrhagic risk was assessed according to the HAS-BLED scale.

Methods

This was a single-center, observational, retrospective study in AF-diagnosed Mexican patients attended to from January 2011 through December 2012 at the Outpatient Clinic of the Cardiology Department, dependent of the Internal Medicine Head Office of the Cd. Madero Petróleos Mexicanos Regional Hospital, which looks after a geographical population of 82,000 inhabitants.

In the present analysis, only patients with non-valvular AF were assessed. Male and female patients, older than 18 years, with recent AF diagnosis documented on any medical report or electrocardiographic registry, and with complete medical history and prior cardiovascular disease diagnoses were included. As an exclusion criterion, previous history of illicit drugs consumption precluded patients' participation in the study.

The types of AF were defined based on the European clinical practice guidelines for the management of AF[3]. Paroxysmal FA was defined as self-limited AF, usually within a 48-h period, although paroxysms can continue for up to 7 days. Persistent AF was considered when an AF episode lasted more than 7 days or when it had to be stopped by cardioversion, either pharmacological or electrical. Long-lasting persistent FA is that which has lasted one year or more by the moment adopting a rhythm-control strategy is decided. Finally, permanent FA is defined when the arrhythmia is accepted by the patient (and the physician).

Stroke risk was assessed for every patient based on CHA_2DS_2-VASc. Hemorrhagic risk was assessed according to the HAS-BLED scale. The frequency of antithrombotic treatment use (antiplatelet or anticoagulant agents) was calculated depending on the results of stroke risk stratification (low risk, moderate risk and high risk) obtained with the CHA_2DS_2-VASc scale.

Descriptive statistics are presented for all variables obtained: mean and standard deviation (SD) for continuous variables and frequencies for categorical variables. All analyses were carried out with the SPSS statistical package, version 16.0.

Results

Of a total of 400 patients, 350 had non-valvular AF. Clinical and demographic characteristics of the patients included in the present article are described in table 1. Patients' mean age was 76.1 ± 10.4 years. Of these, 56.3% were females. HBP was the most common comorbidity in the study population (86.3%). Other comorbidities with high prevalence in the study population were DM (42%), history of ischemic heart disease (22.9%), previous embolism (20%) and heart failure (16%). Previous history of hemorrhage of was found in 6.3%.

With regard to the type of AF, 53.4% of patients had paroxysmal FA, 4.3% persistent FA, 7.4% long-standing persistent FA and 34.9% permanent FA. Of total patients with FA, 43 (12.3%) were not receiving any kind of antithrombotic treatment. 250 (71.3%) were on

Table 1. Clinical and demographic characteristics of patients included in the study

Characteristic	Patients (n = 350)
Age, mean ± SD (years)	76.1 ± 10.4
Females	197 (56.3%)
Alcohol consumption	16 (4.6%)
Current smokers	35 (10%)
High blood pressure	302 (86.3%)
Diabetes mellitus	147 (42%)
Heart failure	56 (16%)
Previous embolisms	70 (20%)
Ischemic heart disease	80 (22.9%)
Cardiac pacemaker	16 (4.6%)
Peripheral artery disease	17 (4.9%)
Impaired renal function	21 (6%)
Impaired liver function	10 (2.9%)
Previous history of hemorrhage	22 (6.3%)
Thyroid disease	31 (8.6%)
Chronic obstructive pulmonary disease	23 (6.6%)

SD: standard deviation

treatment with antiplatelet agents, 54 (15.4%) received anticoagulants and 3 (0.9%) were on treatment with a combination of antiplatelet and anticoagulant agents.

When stroke risk was assessed based on the CHA_2DS_2-VASc scale, 92.9% (n = 325) of patients were at elevated risk (≥ 2 score) of experiencing a stroke and, therefore, candidates to receive anticoagulant treatment (Table 2). However, only 56 patients (17.2%) at high risk for stroke based on the CHA_2DS_2-VASc scale were receiving treatment with anticoagulants (16.3% anticoagulants and 0.9% anticoagulants in combination with antiplatelet agents) (Fig. 1).

Table 3 presents hemorrhagic risk according to the HAS-BLED scale. Up to 72.8% of patients were at high risk of hemorrhage (HAS-BLED ≥ 3). An elevated percentage of patients with non-valvular FA (72.5%) had an elevated risk for stroke and hemorrhage according to the CHA_2DS_2-VASc and HAS-BLED scales (Table 4).

Discussion

Stroke-risk early assessment in patients newly diagnosed with AF and introduction of anticoagulant treatment in patients at high risk can allow for stroke incidence to be decreased. International clinical practice guidelines recommend using stroke risk stratification scales as a simple and easy-to-remember tool that

Table 2. Stroke risk according to the CHA2DS2-VASc scale

CHA_2DS_2-VASc	Risk	Patients (n = 350) n (%)
0	Low risk	10 (2.9)
1	Moderate risk	15 (4.3)
2	High risk	25 (7.1)
3	High risk	66 (18.9)
4	High risk	90 (25.7)
5	High risk	76 (21.7)
6	High risk	33 (9.4)
7	High risk	28 (8.0)
8	High risk	7 (2.0)
9	High risk	0 (0.0)

Table 3. Hemorrhagic risk according to the HAS-BLED scale

HAS-BLED	Risk	Patients (n = 350) n (%)
0	–	1 (0.3)
1	–	29 (8.3)
2	–	65 (18.6)
3	High risk	165 (47.1)
4	High risk	72 (20.6)
5	High risk	13 (3.7)
6	High risk	4 (1.1)
7	High risk	1 (0.3)
8	High risk	–
9	High risk	–

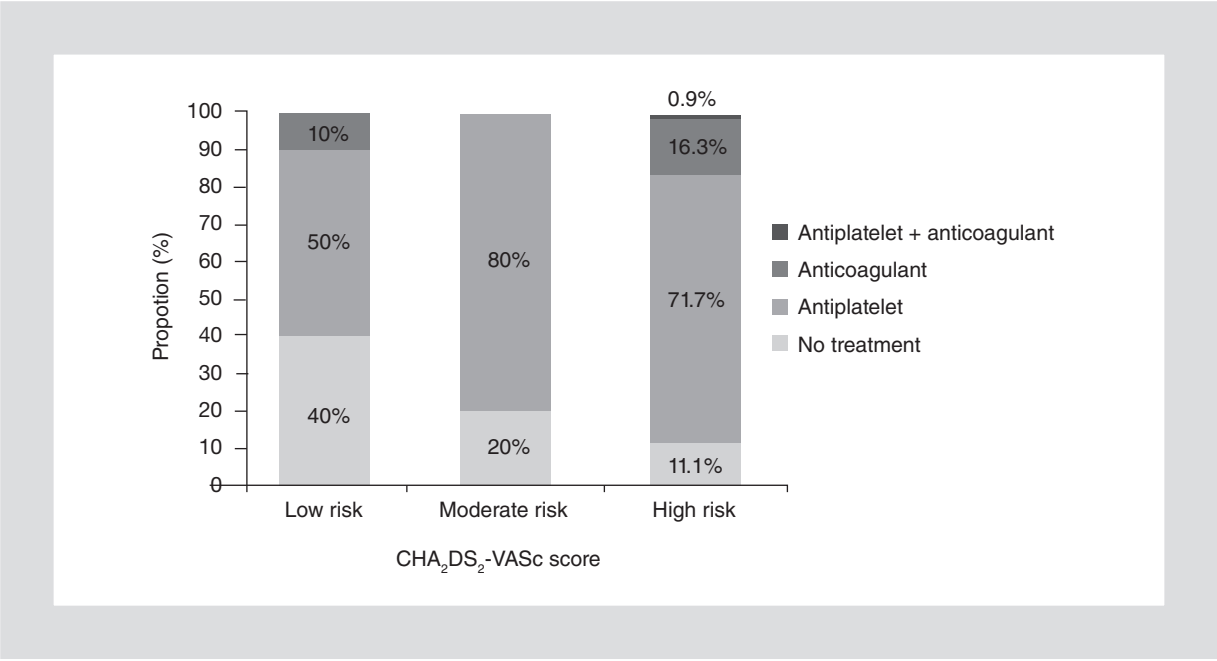

Figure 1. *Antithrombotic treatment received based on stroke risk as measured with the CHA_2DS_2-VASc scale.*

enables helping to decide the best treatment for patients[3]. In patients with $CHADS_2 \geq 2$ or CHA_2DS_2-VASc ≥ 2 classification, prolonged treatment with orally administered anticoagulants is recommended.

The results of the present retrospective study in Mexican patients indicate that an elevated percentage of newly diagnosed patients with non-valvular AF have an risk for stroke: 92.9% according to the CHA_2DS_2-VASc scale. In spite of the elevated thromboembolic risk in the study population, the number of anticoagulant-treated patients is significantly reduced: only 17.2% at high risk according to the CHA_2DS_2-VASc scale.

Several studies conducted in different countries proposed anticoagulants general low-use in spite of evidences in favor of these treatments and of being one of the mainstays of pharmacological treatment for patients with non-valvular AF at high risk of stroke[8-13]. In spite of the large variability of figures between studies, the proportion of patients receiving adequate treatment is estimated to range from 15 to 79%[11]. The rate of anticoagulant underutilization in our series would, therefore, be within the highest among studies conducted in other countries.

Vitamin K antagonists (VKA) are characterized by complex pharmacokinetics, need for prothrombin time continuous monitoring and dose adjustments, risk of hemorrhage, poor treatment compliance, interactions with other drugs and increased costs owing to continuous surveillance and to the treatment itself[11]. The introduction to clinical practice of novel oral anticoagulants, such as dabigatran, rivaroxaban and apixaban, is expected to enable anticoagulant treatment use to be increased in patients with AF at high risk for stroke. The new oral anticoagulants show a series of advantages such as fixed-dose administration, low potential for interaction with other drugs and no need for continuous monitoring of laboratory parameters[14].

Given that oral anticoagulation is not free of downsides, the opportunity to revceive this kind of treatment should always be assessed on an individual basis. The points that should be evaluated include the risk for hemorrhagic complications, the capacity to maintain prolonged anticoagulation and patients' own preferences[3]. Hemorrhagic risk assessment in patients with AF is fundamental for correct management. In the present study we have seen how a large proportion of patients show high risk for stroke and high risk for hemorrhage according to the HAS-BLED scale (72.5%). The use of VKA in these patients should be carried out with extreme caution or the possibility of other alternatives such as the new oral anticoagulants should be assessed. The results of clinical trials conducted with this new generation of anticoagulants have allowed for lower risk of hemorrhage in comparison with conventional

Table 4. Contingency table for hemorrhagic risk and stroke risk based on the CHA_2DS_2-VASc score

	HAS-BLED < 3 (high risk)	HAS-BLED ≥ 3 (high risk)	Total
CHA_2DS_2-VASc < 2 (Low or moderate risk)	24 (6.9%)	1 (0.3%)	25
CHA_2DS_2-VASc ≥ 2 (High risk)	71 (20.3%)	254 (72.5%)	325
Total	95	255	350

anticoagulants to be demonstrated. Thus, one clinical trial that compared apixaban treatment versus warfarin allowed for a reduction in the risk for major hemorrhage higher than 31% in patients treated with this factor Xa inhibitor to be observed[15]. Lower hemorrhagic risk has also been observed with dabigatran[16]. In the case of rivaroxaban, lower risk of intracranial hemorrhage and hemorrhage with fatal outcome has been observed in comparison with warfarin[17].

No previous studies assessing stroke risk in patients with non-valvular AF and their antithrombotic management are available in our country. The only registry in patients with AF is ReMeFa, which was designed with the purpose to gather information of AF management in Mexico, either by rhythm control or rate control[18].

Conclusions

In conclusion, the present study conducted among non valvular FA-diagnosed Mexican patients has allowed evidencing that an elevated percentage of patients at high risk of having a stroke do not receive treatment with anticoagulants in spite of recommendations on their use. The implementation of medical education programs among cardiologists who treat patients with AF might help to establish stroke-prevention adequate strategies based on the presence of risk factors and propitiate, as a consequence, a reduction in the incidence of resulting medical emergencies. The new oral anticoagulants show a wide range of advantages with regard to conventional anticoagulants and constitute a new option of treatment of choice for the clinician, who should individually assess for each patient the thromboembolic and hemorrhageic risks associated with the use of anticoagulants.

Appendix

For the risk factors included in the CHA_2DS_2-VASc scale, HBP was defined by a blood pressure determination higher than 140/190 mmHg, HBP prior diagnosis or the need to take antihypertensive medication.

For the diagnosis of diabetes, previous diagnosis verification in the medical record, specific pharmacological management being followed, or consecutive record of 2 fasting blood-glucose values higher than 126 mg/dl was accepted.

Stroke was regarded as positive if ischemic, hemorrhagic or transient stroke diagnosis was included in the medical record or any medical report.

History of ischemic heart disease was considered to be positive if there was a previous history of acute myocardial infarction, stable or unstable angina pectoris, percutaneous or surgical coronary bypass grafting or positive ischemia-inducing test (ergometry, scintigraphy, stress echocardiography, etc.).

Heart failure was recorded in patients with at least one hospital admission owing to this condition, patients with signs and symptoms of heart failure plus one consistent imaging test (chest X-ray or echocardiogram).

Encoded as peripheral arterial disease was a history of gait claudication, lower limb bypass grafting, amputation or established diagnosis of the condition.

With regard to the risk factors included in the HAS-BLED scale, a patient was defined as having impaired renal function when he/she required dialysis, had received renal transplant or had creatinine concentrations higher than 2.26 mg/dl. The presence of impaired liver function was established in those patients with chronic liver disease (e.g., cirrhosis) or with biochemical evidence of significant hepatic disorder (bilirubin more than twice the upper limit of normal, in association with transaminase levels thrice the upper limit of normal). History of hemorrhage or bleeding was established as a previous history of hemorrhage or bleeding predisposition (e.g., anemia, etc.). Finally, a labile international normalization ratio (INR) was defined as an INR value little time within the therapeutic interval (< 60%).

Funding

The authors did not receive any remuneration at all to carry out this study/article. An agency provided support for editorial development, which was funded by Bristol Myers Squibb de México.

Conflict of interests

The authors declare not having any conflicts of interests.

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