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Analysis of the CHA_2DS_2-VASc score in patients with inadequate anticoagulation control

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Abstract

Among the tools for assessing the risk of thromboembolic events, the CHA_2DS_2-VASc score stands out, which contributes to the identification of patients that are eligible for the use of anticoagulant therapy, which is a great aid in thromboembolic prophylaxis. The present study aims to characterize patients with inadequate control of anticoagulation according to their CHA_2DS_2-VASc score. Information was collected from patients being followed up at an anticoagulation clinic associated with a teaching hospital in Minas Gerais. Patients accompanied at the clinic between August and December 2017, taking warfarin for at least 180 days, with a chronic indication for anticoagulation, and with at least values from two results of the International Normalized List (INR) test were included. 434 patients were identified and 202 with inadequate anticoagulation control. For patients with inadequate control, the CHA_2DS_2-VASc was calculated, which is performed by the sum of risk factor scores for thromboembolic events. Patients were classified as low (0 points), moderate (1 point), or high (≥ 2 points) risk. An association was also made between the score and variables that characterize the context of the patients, such as the municipality of residence and the target therapeutic range of the INR. It is noteworthy that 107 (53.0%) had hypertension; 96 (47.5%) had peripheral arterial, coronary or aortic disease; 62 (30.7%) had a previous stroke; and 27 (13.4%) had diabetes. A considerable percentage of patients with CHA_2DS_2-VASc ≥ 2 (n = 191; 94.5%) was identified, which indicates a high risk for the occurrence of thromboembolic events and reinforces the importance of adequate anticoagulant pharmacotherapy. Regarding the association between demographic characteristics and the results of the CHA_2DS_2-VASc score, an association was identified between the CHA_2DS_2-VASc score and city of residence ($p<0.05$), with no statistical significance being identified between the CHA_2DS_2-VASc score and the INR target therapeutic range ($p>0.05$).

Keywords: Atrial Fibrillation. Warfarin. Aging.

INTRODUCTION

According to the World Health Organization, cardiovascular diseases are currently the leading causes of death in the world[1]. Among these, rheumatic heart disease, congenital heart disease, deep vein thrombosis, and atrial fibrillation (AF) stand out; the latter of which is the most common cardiac arrhythmia in the world[2,3]. According to studies published by the Global Burden of Disease, it is possible to find clear evidence that the prevalence of AF has increased globally, with population aging being one of the main reasons for this increase[4].

It is estimated that, in the United States, the number of adults with AF will double by the year 2050, with a higher prevalence being

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identified among patients with advanced age, ranging from 0.1% among people under 55 years old to 9.0% in patients aged 80 years and over. In addition, there is a higher prevalence among men than among women, regardless of age group[3]. AF directly increases the risk of stroke, hospital admissions, and death, and the use of anticoagulants is indicated for the prevention of these events[5].

Among the drugs used in anticoagulant therapy, warfarin, a competitive inhibitor of vitamin K epoxide reductase, is a coumarin derivative. This enzyme is responsible for reducing vitamin K to its hydroquinone form, which is a substrate in the synthesis of some of the major coagulation factors (II, VII, IX, and X)[6]. As a result of inhibition, vitamin K-dependent coagulation factors will have low biological activity, which reduces the risk of thrombus formation but increases the risk of bleeding complications. In addition, it is known that the use of warfarin requires monitoring, as this drug has interactions with several drugs and foods, resulting in a wide dose-response variability[7].

Patients using warfarin need to undergo tests periodically, and monitoring is done by the International Normalized List (INR)[6]. From a series of INR values, it is possible to assess the quality of anticoagulation by calculating the Time in Therapeutic Range (TTR), which represents the percentage of time the patient had INR values within the therapeutic range. The TTR is influenced by some patient conditions, such as the ability to understand the treatment, medication adherence, and possible drug and food interactions[8].

Among the tools for assessing the risk of thromboembolic events, the CHA_2DS_2-VASc score stands out, which contributes to the identification of patients with AF that are eligible for the use of anticoagulant therapy, which is a great aid in thromboembolic prophylaxis. The CHA_2DS_2-VASc can be used in clinical practice in order to determine the stratification of the patient's thromboembolic risk and to assist in decision making, contributing to the care process.

Assessing the risk of thromboembolic events in patients using warfarin contributes to the validation of the indication for pharmacotherapy. This becomes even more interesting in patients with low anticoagulation quality, as the CHA_2DS_2-VASc score may indicate an unnecessary anticoagulant use in patients who do not show clinical effectiveness with the use of pharmacotherapy. It is considered important to characterize the profile of patients according to this score, especially in middle-income countries such as Brazil, where it is understood that there is a lack of oral anticoagulant indications. The use of the score could help to validate the indication for oral anticoagulants, thus contributing to the rational use of warfarin. Furthermore, the characterization of patients according to the CHA_2DS_2-VASc score can contribute to the identification of patients at higher risk of thromboembolic events as well as the establishment of specific monitoring strategies. Therefore, the aim of this study was to characterize patients with inadequate anticoagulation control in a specialized anticoagulation clinic, according to the CHA_2DS_2-VASc score.

MATERIALS AND METHODS

This was a descriptive study, carried out in an anticoagulation clinic located in Minas Gerais. This clinic was implemented with the aim of offering a multidisciplinary follow-up to patients discharged from the hospital who were referred to a periodic monitoring of warfarin use. The outpatient team is made up of pharmacists, doctors, and nurses.

According to institutional protocol, the patient must have undergone the INR exam within 48 hours before the appointment, and presented the result to the professional (doctor or pharmacist) responsible for their care. At this time, an evaluation of the INR history and complete anamnesis was carried out, including lifestyle habits, eating routines and medications in use. The decision-making involved warfarin dose adjustments, if necessary, and providing guidelines for anticoagulant treatment and rescheduling the next appointment. The frequency with which INR tests should be performed and the magnitude of dose adjustments are indicated by the institutional protocol.

Eligible outpatients were those using warfarin for a period equal to or greater than 180 days, with an indication for chronic anticoagulation, had at least two INR results recorded in the period from August to December 2017, and who presented low TTR (<60%).

Data were extracted from the outpatient's computerized record system, followed by manual checking of 2199 data points generated in the medical records of 434 patients.

The variables collected through the computerized report were: TTR; indication for anticoagulation; and factors for CHA_2DS_2-VASc scoring, namely gender, age, congestive heart failure (CHF) or ventricular ejection fraction (LVEF) below 40%, hypertension arterial disease, diabetes mellitus, previous occurrence of stroke or other thromboembolic event, peripheral, coronary or aortic arterial disease[9]. To assess the association between the score and variables that characterize the context of the patients, their city of residence and the INR target therapeutic range were used. Data were registered in a Microsoft Excel spreadsheet (Office, 2007). Descriptive analysis was performed, with the determination of absolute and relative frequencies of categorical variables, and means and standard deviations of continuous variables. The evaluation of the mean scores for the groups was performed using the ANOVA test in the SPSS® software, version 21.

The calculation of the TTR was performed from the data collected from each patient's INR. This was performed using the Rosessaal method, which uses a historical series of INR results to perform a linear interpolation. To perform this calculation, at least two INR results10 are necessary, which is one of the inclusion criteria for this study. For this, a specific electronic instrument available at www.inrpro.com was used.

In the present study, the calculation of the CHA_2DS_2-VASc was performed for those patients who had low TTR (<60%). It is recommended that the TTR value be greater than 60% for anticoagulant therapy to be benefitial[6,8]. This calculation is performed from the data and values obtained in the CHA_2DS_2-VASc Score[9]. Thus, it was possible to characterize the CHA_2DS_2-VASc of patients with AF using oral anticoagulants (OAC) and those with other indications also using OAC, and determine the stratification for thromboembolisms.

The present work is linked to the clinical trial "Evaluation of the implementation of educational intervention in patients with inadequate control of oral anticoagulation with a vitamin K antagonist treated at a university hospital", which was approved by COEP/UFMG (CAAE: 65928316.3.0000.5149).

RESULTS

A total of 434 patients were followed at the clinic during the study period, and 202 (46.5%) had a TTR below 60%. The sample studied was predominantly female (n = 137; 67.8%) and aged less than 65 years old (n = 114; 56.44%). The mean age of study participants was 61±11 years.

Among the risk factors of sex and age, the most prevalent were female (n = 137; 67.8%) and age < 65 years (n = 114; 56.4%), as shown in table 1.

Among the comorbidity risk factors, peripheral, coronary or aortic arterial disease (n = 96) and arterial hypertension (n = 107) were the most prevalent, as shown in Table 2.

As the CHA_2DS_2-VASc score increased the age also increased (Table 3), while the mean TTR showed variations. Patients with a CHA_2DS_2-VASc score equal to 8 had a lower mean TTR value (24.35) (Table 3). In addition, an average TTR of 37.98% was identified in the studied sample.

Table 4 shows that, among the indications for anticoagulation, the main one was concerning AF/flutter, totaling 136 patients (44.6%), followed by metal prostheses, with a total of 86 patients (28.2%).

Table 1 – Risk factors sex and age according to the CHA_2DS_2-VASc score. Belo Horizonte - MG, 2017.

	CHA_2DS_2-VASc Score								
Risk factor specification	**1** n (%)	**2** n (%)	**3** n (%)	**4** n (%)	**5** n (%)	**6** n (%)	**7** n (%)	**8** n (%)	**Total** n (%)
Female	0 (0)	16 (50.0)	33 (71.7)	34 (73.9)	28 (73.7)	10 (76.9)	14 (100.0)	2 (100.0)	137 (67.8)
Male	11 (100.0)	16 (50.0)	13 (28.3)	12 (26.1)	10 (26.3)	3 (23.1)	0 (0)	0 (0)	65 (32.2)
Total	11 (100.0)	32 (100.0)	46 (100.0)	46 (100.0)	38 (100.0)	13 (100.0)	14 (100.0)	2 (100.0)	202 (100.0)
< 65 years	7 (63.6)	24 (75.0)	30 (65.2)	24 (52.2)	19 (50.0)	3 (23.1)	7 (50.0)	0 (0)	114 (56.4)
≥ 65 and ≤ 74 years	4 (36.4)	4 (12.5)	7 (15.2)	14 (30.4)	11 (28.9)	3 (23.1)	1 (7.1)	0 (0)	44 (21.8)
≥ 75 years	0 (0)	4 (12.5)	9 (19.6)	8 (17.4)	8 (21.1)	7 (53.8)	6 (42.9)	2 (100.0)	44 (21.8)
Total	11 (100.0)	32 (100.0)	46 (100.0)	46 (100.0)	38 (100.0)	13 (100.0)	14 (100.0)	2 (100.0)	202 (100.0)

Table 2 – Comorbidity risk factors according to the CHA_2DS_2-VASc score. Belo Horizonte - MG, 2017.

Comorbidity	CHA_2DS_2-VASc Score								
	1 n (%)	2 n (%)	3 n (%)	4 n (%)	5 n (%)	6 n (%)	7 n (%)	8 n (%)	Total n (%)
Heart failure or VEF[1] below 40%	0 (0)	1 (2.70)	5 (11.30)	12 (27.20)	9 (20.40)	3 (6.80)	12 (27.20)	2 (4.40)	44 (100.00)
Diabetes Mellitus	0 (0)	0 (0)	0 (0)	6 (22.22)	11 (40.75)	3 (11.11)	6 (22.22)	1 (3.70)	27 (100.00)
Peripheral, coronary or aortic arterial disease	0 (0)	9 (9.37)	29 (30.20)	25 (26.05)	21 (21.87)	7 (7.30)	4 (4.16)	1 (1.05)	96 (100.00)
Arterial hypertension	0 (0)	2 (1.86)	14 (13.10)	35 (32.71)	27 (25.23)	13 (12.14)	14 (13.10)	2 (1.86)	107 (100.00)
Previous stroke[2], peripheral embolism or TIA[3]	0 (0)	0 (0)	1 (1.61)	10 (16.12)	24 (38.70)	11 (17.75)	14 (22.60)	2 (3.22)	62 (100)

[1]VEF: Ventricular ejection fraction; [2]CVA: stroke; [3]TIA: Transient ischemic attack

Table 3 – Mean age and TTR of patients, stratified by CHA_2DS_2-VASc score. Belo Horizonte - MG, 2017.

Group Specification	CHA_2DS_2-VASc Score							
	1 (n=11)	2 (n=32)	3 (n=46)	4 (n=46)	5 (n=38)	6 (n=13)	7 (n=14)	8 (n=2)
Average Age	53	56	59	66	64	72	70	80
Average TTR*	37.05	37.19	38.55	39.42	35.74	44.61	35.77	24.35

*TTR: *Time in therapeutic range*

Table 4 – Indications for anticoagulation, stratified by CHA_2DS_2-VASc score. Belo Horizonte - MG, 2017.

Indications for anticoagulation	CHA_2DS_2-VASc Score								Total
	1 n (%)	2 n (%)	3 n (%)	4 n (%)	5 n (%)	6 n (%)	7 n (%)	8 n (%)	n (%)
Stroke	2 (5.00)	4 (10.30)	1 (2.60)	6 (15.40)	12 (30.80)	4 (10.30)	9 (23.00)	1 (2.60)	39 (12.80)
Heart disease	1 (3.00)	7 (21.90)	8 (25.00)	6 (18.80)	4 (12.50)	2 (6.30)	3 (9.40)	1 (3.10)	32 (10.50)
Thromboembolism	2 (16.8)	1 (8.30)	1 (8.30)	4 (33.30)	3 (25.00)	1 (8.30)	0 (0.00)	0 (0.00)	12 (3.90)
Atrial fibrillation/flutter	8 (5.90)	16 (11.80)	31 (22.70)	34 (25.00)	27 (19.90)	9 (6.60)	9 (6.60)	2 (1.50)	136 (44.60)
Metal prosthesis	1 (1.2)	15 (17.4)	24 (27.9)	28 (32.5)	14 (16.3)	3 (3.5)	1 (1.2)	0 (0.0)	86 (28.20)

Table 5 – Assessment of the association between the CHA_2DS_2-VASc score and the target INR[1] and City of residence.

Characteristics		CHA_2DS_2-VASc Score	
INR target therapeutic range	**N**	**Mean (SD[2])**	**Valor p***
2 to 3	144	3.28 (1.73)	
2.5 to 3.5	54	2.76 (1.13)	0.088
3 to 3.5	4	2.50 (1.29)	
City of residence			
Capital	112	3.28 (1.62)	
Metropolitan Region	71	3.15 (1.53)	0.018
Interior	19	2.16 (1.46)	

[1] INR: International Standardized Ratio; [2]SD: Standard deviation; *Refers to the ANOVA test association.

DISCUSSION

According to the data obtained in this study, it was observed that most patients who demonstrated a low TTR were female (n = 137; 67.8%). Among the risk factors for the development of thromboembolic events, there is a difference between the sexes, since being female results in a score of 1 on the CHA_2DS_2-VASc score, while no points are given for being a male[11].

Among the most prevalent risk factors for the development of thromboembolic events in the studied sample, the presence of arterial hypertension is highlighted. This health problem is among the main factors that favor the development of cardiovascular diseases and stroke, which are important causes of death in elderly patients[12].

It was also observed that most of the studied sample was over 60 years old, which is in the elderly age group. The increase in the CHA_2DS_2-VASc score was proportional to the increase in age, which suggests a higher risk of developing thromboembolic events in older individuals. It is known that most of the elderly population in Brazil has chronic diseases and functional limitations[13], which is corroborated with the results found in the study herein. The number of patients with cardiovascular disease is steadily increasing in the population. This scenario is the result, among other factors, of the accelerated growth of the elderly population, which has a higher incidence of these morbidities[12,14,15].

Among the various indications for anticoagulation, AF/flutter (n = 136; 44.6%) and the use of metal prostheses (n = 86; 28.2%) stand out, with the latter presenting a distinct therapeutic range (between 2.50 and 3.50). AF is an independent risk factor for the occurrence of thromboembolic events, and is an important trigger of stroke, which is the second leading cause of death in the world[11,16]. In addition, AF represents a major problem in the public health system. Its expenditures are estimated to be between 16 to 26 billion dollars per year in the United States[17,18]. The incidence of AF increases with aging. It is estimated that only 1% of patients with AF are not elderly, and up to 12% are patients aged between 75 and 84 years[19].

TTR follow-up provides monitoring of the effectiveness and safety of pharmacotherapy. The population of this study varied with an average TTR of 38.0%, a value below the desired value of around 60.0%. Several factors can interfere with TTR, such as

the patient's low understanding of their health problem, lack of adherence to drug treatment, and drug and food interactions[8].

Elderly patients usually have more than one chronic disease, thus practicing polypharmacy, which increases the risk of adverse events[20]. This demonstrates the importance of quality of care for the patient, who, in addition to using warfarin, may be using other interacting drugs, generating greater difficulty in controlling the INR, and therefore, a lower TTR.

There are many variables available to patients who use anticoagulants. Identifying the difficulties and understanding them is the best way to develop a health system that is prepared for adversity. The CHA_2DS_2-VASc score was initially proposed to stratify thromboembolic risk in patients with AF/flutter; however, it has been validated in several independent cohort studies that indicate that the score is also predictive of stroke and mortality in patients with different indications of AF/flutter and patients not treated with OAC[21]. Therefore, the importance of using this score for patients with other indications, favoring the care for those at higher risk, is emphasized. The elderly population is growing rapidly on a global level, which indicates that the health system and its professionals need to be prepared to use instruments that can offer greater safety to the patient care process.

When evaluating the association between demographic characteristics with the results of the CHA_2DS_2-VASc score, it was possible to observe that individuals residing in the interior of the state had a lower mean CHA_2DS_2-VASc scores. This finding may be related to the possibility of underdiagnosing the risk factors associated with the calculation of this score. This underdiagnosis may be associated with difficulties in accessing health services. The fact that these individuals are sent from the countryside to undergo follow-up in the capital may reflect difficulties in offering specialized services. Although difficulties in accessing health services in Brazil is a topic widely discussed in the literature, studies addressing specific associations between the CHA_2DS_2-VASc score and the profile of the city of residence and the INR target therapeutic range were not identified[22,23]. This information should be considered as unique in the scientific literature, as well as the focus on individuals residing in the context of a middle-income country.

It is noteworthy that the CHA_2DS_2-VASc score has been validated for patients with AF[24]. As there are no specific thromboembolism risk score calculation tools for other indications of oral anticoagulants, this score has been used in clinical practice for patients with other indications of anticoagulants, which correspond to the profiles of patients addressed in this study[25].

Anticoagulation clinics play an essential role in the quality of anticoagulant pharmacotherapy. The work performed contributes to the identification of the difficulties presented by inadequate education on the part of the patient[26]. Although there are these benefits, the present study identified a considerable number of patients with inadequate control of anticoagulation (202 patients), with 191 patients with CHA_2DS_2-VASc above and/or equal to 2, representing 94.5% of the population, which classifies them as high-risk patients. 11 patients (5.4%) were also identified with a score equal to 1, which represents moderate-risk patients who may or may not be indicated for the use of OAC; therefore, these are patients that should be evaluated regarding their need for use. Since all individuals present in this study use OAC, there were no patients with a score of 0.

Thus, it is necessary to invest in educational strategies on the management of pharmacotherapy, the risks involved and the patient's perception of the treatment.

The present study focuses on patients who presented an inadequate TTR, as it is understood that they are at higher risk for complications from warfarin treatment and deserve greater investments to improve the care process. This study has as a limitation the fact that a convenience sample was used and, therefore, it was not possible to use inferential analytical techniques to further deepen the assessment. Future studies can be carried out to assess the behavior of data regarding polypharmacy, treatment adherence, and understanding of this pharmacotherapy.

CONCLUSION

This study allowed us to verify that most patients had a CHA_2DS_2-VASc score above or equal to 2, where the most prevalent indication was AF/flutter. According to the CHA_2DS_2-VASc, this number represents a high risk for the development of thromboembolic events, which validates the indication for the use of the oral anticoagulant warfarin. These results open a discussion of the need for anticoagulant pharmacotherapy in these patients and the investment in educational strategies for a better understanding of pharmacotherapy, with the consequent achievement of greater effectiveness. Regarding the association between demographic characteristics and the results of the CHA_2DS_2-VASc score, an association was identified between the CHA_2DS_2-VASc score and city of residence ($p<0.05$), with no statistical significance being identified between the CHA_2DS_2-VASc score and the INR target therapeutic range ($p>0.05$).

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