Trends and Predictors of Oral Anticoagulation in Patients with Atrial Fibrillation: A Serial Cross-Sectional Study from 2011 to 2016

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Abstract

Background: Despite the efficacy of vitamin K antagonists against stroke in patients with atrial fibrillation (AF), the underuse of this therapy is well documented.

Objectives: To evaluate trends and predictors of oral anticoagulants utilization in patients with AF.

Methods: Observational, retrospective, serial cross-sectional study between 2011-2016. Comparisons between groups were performed using the Student t, Mann-Whitney and Chi-square tests. Logistic regression was used to identify independent predictors of anticoagulation. A p value < 0.05 was considered significant.

Results: A total of 377 patients were analyzed. The mean age was 70 ± 15 years; 52% were male and 75% were anticoagulated (20% with VKA and 55% with DOAC). Over 5 years, the overall frequency of anticoagulation increased by 22.4%. The use of DOACs increased from 29% to 70%, whereas the use of VKA decreased from 36% to 17%. The use of antiplatelet agents alone also fell from 21% to 6%. The predictors of anticoagulation were previous episodes of AF (OR 3.1, p < 0.001), hypertension (OR 3.0, p < 0.001) and HASBLED score (OR 0.5, p < 0.001). The predictors of DOAC use were serum creatinine (OR 0.2, p = 0.002), left atrial size (OR 0.9, p = 0.003) and biological valve prosthesis (OR 0.1, p = 0.007). Of the 208 patients using DOACs, 63 (30%) received inadequate prescriptions: 5 with severe drug interactions and 58 with incorrect dosing.

Conclusions: Between 2011 and 2016, DOACs were rapidly incorporated into clinical practice, replacing AVKs and antiplatelets, and contributing to greater use of anticoagulation in patients with AF. (Int J Cardiovasc Sci. 2020;33(1):68-78)

Keywords: Atrial Fibrillation; Anticoagulants; Brain Ischemia; Vitamin K/antagonists & inhibitors; Thromboembolism/ prevention & control.

Introduction

Atrial fibrillation (AF) affects about 1–2% of the world's population and is associated with a five-fold increased risk of stroke. The use of vitamin K antagonists (VKA) as anticoagulants reduces the risk of stroke or systemic embolism by 64% and all-cause death by 26%.[1-7] However, observational studies have shown that only 50–60% of patients with AF eligible for the use of anticoagulants are anticoagulated. Reasons for underutilization of VKAs include numerous drug and food interactions and the inconvenience of laboratory monitoring process, which make it difficult to maintain the International Normalized Ratio (INR) in the narrow therapeutic range, placing patients at risk for ischemic and hemorrhagic events.[8-10]

Over the past 10 years, several randomized trials, involving more than 70,000 patients with AF, compared the use of AVK with direct-acting oral anticoagulants (DOACs). In these studies, DOACs were at least as effective as VKAs in preventing thromboembolic events and promoted a significant reduction in the frequency of intracranial hemorrhage.[11] In addition, DOACs

do not require laboratory monitoring to determine effective therapeutic level and have few significant drug interactions.

The purpose of this study is to determine the pattern and predictors of the use of anticoagulants in eligible patients with AF and how fast DOACs are incorporated in this context.

Methods

Reference population

Data were collected from an electronic medical record of all hospitalized patients diagnosed with AF and/or atrial flutter at a private tertiary institution in Salvador, Bahia, from May 23, 2011 (date of approval of dabigatran in Brazil) to June 30, 2016. Patients were screened from ICDs I48 and R00, and only those with documented AF or atrial flutter were recruited.

Study design

Retrospective observational study based on electronic chart review, with annual cross-sections for five consecutive years (trends study).

Inclusion and exclusion criteria

Inclusion criteria were: age ≥ 18 years, AF diagnosis and/or atrial flutter confirmed by ECG and/or Holter. Patients without electronic prescription of discharge were excluded, as this was the source of the data regarding the use of anticoagulant. On readmissions, the most recent admission was chosen for analysis.

Data collected and definitions

Demographic and anthropometric data were collected, in addition to the cardiovascular risk factors traditionally related to AF (systemic arterial hypertension [SAH], diabetes, valve disease, myocardial infarction, heart failure, history of bleeding, medications). The risk scores for stroke and bleeding were CHA_2DS_2VASc and HASBLED, validated in international studies.[12-14] AF was classified according to the II Brazilian Guidelines for Atrial Fibrillation of the Brazilian Society of Cardiology.[15] When there was insufficient information for classification, AF was considered of indefinite duration. Prior AF was defined as the identification of episodes of this arrhythmia prior to the reference admission during review of medical records.

Echocardiographic data were collected from the most recent test, respecting the period of up to 1 year before admission. Valvular heart disease was defined as the presence of any moderate or severe mitral or aortic lesion. The presence of a valve prosthesis was defined by echocardiogram or clinical history.

Electronic prescription of discharge was used to collect information on anticoagulants, antiplatelets and their doses, and other drugs with potential for drug interaction.

All information regarding hemorrhagic events was collected, but only major bleeding — intracranial hemorrhage, need for blood products or corrective surgical treatment — were considered for analysis.

The following were considered absolute contraindications for oral anticoagulants: active bleeding, severe hemorrhagic diathesis, thrombocytopenia < 50,000, invasive surgery or procedure to be done, major trauma, hemorrhagic stroke, intracranial or spinal tumor, spinal anesthesia, uncontrolled SAH. Relative contraindications included: end-stage neoplasia, active peptic ulcer, advanced dementia (without a caregiver), alcoholism and frequent falls (more than three per year). Patients with zero CHA_2DS_2-VASc were not considered candidates for anticoagulation.

Inappropriate use of DOAC[16] was defined as follows: prescriptions containing drugs with strong drug interaction potential; dose inconsistent with the dosage recommended by the manufacturer, considering patient's age, weight and renal function; presence of absolute contraindications (mechanical cardiac valve prosthesis or moderate to severe mitral stenosis).

Statistical analysis

Continuous variables were summarized by mean and standard deviation or median and interquartile distance, as indicated by the frequency distribution. Comparisons of quantitative variables between 2 groups were done using Student's t test for independent samples and Mann-Whitney. Categorical variables were summarized using simple and relative frequencies, compared between groups using the chi-square test. For analysis of correlation between the HASBLED and CHA_2DS_2-VASc scores, the Spearman's technique was used.

To identify predictors of anticoagulation and anticoagulant type, we used binary logistic regression. Firstly, we made a selection of variables using univariate logistic regression. The variables associated with anticoagulation and use of DOAC with p value < 0.05 in

the univariate analyses were later included in multivariate logistic regression models using the backward stepwise method. The variables that reached p < 0.05 in the final analyses were considered statistically significant.

All analyses were conducted in the Statistical Package for the Social Sciences (SPSS) version 23.

Ethical issues of research

This study was approved in a plenary session at the Ethics Research Committee Prof. Celso Figuerôa, Hospital Santa Izabel on 11-24-2014, according to Resolutions 466/12 and 251/97, protocol number 917.116.

Results

From 2011 to 2016, there were 464 admissions with diagnosis of AF discharge. Of these, 87 patients were excluded: 28 for not presenting AF (coding error); 26 hospital readmissions; 20 deaths during admission; 13 for not having electronic prescription of discharge. The final population analyzed consisted of 377 patients.

Demographic and clinical data

Patients were separated into two groups: patients with and without anticoagulants. The group on anticoagulants was subsequently divided into patients using VKA or DOAC (Table 1). The mean age of the patients was 70 ± 15 years, and 52% were male with mean body mass index (BMI) of 27 ± 6. Regarding the type of AF, 42% had paroxysmal AF, 12% had persistent AF, 27% had permanent AF, 19% with indefinite duration; 10% of the patients had atrial flutter. There was a high prevalence of comorbidities, with 71% of hypertensive patients, 23% of diabetics, 26% with a history of heart failure, 7.4% with a history of myocardial infarction and 18% had ischemic stroke. Of the study population, 25% had moderate or severe valvulopathy, 3.9% had biological valve prosthesis and 1.8% had mechanical valve prosthesis (Table 1).

Mean CHA_2DS_2-VASc risk score was 3.4 ± 2.0 and the HASBLED score was 1.2 ± 1.0, with 11.2% of these having HASBLED 3 and 79.8% having CHA_2DS_2-VASc ≥ 2 (Chart 1).

Use of anticoagulant therapy

Considering the total population over a 5-year period, 75% of the patients were discharged on anticoagulants (20% received VKA and 55% received DOACs), 15% were on antiplatelets alone and 10% were not on antithrombotic therapy.

Table 1 - Demographic and clinical characteristics of 377 adult patients admitted with atrial fibrillation at a tertiary hospital in Salvador, Bahia, Brazil

Variable	Without anticoagulant (n = 93)	With anticoagulant (n = 284)	p*	VKA (n = 76)	DOACs (n = 208)	p†
Age (years)	73 ± 18	69 ± 13	0.059	70 ± 13	69 ± 14	0.493
Male	42 (45.2)	155 (54.6)	0.115	41 (53.9)	114 (54.8)	0.897
Weight (kg), n = 370	71.8 ± 15.5	78.4 ± 20.6	0.002	75.8 ± 21.4	79.3 ± 20.3	0.207
Height (meters), n = 370	1.64 ± 0.11	1.66 ± 0.10	0.036	1.65 ± 0.10	1.67 ± 0.10	0.114
SAH	59 (63.4)	210 (73.4)	0.052	59 (77.6)	151 (72.6)	0.392
DM	27 (29)	61 (21.5)	0.135	18 (23.7)	43 (20.7)	0.584
CHF	23 (24.7)	77 (72)	0.652	30 (39.5)	47 (22.6)	0.005
AMI in the past year	10 (10.8)	18 (6.3)	0.159	5 (6.6)	13 (6.3)	0.920
TCA in the past year	4 (4.3)	4 (1.4)	0.093	1 (1.3)	3 (1.4)	0.936
History of TIA/ischemic stroke	25 (26.9)	42 (14.8)	0.008	10 (13.2)	32 (15.4)	0.640
History of hemorrhagic stroke	0 (0)	2 (0.7)	0.417	1 (1.3)	1 (0.5)	0.456
History of AF n=357	42 (50)	191 (70)	0.001	49 (70)	142 (69.9)	0.994

Cont. Table 1 - Demographic and clinical characteristics of 377 adult patients admitted with atrial fibrillation at a tertiary hospital in Salvador, Bahia, Brazil
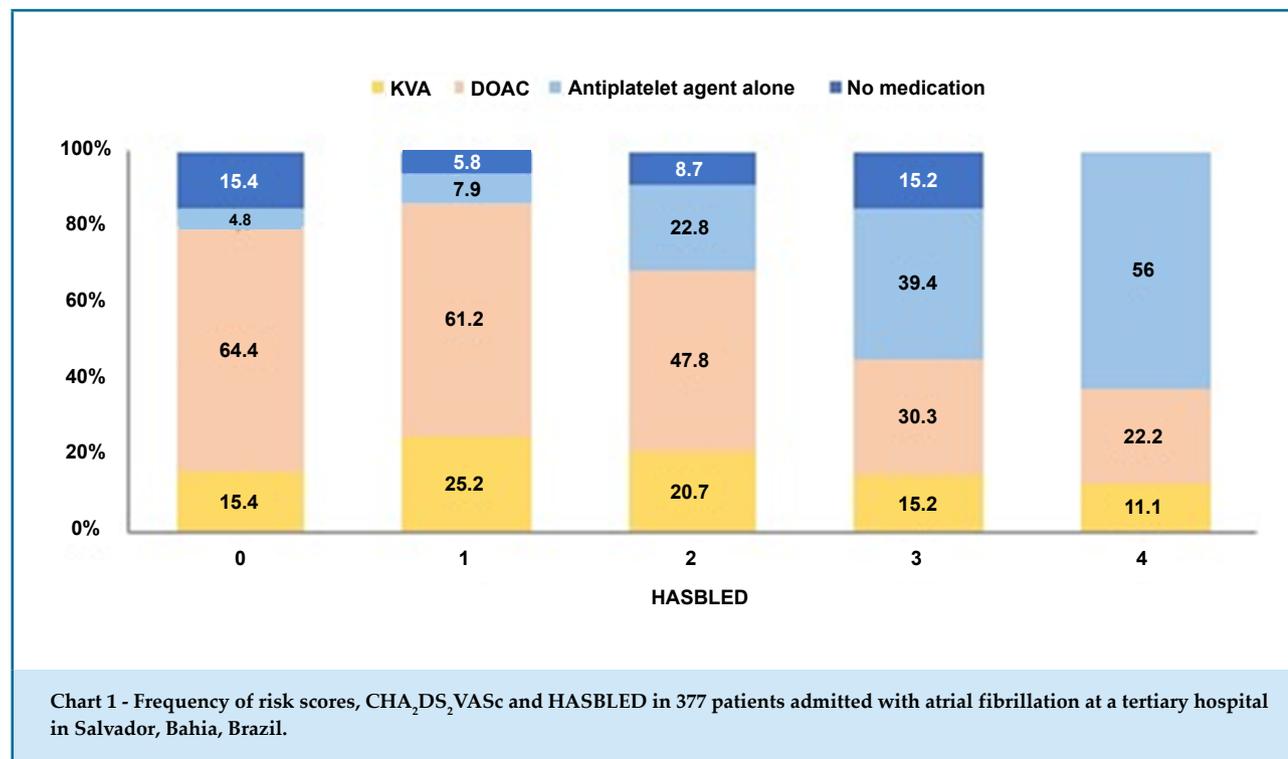
Variable	Without anticoagulant (n = 93)	With anticoagulant (n = 284)	p*	VKA (n = 76)	DOACs (n = 208)	p†
AF classification n = 339						
Paroxysmal	35 (41.7)	106 (41.6)		20 (27.8)	86 (47)	
Persistent	5 (6)	35 (13.7)	0.185	13 (18.1)	22 (12)	0.002
Permanent	28 (33.3)	64 (25.1)		28 (38.9)	36 (19.7)	
Undetermined	16 (19)	50 (19.6)		11 (15.3)	39 (21.3)	
CHA_2DS_2-VASc	4 (0 to 8)	3 (0 to 9)	0.010	3 (0 to 8)	3 (0 to 9)	0.199
HASBLED	2 (0 to 4)	1 (0 to 4)	< 0.001	1 (0 to 4)	1 (0 to 4)	0.089
Recent ischemic stroke/TIA	4 (4.3)	21 (7.4)	0.298	6 (7.9)	15 (7.2)	0.846
Recent hemorrhagic stroke	2 (2.2)	0 (0)	0.013	0	0	
Biological prosthesis	2 (2.2)	13 (4.6)	0.299	9 (11.8)	4 (1.9)	< 0.001
Metallic prosthesis	0 (0)	7 (2.5)	0.126	7 (9.2)	0 (0)	< 0.001
Valvular heart disease	23 (24.7)	70 (24.6)	0.987	28 (36.8)	42 (20.2)	0.004
Hemorrhage	9 (9.7)	12 (4.2)	0.047	5 (6.6)	7 (3.4)	0.233
Major bleeding	4 (4.3)	5 (1.8)	0.164	2 (2.6)	3 (1.4)	0.500
Interaction with DOAC	60 (64.5)	225 (79.2)	0.004	67 (88.2)	158 (76)	0.025
Creat. (mg/dl), n = 350	1.1 ± 0.9	1.1 ± 0.7	0.986	1.3 ± 1.3	1 ± 0.3	0.031
LA (mm), n = 349	42.6 ± 7.4	43.5 ± 6.6	0.283	47.3 ± 6.14	42.2 ± 6.3	< 0.001
LVEF (%), n = 349	62.1 ± 12.9	59.8 ± 15	0.176	55.1 ± 16	61.5 ± 14.5	0.002
Arrhythmia reversal						
Electric	10 (10.8)	82 (28.9)		19 (25)	63 (30.3)	
Not Executed	41 (44.1)	100 (35.2)		40 (52.6)	60 (28.8)	
Chemical	30 (32.3)	41 (14.4)	< 0.001	6 (7.9)	35 (16.8)	0.005
Spontaneous	10 (10.8)	41 (14.4)		7 (9.2)	34 (16.3)	
Ablation	02 (2.2)	20 (7)		4 (5.3)	16 (7.7)	
Antiplatelet agents	56 (60.2)	3 (15)	< 0.001	13 (17.1)	30 (14.4)	0.577

For continuous variables n (± standard deviation) and for continuous variables n (%); in case of missing data, total n was placed next to the variable; p* refers to comparison between groups with and without anticoagulants; p† refers to comparison between the groups with VKA and DOAC; TCA: transcutaneous coronary angioplasty; TIA: transient ischemic attack; Creat.: serum creatinine; LA: left atrium; LVEF: left ventricular ejection fraction.

From 2011 to 2015, there was a progressive increase in the use of anticoagulants from 64% to 87%, largely at the expense of an increase in the use of DOACs, which rose from 29% to 70% (a relative increase of 144.8%), and reduced use of VKA and antiplatelets alone in the same period. Average annual incorporation of DOACs was 10.4% (Chart 2). About 25% of the patients were on antiplatelets alone or combined with anticoagulants.

The prevalence of prescription of oral anticoagulants, antiplatelets and no antithrombotic drugs stratified by risk category according to the CHA_2DS_2-VASc and HASBLED scores are shown in charts 3 and 4. There

Chart 1 - Frequency of risk scores, CHA$_2$DS$_2$VASc and HASBLED in 377 patients admitted with atrial fibrillation at a tertiary hospital in Salvador, Bahia, Brazil.

was a strong correlation between the HASBLED and CHA$_2$DS$_2$-VASc scores (Spearman's r 0.706).

Predictors of use and type of anticoagulants

Most patients who had anticoagulants prescribed on hospital discharge had a history of previous episodes of AF (p = 0.001) and TIA/stroke (p = 0.008), were older (p = 0.056), had lower mean HASBLED (p < 0.001), higher mean weight (p = 0.002) and higher prevalence of SAH (p = 0.052) than non-anticoagulated patients. In the multivariate logistic regression analysis, the following remained as independent predictors of anticoagulation: previous episodes of AF, SAH and HASBLED (p < 0.001) (Table 2).
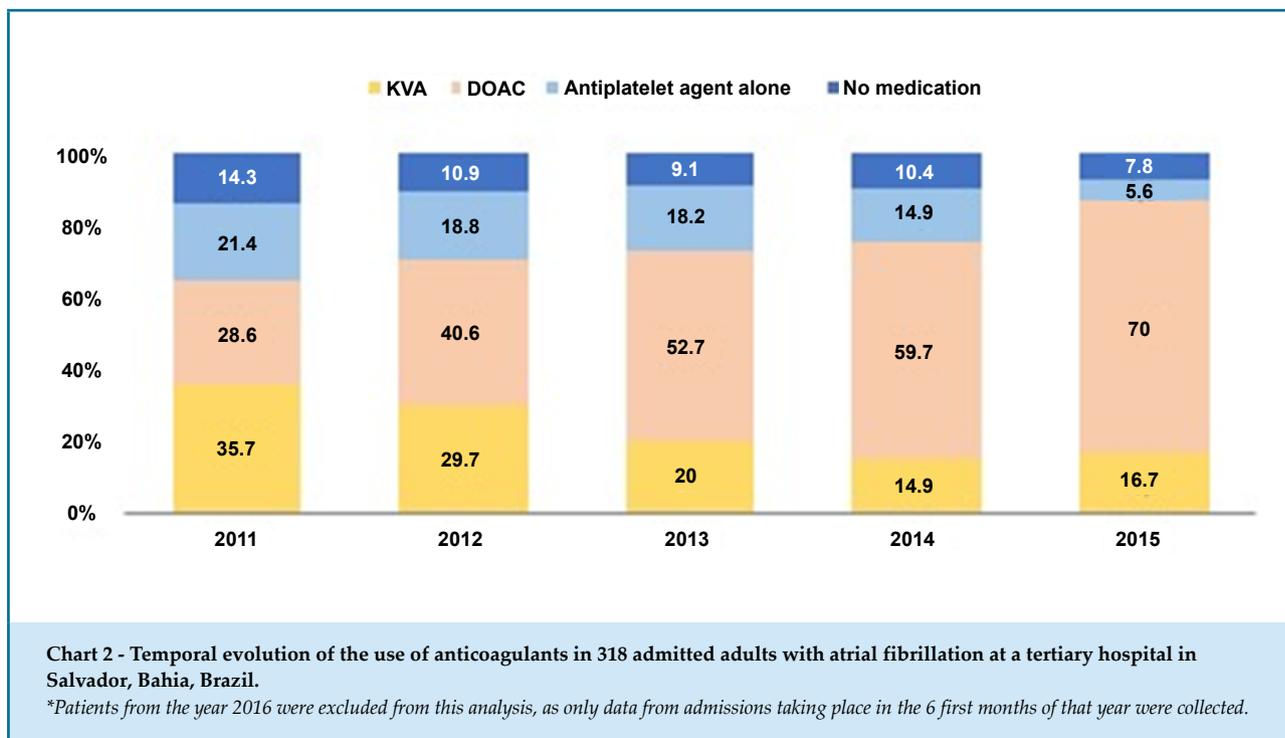
To identify variables associated with the prescription of a given class of anticoagulants, we built a multiple logistic regression model using DOAC as a dependent variable and paroxysmal AF, CHF, serum creatinine, left ventricular ejection fraction, LA diameter, biological valve prosthesis, moderate valvular heart disease and electrical or chemical CV as independent variables. The variables serum creatinine (p < 0.002), LA diameter (p = 0.003) and biological valve prosthesis (p = 0.007) were inversely associated with the prescription of a DOAC, that is, were predictors of VKA prescription (Table 3).

Appropriateness of the use of anticoagulants

Of the 93 patients with AF whose discharge prescriptions did not contain anticoagulants, 43 had legitimate reasons for doing so: 14 with zero CHA$_2$DS$_2$VASc, 16 with absolute contraindications and 13 with relative contraindications. In the other 50 patients (54%), no reasons were found for the non-prescription of anticoagulants (45 patients) or the reasons on record were inconsistent with the literature (5 patients) — "requested by the attending physician"; "already had an indication of using anticoagulants and the attending physician did not prescribe"; "has bronchiectasis and history of bleeding"; "due to the risks of anticoagulation"; "will have pacemaker implanted" (Table 4).

Discussion

This is the first Brazilian study to demonstrate an increase in the use of oral anticoagulants in patients with AF as a result of progressive incorporation of DOACs into clinical practice. Despite the high thromboembolic risk of the study population, one-quarter of patients with AF were discharged without anticoagulant prescription, confirming findings from contemporary international registries. However, over the study period

Chart 2 - Temporal evolution of the use of anticoagulants in 318 admitted adults with atrial fibrillation at a tertiary hospital in Salvador, Bahia, Brazil.
Patients from the year 2016 were excluded from this analysis, as only data from admissions taking place in the 6 first months of that year were collected.

(2011–2016), there was a significant increase in the rate of anticoagulant use, which is largely due to the rapid incorporation of DOACs into clinical practice, which progressively replaced VKAs and antiplatelet agents. We did not find any other Brazilian study showing the evolution of anticoagulation rates in patients with AF after the introduction of DOACs on the market. A cross-sectional study involving 407 patients with AF treated at the emergence service of a tertiary center in Porto Alegre evaluated the rate of anticoagulant use. Only 34% of these patients received anticoagulation, and even in patients with $CHA_2DS_2\text{-}VASc \geq 2$, only 40% had anticoagulants prescribed.[17]
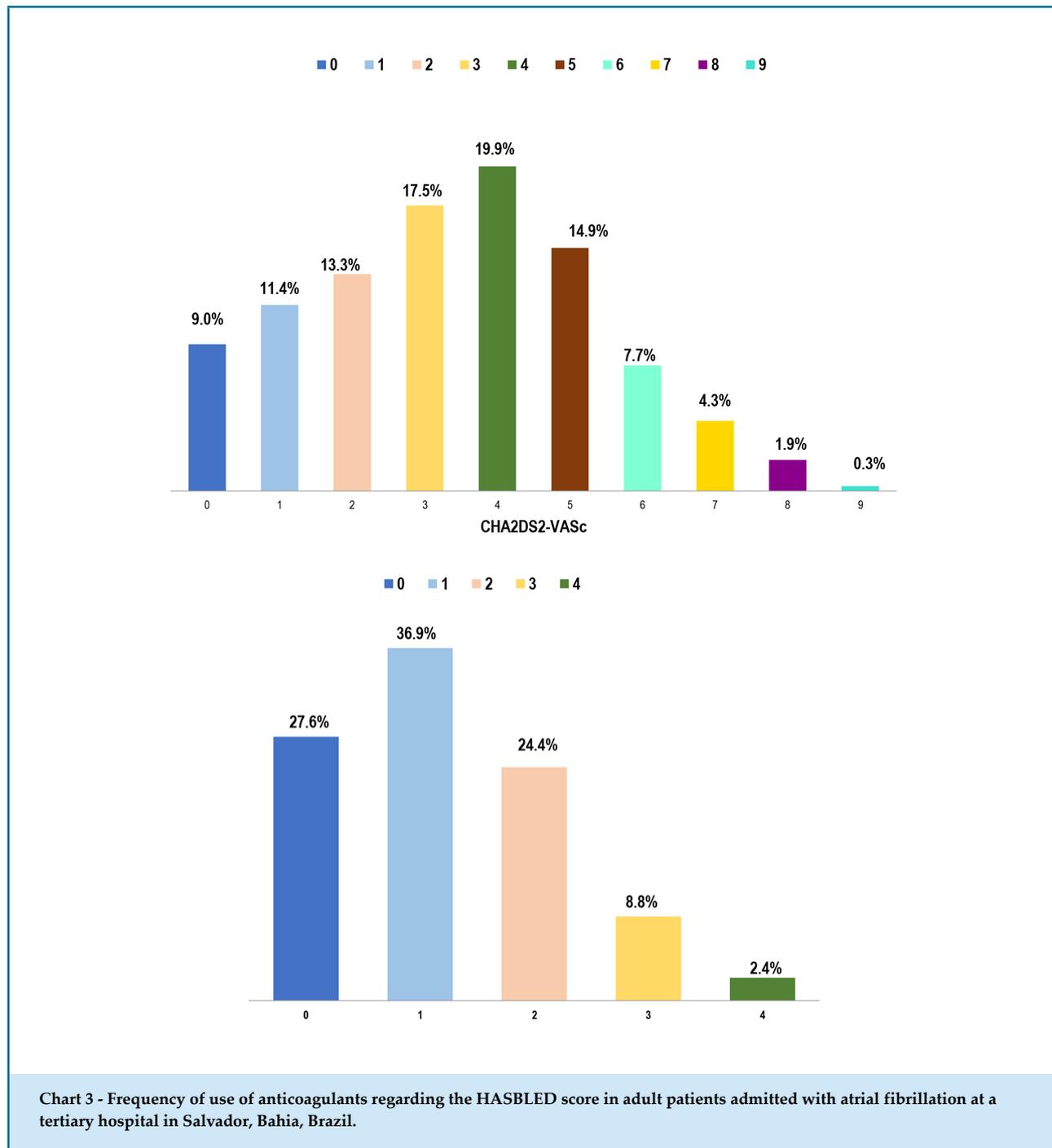
ANVISA approved the first DOAC in Brazil — dabigatran in 2011 — then two new direct inhibitors of factor Xa: rivaroxaban and apixaban. This study documented a rapid incorporation of these new anticoagulants (annual average of 10.4%), rising from 28% in 2011 to 70% in 2016. This was the determining factor in the 34.8% increase in the overall use of anticoagulants in our population of patients with AF.

Most contemporary international registries show the same trend. The GARFIELD AF registry (The Global Anticoagulant Registry in the FIELD-Atrial Fibrillation), which started in 2011, with completed recruitment in follow-up phase, also showed a significant increase

in the use of DOACs (4.2% to 37%) associated with to an absolute increase of 13.7% (57.4% to 71.1%) in the frequency of anticoagulant use. Likewise, the GLORIA-AF registry documented a marked increase in the overall rate of anticoagulant use (64% to 80%) between phase 1 and 2 of the study, concomitantly with the introduction and incorporation of DOACs into clinical practice, now used by 48% of patients, compared to 32% of VKA users. Both GLORIA AF and GARFIELD AF registries observed a marked decrease in the use of antiplatelet agents.[18,19]

These changes in the pattern of anticoagulant use seem to be occurring in almost all regions of the world, according to GLORIA AF data, except for Asia, where more than 40% of patients with AF do not receive anticoagulants yet. Also in this registry, Latin America presented high rates of oral anticoagulants and DOACs, of 85% and 56%, respectively. It seems clear that the greatest factor for the improvement in the global anticoagulation rates in AF observed in international registries and in this study over the past 5 years was the emergence of DOACs. These drugs overcame many difficulties and limitations associated with the practical use of traditional anticoagulants, which strongly impacted the decision on its use.

In addition to the DOACs, the latest therapeutic guidelines for AF may have contributed to an increase in

Chart 3 - Frequency of use of anticoagulants regarding the HASBLED score in adult patients admitted with atrial fibrillation at a tertiary hospital in Salvador, Bahia, Brazil.

the number of AF patients receiving oral anticoagulants, since they no longer consider antiplatelet agents as acceptable alternatives to anticoagulants in patients with lower thromboembolic risk.[16,20]

Another important finding of our study was the lack of linearity between thromboembolic risk and the percentage of anticoagulant use. The frequency of anticoagulant prescription increased with the

thromboembolic risk score up to CHA_2DS_2-VASc 3. However, in scores > 3, there was a progressive decrease in the use of anticoagulants. Similar findings were observed in other cohort studies, where anticoagulation rates peaked at CHA_2DS_2-VASc 3-4 scores, followed, unlike our study, with a plateau without an observable decline.[18,19] Thus, despite the known increase in the annual risk of stroke at each point of the CHA_2DS_2-VASc

Chart 4 - Frequency of use of anticoagulants regarding the CHA_2DS_2-VASC score in adult patients admitted with atrial fibrillation at a tertiary hospital in Salvador, Bahia, Brazil.
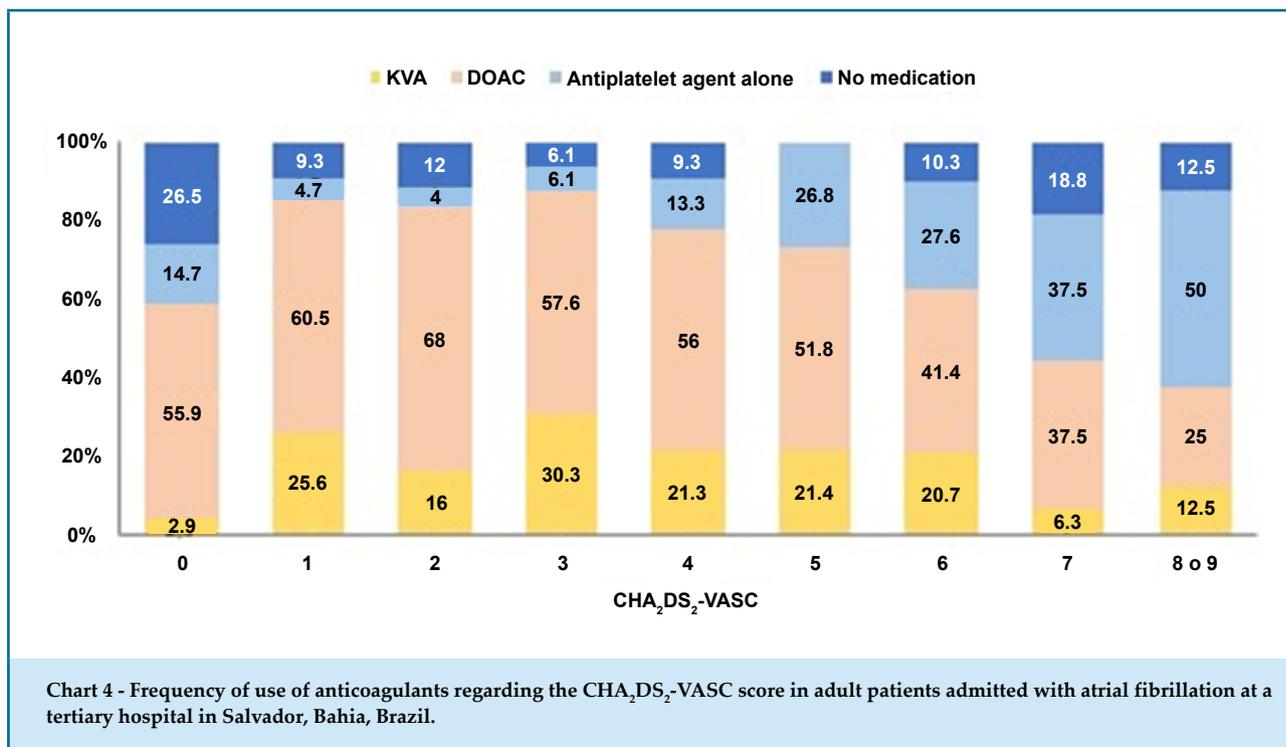
Table 2 - Multivariate logistic regression model for predictors of anticoagulant use in patients admitted with atrial fibrillation at a tertiary hospital in Salvador, Bahia, Brazil

Variable	OR (95% CI)	p
History of AF	3.13 (1.80 to 5.44)	< 0.001
SAH	3.05 (1.66 to 5.62)	< 0.001
HASBLED	0.50 (0.38 to 0.66)	< 0.001

Table 3 - Multivariate logistic regression model for predictors of DOAC use in adult patients admitted with atrial fibrillation at a tertiary hospital

Variable	OR (95% CI)	p
Serum creatinine (mg/dL)	0.18 (0.06 to 0.52)	0.002
LA diameter (mm)	0.92 (0.87 to 0.97)	0.003
Biological valve prosthesis	0.12 (0.03 to 0.57)	0.007
CV (electrical or chemical)	2.02 (0.97 to 4.22)	0.060

Electrical or chemical CV; CV: electrical cardioversion; LA: left atrium.

Table 4 - Frequency of inappropriate use of DOACs in 208 patients with atrial fibrillation, with indication for use of anticoagulants at a private tertiary hospital in Salvador, Bahia, Brazil

DOAC used	DOAC misuse frequency n (%)	Contraindication for drug interaction n (%)	Improper dose reduction n (%)	Improper full dose n (%)
Dabigatran (n = 60)	33 (55)	2 (3.3)	29 (67)	2/17 (11.8)
Rivaroxaban (n = 119)	22 (18.5)	1 (0.8)	18 (48.6)	3/82 (3.6)
Apixaban (n = 29)	8 (27.6)	2 (6.9)	6 (46.1)	0/16 (0)

score, 20–50% of high-risk patients remain unprotected without anticoagulants. Several reasons may have contributed to these findings. Many physicians may not use any tools as structured as CHA_2DS_2-VASc for evaluation of thromboembolic risk in AF, using only their imprecise clinical impression[12] and failing to capture the actual risk of some patients. Besides, patients with higher CHA_2DS_2-VASc have a higher prevalence of comorbidities associated with both higher risk of stroke and bleeding risk. Exploring this assumption, we demonstrated a strong correlation between the CHA_2DS_2-VASc and HASBLED scores (Spearman's r 0.706). Physicians may be fearful of prescribing anticoagulants for patients with higher CHA_2DS_2-VASc if they also present higher risk of bleeding, translated by higher HASBLED. Additionally, since many of these patients are also older and have higher prevalence of atherosclerotic disease, a significant percentage already use antiplatelet agents, which adds to the risk of bleeding and reluctance to prescribe anticoagulants.

Predictors of use of anticoagulants and DOACs

In our study, history of AF episodes and the presence of SAH individually increased by three-fold the chances of patients receiving anticoagulant prescription at discharge. On the other hand, at every 1 point where HASBLED increased, the chance of anticoagulation was reduced by 50%. These are logical and intuitive predictors of anticoagulation, since the first two increase the perception of thromboembolic risk and the last one increases the risk of bleeding. In the NCDR PINNACLE registry, there were more hypertensives among patients taking anticoagulants than among those who did not use anticoagulants (80% versus 74%; p < 0.001).[21]

In an analysis of participants from the 2nd and 5th cohorts of the GARFIELD-AF study in the UK, the two main reasons for the physician to avoid using anticoagulant in patients with CHA_2DS_2-VASc ≥ 2 were risk of fall and hemorrhagic event, respectively.[22]

Regarding the predictors of use of DOACs, we observed that for each 1.0 mg/dl increase in serum creatinine, there was 82% less chance of the patient being discharged on DOAC. For 1 year, Luger et al. analyzed AF patients who had stroke or TIA and concluded that the decision on the use of VKA or DOAC was mainly determined by the patient's renal function and absence of previous anticoagulant therapy, both reducing the chance of using DOAC.[23]

In addition to renal function, the presence of a biological valve prosthesis also significantly reduced the chance of DOAC prescription. Although not all studies comparing DOACs with VKA excluded patients with biological prostheses, which do not represent contraindication for the use of DOACs, the unfavorable experience of dabigatran in patients with mechanical prostheses[24] may cause some fear of using these anticoagulants in the context of any valve prosthesis.

Appropriateness of DOAC prescription

Our study demonstrated that in 28% of DOAC prescriptions, the doses were inadequate for the patients' clinical profile. However, as opposed to the findings of the cited studies, the most frequent dosing error was improper reduction of DOAC dose, rather than lack of adjustment. Both the lack of adjustment and improper dose reduction may compromise the efficacy and safety of anticoagulant therapy with DOACs. The randomized cluster study IMPACT-AF showed that multifaceted educational interventions were able to improve the frequency of anticoagulation and reduce the incidence of stroke.[25]

Limitations

Limitations of this paper include its retrospective design based on electronic medical records, making it subject to registration bias due to lack of information in medical records. In some cases, for example, it was not possible to assess the suitability of the DOAC dose because we did not have serum creatinine, weight or height information. Some patients were excluded because they did not have electronic prescription for discharge. However, these events were infrequent and did not compromise the results found.

Regarding the possibility of generalizing our findings to other populations, although it was conducted in a single center, the characteristics of the study population are similar to those of major international registries of AF. However, because it was conducted in a private medical center, our data cannot be extrapolated to patients with AF from the public healthcare system.

Conclusions

This study demonstrated that, following the approval of DOACs for clinical use in Brazil in 2011, these anticoagulants were rapidly incorporated into clinical

practice, becoming the therapy of choice for patients with AF and contributing decisively to the increase of anticoagulation rates in this group of patients. Despite this important achievement, 13% of eligible patients remained without anticoagulation. Additionally, besides the long-standing historical difficulty of keeping patients on VKA in the narrow therapeutic range, at least 25% of patients using DOACs are exposed to inappropriate doses, compromising its efficacy and safety.

The data and reflections described in this study should serve to guide the leaders of our healthcare system and medical societies towards building educational and awareness-raising strategies for health professionals and patients regarding the importance of correct prescription and adherence to anticoagulant therapy in AF.

Author contributions

Conception and design of the research: Geraldes MFA, Darze ES, Rocha PN. Acquisition of data: Geraldes MFA. Analysis and interpretation of the data: Geraldes MFA, Darze ES, Rocha PN. Statistical analysis: Geraldes MFA, Darze ES, Rocha PN. Writing of the manuscript: Geraldes MFA, Darze ES, Rocha PN. Critical revision of the manuscript for intellectual content: Geraldes MFA, Darze ES, Rocha PN.

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