Application and Comparison of the CHADS$_2$ and CHA2DS$_2$-VASc Risk Scores in a Population with Atrial Fibrillation

DARÍO DI TORO[MTSAC], CLAUDIO HADID[MTSAC], SEBASTIÁN GALLINO[†], CARLOS LABADET[MTSAC], IN REPRESENTATION OF THE RESEARCH AREA OF THE ARGENTINE SOCIETY OF CARDIOLOGY AND THE PARTICIPATING INVESTIGATORS OF THE FIRST NATIONAL, MULTICENTRIC, PROSPECTIVE STUDY OF CHRONIC ATRIAL FIBRILLATION IN THE ARGENTINE REPUBLIC

ABSTRACT

Introduction
The CHADS$_2$ score and the CHA2DS$_2$-VASc score recently adopted by the medical community have been developed with international registry data and are widely used in clinical practice. However, they have not been evaluated in national registries.

Objectives
The aims of this study were first to evaluate the predictive power of the CHADS$_2$ and CHA2DS$_2$-VASc stroke risk scores in the Atrial Fibrillation Registry conducted by the Argentine Society of Cardiology Research Area and second to compare both scoring systems.

Methods
The Atrial Fibrillation Registry of 2001 was a multicenter, prospective study of all consecutive patients with chronic atrial fibrillation (permanent and persistent) treated in 70 medical centers in Argentina. Demographic data, socioeconomic characteristics, background and clinical features were obtained. A 2-year follow-up was performed to assess stroke rate. For the present analysis patients without anticoagulant treatment were selected. In this population, the two risk score systems were assessed; a ROC curve was built for each score (reported as C statistic) and both scoring systems were compared.

Results
The study population consisted of 303 patients (49.3 %) not receiving anticoagulant therapy. The stroke rate in the selected population was 9.5%. Both scoring systems predicted significant stroke risk.
The stroke rate increased as the CHADS$_2$ and the CHA2DS$_2$-VASc scores were higher, and were similar in both risk scales.
The CHADS$_2$ and CHA2DS$_2$-VASc scores had C statistic values of 0.67 (0.55-0.78) and 0.69 (0.59 to 0.78), respectively, without significant differences between them.
The score analyses divided into three risk profiles -low, moderate and high- revealed that the predictive power decreased markedly. The C statistic of the CHADS$_2$ was 0.63 (95% CI 0.57-0.68) and that of the CHA2DS$_2$-VASc score was 0.57 (95% CI 0.51-0.62, with a slightly better predictive trend for the CHADS$_2$ score but without statistical significance.

Conclusions
The two scoring systems used to predict stroke in an Argentine population of patients with persistent and permanent atrial fibrillation have a similar predictive power comparable to results reported in the literature.

Abbreviations >

SAF	Atrial fibrillation		**HF**	Heart failure
CVA	Stroke		**HTN**	Hypertension
DM	Diabetes mellitus		**TIA**	Transient ischemic attack

Research Area, Argentine Society Of Cardiology, Buenos Aires, Argentina
[MTSAC] Full Member of the Argentine Society of Cardiology
[†] To apply as Full Member of the Argentine Society of Cardiology

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia observed in clinical practice. (1)

Its prevalence increases with age (observed in up to 9% of the population over 80 years) (2) and with the presence of organic heart disease (hypertensive heart disease, heart failure and coronary artery disease).

Atrial fibrillation produces a significant increase in morbidity and mortality due to higher risk of developing thromboembolic events and stroke (CVA). (3)

The $CHADS_2$ risk score was published in 2001 and adopted by guidelines and the medical community due to its good predictive power and simplicity. (4) After its publication the $CHADS_2$ score received some criticism. One of the most important was underestimation of risk factors for thromboembolic events, especially in the low-risk population. Therefore, it was necessary to create a new score contemplating variables previously not taken into account.

Nine years later the CHA2DS$_2$-VASc score came to address the $CHADS_2$ score difficulty in estimating risk in patients with low embolic risk. (5)

European guidelines promptly adopted the latter score and at present it is preferably recommended over its predecessor. (6)

All studies comparing both scoring systems were performed retrospectively and at present the published information is controversial.

One of the faculties of a good scoring system is the ability to predict the event in question in a population other than the one used for its development (external validation). For this reason, the aim of this study was to evaluate the prediction of both scoring systems in a national registry and to compare their predictive power in a population with permanent and persistent AF in Argentina.

METHODS

The Atrial Fibrillation registry performed in 2001 was a multicentric and prospective study of all consecutive patients treated for chronic ventricular fibrillation (permanent and persistent) in 70 medical centers of Argentina. Patient demographic data, socioeconomic background, medical history and clinical characteristics were obtained. A 2-year follow-up was conducted and at the end of this period the rate of CVA was assessed by telephone contact.

Inclusion and exclusion criteria of the Chronic Atrial Fibrillation Registry of Argentina have been previously published. (7) In 615 patients, vital status and outcome after entering the study were verified. Among these patients, 49.3% (n = 303) did not receive anticoagulant therapy according to the treating physician´s criterion and were selected as the study population. The primary endpoint was CVA during follow-up.

Definitions

Stroke (CVA): clinically diagnosed neurological irreversible impairment (images were not mandatory)

Hypertension (HTN): every patient receiving antihypertensive drugs.

Diabetes mellitus (DM): patients receiving treatment with hypoglycemic agents or insulin in any of its forms.

Heart failure (HF): patients with history of heart failure according to the treating physician and/or ventricular dysfunction on the echocardiogram.

Statistical analysis

Discrete variables were expressed as percentages and continuous variables as mean ± standard deviation. Multiple logistic regression analysis was performed to explore the independent association among the different variables involved in the study and the primary and secondary endpoints.

Logistic regression was done with every possible scenario, with scores as independent variable and CVA as dependent variable. First, the score was applied according to the scoring system recommended in the literature and then it was analyzed dividing it into three risk scenarios (score = 0 low risk, score =1 intermediate risk, score ≥ 2 high risk).

The prognostic power of both scores was determined calculating the area under the receiver operating characteristic (ROC) curve and the C statistic value. The latter quantifies the discriminating capacity of the predictive model. Areas under the ROC curve for the different scores were compared (adding the points of each variable and as risk profile) and was reported as C statistic or area under the curve. A p value < 0.05 was considered statistically significant. Stata version 10.0 was used to perform statistical analyses.

RESULTS

Scores were compared in 303 patients included in the study, which were followed-up for a mean of 815 days (95% CI 804-827). Stroke developed in 9.5% of patients during follow-up. Baseline population characteristics are shown in Table 1. Population mean age was 73.5 ± 10.1 years; 47.2% were female and 8.3% had previous CVA. Figure 1 illustrates in both risk scales the incidence of CVA with increasing score. It can be seen that with each increase of the score value there is higher prevalence of the endpoint, a response observed more clearly for the $CHADS_2$ score, as the CHA2DS$_2$-VASc score presents more fluctuations between values. The $CHADS_2$ score median value was 2, while that of the CHA2DS$_2$-VASc score was 3.

Both scoring systems significantly predicted CVA on the logistic regression analysis (with both forms of analysis). The area under the $CHADS_2$ score was 0.67 (95% CI 0.55-0.78) when analyzed adding points, as originally published. Employing the same analysis, the area under the CHA2DS$_2$-VASc score was 0.69 (95% CI 0.59-0.78). Figure 2 shows that there were no significant differences between both curves (p = 0.44).

When scores were divided into three risk profiles -low, moderate and high- the predictive power decreased markedly; the C statistic for the $CHADS_2$ score was 0.63 (95% CI 0.57-0.68) and that of the CHA2DS$_2$-VASc score was 0.57 (95% CI 0.51-0.62) with the $CHADS_2$ score showing a slightly better predictive trend, but without statistical significance.

DISCUSSION

It is extremely important to validate predictive models in different populations, as this external validation gives the scoring system a strength it that does not possess at the time of its publication.

The CHADS$_2$ score was developed in a population in the United States and the CHA2DS$_2$-VASc score in a European population. We believe it is useful to know whether these models applied in our population have the same predictive ability.

The first helpful finding of our study was that both scoring systems significantly predicted CVA in a population of Argentina, either analyzed as score or divided into three risk categories. The second finding of this study in order of importance is that the comparison between the CHADS$_2$ and CHA2DS$_2$-VASc scores showed no significant differences in the prediction of CVA in the same population.

Several studies have compared both risk scores in terms of CVA risk prediction. Olesen et al. published the Danish registry that included 73538 patients followed-up for 1, 5 and 10 years, in which the primary endpoint was hospitalization with or without death for a thromboembolic event. (8) In these patients the predictive value of both risk scores was similar when used adding points, with a C statistic of 0.66 for the CHADS$_2$ score at one year and 0.76 at 5 years, and an area under the curve of 0.66 for the CHA2DS$_2$-VASc score at one year and 0.75 at 5 years. Interestingly, when the scores were used in the three risk categories, the predictive ability of the CHA2DS$_2$-VASc score was better than that of the CHADS$_2$ score, both at one and 5 years, reaching values of area under the curve higher than those reported in the original article (0.85 at one year and 0.88 at 5 years for the CHA2DS$_2$-VASc score compared with 0.72 and 0.79, respectively).

In our study, when analyzed by risk group, the CHADS$_2$ score was better than the CHA2DS$_2$-VASc score in predicting brain embolism, though this difference was not statistically significant.

Poli et al. recently evaluated six predictive CVA models in 662 patients with AF, a mean age of 74 years and follow-up of 3.6 ± 2.7 years. (9) These two risk scores were among the models tested. Of all the assessed models, the CHADS$_2$ and CHA2DS$_2$-VASc scores were the best predictors of embolic events with an area under the curve of 0.71 and 0.72, respectively. The prediction was quite modest, but no significant differences were found between both scores.
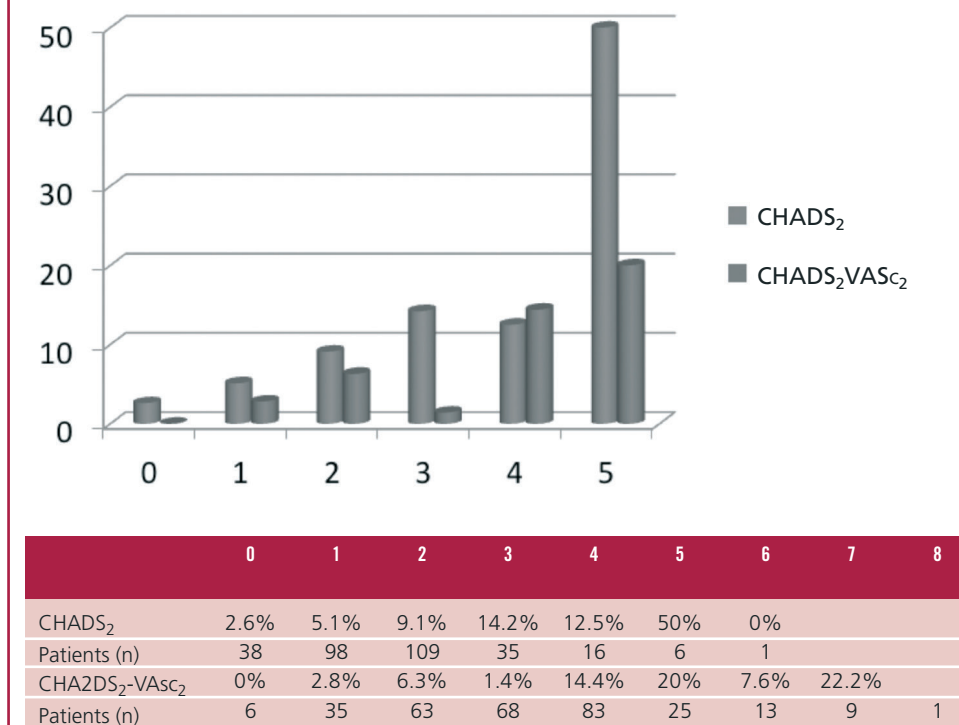
The difference between Poli´s work and our study

Table 1. Baseline population characteristics (N=303)

Variable	
Age, years	73.5 ± 10,1
Female gender, % (n)	47.2 (143)
Heart failure, % (n)	29.7 (90)
Hypertension, % (n)	66.7 (39)
Diabetes mellitus, % (n)	12.9 (202)
History of CVA, % (n)	8.3 (39)
Vascular disease, % (n)	21.5 (25)
Coronary disease, % (n)	16.8 (65)
Amiodarone, % (n)	36.3 (51)
Betablockers, % (n)	18.5 (110)
Pacemaker, % (n)	6.9 (56)
LA diameter, mm	48.5 ± 8.0 (21)

CVA: Stroke. LA: Left atrial.

Fig. 1. Stroke incidence with increasing risk scores.

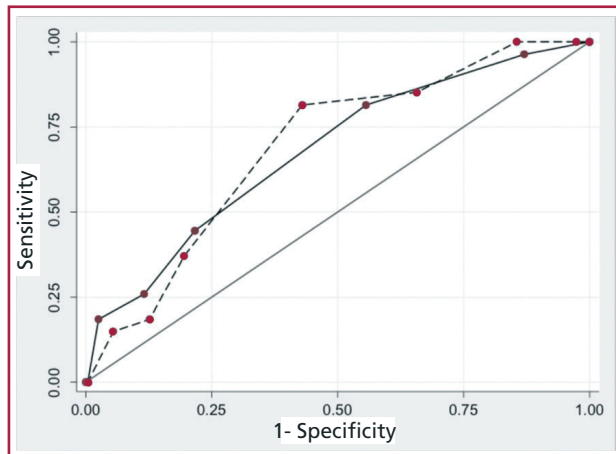|	0	1	2	3	4	5	6	7	8
CHADS$_2$	2.6%	5.1%	9.1%	14.2%	12.5%	50%	0%		
Patients (n)	38	98	109	35	16	6	1		
CHA2DS$_2$-VASc$_2$	0%	2.8%	6.3%	1.4%	14.4%	20%	7.6%	22.2%	
Patients (n)	6	35	63	68	83	25	13	9	1

Fig. 2. Comparison of ROC curves for the CHADS$_2$ (*solid line*) and the CHA2DS$_2$-VASc (*dotted line*) scores.

is that patients in the Italian study were anticoagulated with a high rate of prior CVA (20%) and a high rate of previous transient ischemic attack (TIA) (11%). In our study all anticoagulated and non-anticoagulated registry patients could have been analyzed, but we believe that the anticoagulant changes CVA risk and alters sample homogeneity.

The sample size of the Swedish register is impressive, reaching almost 2% of the total Swedish population. Of the 170291 patients enrolled, 90490 received no anticoagulants and were assessed by both risk scales and followed-up for a mean of 1.4 years. (10) The register assessed the CHADS$_2$ score in three different ways: one as score by adding points, a second one called classic where a score of 1-2 was considered as intermediate risk and a third one defined as revised whereby a score ≥2 was regarded as high risk.

When both scales were used by adding points, both systems had the same predictive ability with a similar area under the curve (0.67 for the CHA2DS$_2$-VASc score and 0.66 for the CHADS$_2$ score; p = ns). When the scoring systems were compared according to risk with either of the two ways of categorization, the CHADS$_2$ score was significantly better at predicting CVA and peripheral embolism than the CHA2DS$_2$-VASc score.

This result was quite similar to ours in terms of the slightly better prediction of the CHADS$_2$ score divided into risk profiles.

These findings were observed despite the large number of events that occurred in patients with the CHADS$_2$ 1 score compared with the CHA2DS$_2$-VASc 1 score (4.9% vs. 0.9 %, respectively).

We believe that at present there is no evidence to show superiority of one risk score over the other in terms of predicting embolic events or CVA.

The CHA2DS$_2$-VASc score seems slightly better in identifying patients with real low risk. No events were registered in the group with CHA2DS$_2$-VASc = 0 while events were identified in patients with CHADS$_2$

= 0 (2.6 %). But despite this advantage of one system over the other, the latest developed score fails to predict overall risk better than the former.

Limitations

Some limitations of our study were those of the original registry, as for example lack of inclusion of paroxysmal AF, although it has been shown that the risk of embolism is similar in all three forms of AF. (11) Moreover, the presence of permanent and persistent AF includes patients with more comorbidities and higher score in the risk scale. Another limitation was that patient follow-up was done by telephone. Although there may be some bias in patient recollection of the event in question, it seems reasonable to assume that a CVA is very well remembered by the patient and not so a TIA, which was therefore excluded from the analysis. This decision might have led to an underestimation of the total number of brain embolic events.

Since patients who did not receive anticoagulation were selected to compare both risk scores, our sample was lower than the original one. This can reduce the number of patients in some score values, thus decreasing the predictive power of that value, but when we divide the scoring system into three risk areas this phenomenon is diluted and it can be seen that the predictive ability does not vary substantially.

CONCLUSIONS

This work shows that in a predominantly Argentine population, CVA risk scores predict this event similarly to those reported in the literature. The areas under the curve were similar to those of records published and no significant differences were found between both scales, either analyzed as score or as a risk profile.

RESUMEN

Aplicación y comparación de los puntajes de riesgo CHADS$_2$ y CHA2DS$_2$-VASc en una población con fibrilación auricular

Introducción

El puntaje CHADS$_2$ y el recientemente adoptado por la comunidad médica CHA2DS$_2$-VASc se han elaborado con datos de registros internacionales y son ampliamente usados en la práctica clínica. Sin embargo, no se han evaluado en registros nacionales.

Objetivos

Evaluar el poder de predicción de los puntajes de riesgo de accidente cerebrovascular CHADS$_2$ y CHA2DS$_2$-VASc en el Registro de Fibrilación Auricular realizado por el Área de Investigación de la Sociedad Argentina de Cardiología y secundariamente comparar ambos sistemas de puntaje.

Material y métodos

El Registro de Fibrilación Auricular realizado en 2001 fue un estudio multicéntrico y prospectivo de todos los pacientes consecutivos asistidos por fibrilación auricular crónica (permanente y persistente) en 70 centros médicos de la

Argentina. Se obtuvieron los datos demográficos, las características socioeconómicas, los antecedentes y las características clínicas. Se realizó un seguimiento a 2 años en el que se evaluó la tasa de accidente cerebrovascular. Para el presente análisis se seleccionaron los pacientes sin tratamiento anticoagulante. En esta población se evaluaron los dos sistemas de puntaje de riesgo, se confeccionó una curva de ROC para cada puntaje (que se informa como estadístico C) y se realizó una comparación entre ambos sistemas de puntaje.

Resultados
El 49,3% (303 pacientes) de los pacientes seguidos no recibían tratamiento anticoagulante y constituyeron nuestra población en estudio. La tasa de accidente cerebrovascular en la población seleccionada fue del 9,5%. Los dos sistemas de puntaje de riesgo predijeron el accidente cerebrovascular significativamente.

La tasa de accidente cerebrovascular fue aumentando a medida que aumentaba el puntaje del CHADS$_2$ y el del CHA2DS$_2$-VASc; este aumento fue similar en ambas escalas de riesgo.

El estadístico C para accidente cerebrovascular del CHADS$_2$ fue de 0,67 (0,55-0,78) y el del CHA2DS$_2$-VASc fue de 0,69 (0,59-0,78), sin diferencias significativas entre ambos.

Con el análisis de los puntajes divididos en tres perfiles de riesgo bajo, moderado y alto se observó que el poder de predicción disminuyó notablemente; el valor del estadístico C del CHADS$_2$ fue de 0,63 (IC 95% 0,57-0,68) y el del CHA2DS$_2$-VASc fue de 0,57 (IC 95% 0,51-0,62), con una ligera tendencia a predecir mejor el CHADS$_2$ pero sin significación estadística.

Conclusiones
En una población con fibrilación auricular de la República Argentina se observó que los dos sistemas de puntaje de predicción de accidente cerebrovascular en pacientes con fibrilación auricular permanente y persistente tienen un poder de predicción similar entre ellos y similar al referido en la bibliografía.

Palabras clave > Fibrilación auricular - Embólia Accidente cerebrovascular

Conflicts of interest
None declared.

REFERENCES

1. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. Arch Intern Med 1995;155:469-73. http://doi.org/fxch32
2. Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). Am J Cardiol 1994;74:236-41. http://doi.org/d9wc3x
3. Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham study. N Engl J Med 1982;306:1018-22. http://doi.org/bdb3bm
4. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke results from the National Registry of Atrial Fibrillation. JAMA 2001;285:2864-70. http://doi.org/djqhd4
5. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: The Euro Heart Survey on Atrial Fibrillation. Chest 2010;137:263-72. http://doi.org/c43wcq
6. Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. ESC Committee for Practice Guidelines (CPG). 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J 2012;33:2719-47. http://doi.org/n97
7. Labadet C, Liniado G, Ferreirós E, Molina Viamonte V, Di Toro D, Cragnolino R et al. First National Prospective Multicenter Study of Chronic Atrial Fibrillation in Argentina. Rev Argent Cardiol 2001:69:49-67.
8. Olesen JB, Lip GY, Hansen ML, Hansen PR, Tolstrup JS, Lindhardsen J. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:D124. http://doi.org/dbfsfg
9. Poli D, Lip GY, Antonucci E, Grifoni E, Lane D. Stroke Risk Stratification in a "real-world" elderly anticoagulated atrial fibrillation population. J Cardiovasc Electrophysiol 2011;22:25-30. http://doi.org/d3sp96
10. Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J 2012;33:1500-10. http://doi.org/fzbh2k
11. Friberg L, Hammar N, Rosenqvist M. Stroke in paroxysmal atrial fibrillation: report from the Stockholm Cohort of Atrial Fibrillation. Eur Heart J 2010;31:967-75. http://doi.org/bq7p7n