Stroke risk scores to predict hospitalization for acute decompensated heart failure in atrial fibrillation patients

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Introduction. Atrial fibrillation (AF) is the most frequent hospitalized arrhythmia. It associates increased risk of death, stroke and heart failure (HF). Stroke risk scores, especially CHA₂DS₂-VASc, have been applied also for populations with different diseases. There is, however, limited data focusing on the ability of these scores to predict HF decompensation.

Methods. We conducted a retrospective observational study on a cohort of 204 patients admitted for cardiovascular pathology to the Cardiology Ward of our tertiary University Hospital. We aimed to determine whether the stroke risk scores could predict hospitalisations for acute decompensated HF in AF patients.

Results. C-statistics for CHADS₂ and R₂CHADS₂ showed a modest predictive ability for hospitalisation with decompensated HF (CHADS₂: AUC 0.631 p = 0.003; 95%CI 0.560–0.697. R₂CHADS₂: AUC 0.619; 95%CI 0.548–0.686; p = 0.004), a marginal correlation for CHA₂DS₂-VASc (AUC 0.572 95%CI 0.501-0.641 with a p value of only 0.09, while the other scores failed to show a correlation. A CHADS₂ ≥ 2 showed a RR = 2.96, p < 0.0001 for decompensated HF compared to a score < 2. For R₂CHADS₂ ≥ 2, RR = 2.41, p = 0.001 compared to a score < 2. For CHA₂DS₂-VASc ≥ 2 RR = 2.18 p = 0.1, compared to CHA₂DS₂-VASc < 2. The correlation coefficients showed a weak correlation for CHADS₂ (r = 0.216; p = 0.001) and even weaker for R₂CHADS₂ (r = 0.197; p = 0.0047) and CHA₂DS₂-VASc (r = 0.14; p = 0.035).

Conclusions. Among AF patients, CHADS₂, CHA₂DS₂-VASc and R₂CHADS₂ were associated with the risk of hospitalisation for decompensated HF while ABC and ATRIA failed to show an association. However, predictive accuracy was modest and the clinical utility for this outcome remains to be determined.

Key words: acute decompensated heart failure, atrial fibrillation, stroke risk scores.

INTRODUCTION

Atrial fibrillation (AF) is the most frequent persistent arrhythmia, affecting 2–3% of the global population [1, 2]. The latest estimates show that there are 8.8 million AF patients in Europe [3]. It is a public health problem worldwide, with a constantly increasing prevalence and incidence [4–7]. AF is also the most common rhythm disorder for which patients are hospitalized, being responsible for approximately 33% of hospitalizations for arrhythmias [8]. AF associates increased risk of HF, hospitalizations and death [9].

HF and AF have common risk factors and pathophysiology [10]. They can cause each other or cause exacerbation of the other one by complex mechanisms including structural remodeling, neurohormonal activation, LV dysfunction (tachycardiomyopathy).

Various risk models were developed over the past years aiming to stratify the thromboembolic risk in AF patients and to discriminate those that benefit from antithrombotic therapy. Currently, the most validated and widely used score is CHA₂DS₂-VASc [11].

Among the first studies to evaluate thromboembolic risk factors in AF were AFI (the Atrial Fibrillation Investigators) [12] and SPAF (Stroke prevention in atrial fibrillation clinical trial) [13]. CHADS₂ score, with superior accuracy in stroke prediction was obtained combining the two previous scores [14].

In 2010, G. Lip *et al.* [11] developed the CHA₂DS₂-VASc score refining the CHADS₂ score with so-called “risk modifying” factors. Unlike the previous score, CHA₂DS₂-VASc has the great advantage of identifying patients who are really at low risk of stroke and who most likely do not require antithrombotic medication.

R₂CHADS₂ score was created by adding two points for a ClCr <60 ml/min, to the already established CHADS₂. The R₂CHADS₂ score was validated on the cohorts from the ROCKET-AF and ATRIA studies [15, 16].

ATRIA is one of the newest scores proposed to assess thromboembolic risk and was derived from the ATRIA cohort [17]. It was validated on the ATRIA-Cardiovascular Research Network (CVRN) cohort [18]. This score tried to evaluate severe thromboembolic events (Rankin ≥ 3 at discharge or death in the first 30 days), the predictive value being higher for this category of patients than for those without thromboembolic events [18].

The ABC score contains only 4 variables: age (A), biomarkers (troponin and NT-proBNP) (B), history of stroke/TIA (C). It was developed using the cohort from the ARISTOTLE study (a highly selected cohort of anticoagulated AF patients) and was subsequently validated on a smaller cohort from the RE-LY study [19, 20].

ABC is the only score that uses biomarkers, which add important information about subclinical cardiovascular dysfunction and are associated with

vascular vulnerability [21]. ABC includes the variables with the highest prognostic power in multivariate COX analysis.

Although CHA₂DS₂-VASc and CHADS₂ were originally designed to stratify the risk of stroke in AF patients, recently they have been applied in studies with populations of various other pathologies [22, 23]. For the other stroke risk scores, there is limited data on their ability to predict hospitalisation for HF decompensation [24, 25].

Therefore, we aimed to determine whether the stroke scores could also predict decompensated HF in AF patients.

MATERIAL AND METHODS

We included 204 patients, aged 18 to 80, with either previously diagnosed or new onset AF, that were admitted to the Cardiology Ward of the Colentina Clinical Hospital in 2015.

The inclusion and exclusion criteria are listed in Figure 1.

Figure 1. Inclusion and exclusion criteria.

Although we screened a much higher number of patients, many of them were excluded for missing data. Being a retrospective analysis, we used data from patients charts or discharge summary. The most frequent causes for exclusion were missing parameters (needed for calculating all the risk scores included in our study) and lack of follow-up.

We calculated the following scores for each patient: CHADS₂, CHA₂DS₂-VASc, R₂CHADS₂, ABC, ATRIA.

Patients were evaluated after a mean follow-up period of 365 days. The main outcome of interest was hospitalisation for acute decompensated HF after the index date.

All patients signed a written consent for agreeing to participate in research activity with anonymized data. The research protocol was in accordance with the ethical guidelines of the Declaration of Helsinki.

Statistical analysis

Demographic and clinical characteristics at index evaluation are summarized using means $\pm$ standard deviation for continuous variables and percentages for categorical variables.

The prediction ability of each scoring system was analysed with C-statistics and compared by the differences in the area under the curve (AUC) according to the ROC curve. We compared the AUCs for all scores using DeLong method.

The statistical analysis was performed using Microsoft Excel 16.34, SPSS Statistics 23 and MedCalc 19.2. The p value for statistical significance was set at < 0.05 .

RESULTS

The baseline characteristics of the study population are shown in Table 1. The mean age at admission was 66 years old and the proportion of male patients was slightly smaller than that of women (46% vs 54%). 139 (68.1%) patients were classified as having permanent AF while 23 (11.2%) had persistent AF and 42 (20.5%) paroxysmal AF.

Table 1

Baseline characteristics of the study population

Baseline characteristics	Total	Patients with hospitalisation for HF	Patients without hospitalisation for HF	P value
	N = 204	N = 60	N = 144	
Mean age (yr $\pm$ SD)	66 (± 8.68)	67 (± 8.53)	65 (± 8.7)	0.29
Gender (male)	95 (46%)	29 (48.3%)	67 (46.5%)	0.93
AF type	Paroxysmal 42 (20.5%)	8 (13.3%)	34 (23.6%)	0.09
	Persistent 23 (11.2%)	10 (16.6%)	13 (12.5%)	0.11
	Permanent 139 (68.1%)	42 (70%)	97 (67.3%)	0.71
HTN	157 (77%)	50 (83.3%)	107 (74.3%)	0.22
CHF	56 (27.5%)	32 (53.3%)	24 (16.6%)	<0.0001
Diabetes mellitus	53 (25%)	21 (35%)	32 (22.2%)	0.08
Dyslipidaemia	71 (34.8%)	18 (30%)	53 (36.8%)	0.44
History of stroke/TIA	18 (8.8%)	3 (5%)	15 (10.4%)	0.45
Coronary artery disease	78 (38.6%)	29 (48.3%)	49 (34%)	0.09
EF ($\pm$ SD)	45.8% (± 11.6)	40% (± 12.9)	48% (± 10.2)	0.01

Table 2 shows patients medication at index evaluation. 168 patients were anticoagulated, most of them with VKA (137; 67.2%) and only 31 (15.2%) NOAC. The remaining 36 (17.6%) were not receiving oral anticoagulation.

Figure 2 and Tables 3–7 show the distribution of patients based on the values of the risk scores.

The AUC showed that CHADS₂ and R₂CHADS₂ have a modest predictive ability for

decompensated HF (CHADS₂: AUC 0.631 95% CI 0.560–0.697; $p = 0.003$. R₂CHADS₂: AUC 0.619; 95% CI 0.548–0.686; $p = 0.004$), while the other stroke risk scores failed to show a correlation (ABC: AUC 0.514; 95% CI 0.426–0.601; $p = 0.76$. ATRIA: AUC 0.537 95% CI 0.46–0.6; $p = 0.37$). CHA₂DS₂-VASc had a AUC of 0.572 (95% CI 0.501–0.641) but with $p = 0.09$ (Figure 3).

Table 2

Medical therapy of the study population

Medication at index evaluation		Total	Patients with hospitalisation for HF	Patients without hospitalisation for HF	P value
		N = 204	N = 60	N = 144	
Beta blockers		156 (76.5%)	40 (66.7%)	116 (80.6%)	0.0512
ACEIs/sartans		154 (75.5%)	48 (80%)	106 (73.6%)	0.47
Digoxin		65 (31.9%)	27 (45%)	38 (26.4%)	0.0149
Antiarrhythmic	Total	21 (10.3%)	6 (10%)	155 (10.4%)	0.87
	Amiodarone	19 (9.31%)	6 (10%)	13 (9.02%)	0.96
	Propafenone	2 (0.98%)	0	2 (1.38%)	0.89
Loop diuretics		84 (41.2%)	35 (58.3%)	49 (34%)	0.022
OAC	VKA	137 (67.2%)	47 (78.3%)	90 (62.5%)	0.4
	NOAC	31 (15.2%)	5 (8.3%)	26 (18.1%)	
No OAC		36 (17.6%)	8 (13.3%)	28 (19.4%)	0.4
Ca ch. antagonists	DHP	23 (11.3%)	8 (13.3%)	15 (10.4%)	0.98
	Non DHP	12 (5.9%)	4 (6.7%)	8 (5.6%)	0.72
Statins		128 (62.7%)	39 (65%)	89 (61.8%)	0.78

Figure 2. Frequency distribution of each score model.

Table 3

Distribution of patients based on the CHA₂DS₂-VASc score

	CHA ₂ DS ₂ -VASc		
	low risk (0 for males/ 1 for female)	intermediate risk (1 for males/ 2 for females)	high risk (≥2 for males/ ≥3 for females)
Without HF hospitalisation	6 (2.94%)	33 (16.17%)	105 (51.47%)
With HF hospitalisation	0	12 (5.88%)	48 (23.50%)
Total	6 (2.94%)	45 (22.05%)	153 (71.90%)

Table 4

Distribution of patients based on the CHADS₂ score

	CHADS ₂						
	0	1	2	3	4	5	6
Without HF hospitalisation	15 (10.4%)	51 (35.4%)	41 (28.5%)	28 (19.4%)	8 (5.6%)	1 (0.7%)	0 (0%)
With HF hospitalisation	2 (3.3%)	13 (21.7%)	19 (31.7%)	20 (33.3%)	4 (6.7%)	1 (1.7%)	1 (1.7%)
Total	17 (8.3%)	64 (31.4%)	60 (29.4%)	48 (23.5%)	12 (5.9%)	2 (1%)	1 (0.5%)

Table 5

Distribution of patients based on the R₂CHADS₂ score

	R ₂ CHADS ₂								
	0	1	2	3	4	5	6	7	8
Without HF hospitalisation	13 (9%)	39 (27.1%)	34 (23.6%)	27 (18.8%)	15 (10.4%)	14 (9.7%)	2 (1.4%)	0 (0%)	0 (0%)
With HF hospitalisation	2 (3.3%)	10 (16.7%)	13 (21.7%)	16 (26.7%)	6 (10%)	8 (13.3%)	5 (8.3%)	0 (0%)	0 (0%)
Total	15 (7.4%)	49 (24%)	47 (23%)	43 (21.1%)	21 (10.3%)	22 (10.8%)	7 (3.4%)	0 (0%)	0 (0%)

Table 6

Distribution of patients based on the ATRIA score

	ATRIA											
	0	1	2	3	4	5	6	7	8	9	10	11
Without HF hospitalisation	11 (7.6%)	17 (11.8%)	24 (16.7%)	8 (5.6%)	18 (12.5%)	19 (13.2%)	10 (6.9%)	12 (8.3%)	12 (8.3%)	6 (4.2%)	6 (4.2%)	1 (0.7%)
With HF hospitalisation	1 (1.7%)	5 (8.3%)	8 (13.3%)	9 (15%)	7 (11.7%)	11 (18.3%)	5 (8.3%)	5 (8.3%)	4 (6.7%)	1 (1.7%)	4 (6.7%)	0 (0%)
Total	12 (5.9%)	22 (10.8%)	32 (15.7%)	17 (8.3%)	25 (12.3%)	30 (14.7%)	15 (7.4%)	17 (8.3%)	16 (7.8%)	7 (3.4%)	10 (4.9%)	1 (0.5%)

Table 7

Distribution of patients based on the ABC score

	ABC			
	0–1%	1–2%	2–3%	>3%
Without HF hospitalisation	107 (74.3%)	30 (20.8%)	5 (3.47%)	2 (1.38%)
With HF hospitalisation	41 (68.3%)	17 (28.3%)	1 (1.6%)	1 (1.6%)
Total	148 (72.5%)	47 (23%)	6 (2.9%)	3 (1.47%)

Diagonal segments are produced by ties.

Figure 3. Comparison of the ROC curves for the prediction of hospitalization for decompensated heart failure.

The values are relatively similar between scores, with the highest positive predictive values (PPV) for R₂CHADS₂ (37.6% vs 36.5% (CHADS₂) vs 33% (CHA₂DS₂-VASC) and the highest negative predictive values (NPV) for CHADS₂ (81.48% vs 76.6% (CHA₂DS₂-VASC) vs 77.45% (R₂CHADS₂)), the PPV are poor but with fairly good NPV, indicating that these scores could be useful in identifying patients at low risk for decompensated HF.

DeLong comparison of AUCs showed the following to be significantly different: CHADS₂ vs CHA₂DS₂-VASC ($p = 0.02$), CHADS₂ vs ATRIA ($p = 0.01$), CHADS₂ vs ABC ($p = 0.02$), R₂CHADS₂ vs ATRIA ($p = 0.03$) and R₂CHADS₂ vs ABC ($p = 0.04$).

The correlation coefficient showed a weak correlation for CHADS₂ ($r = 0.216$; $p = 0.001$) and even weaker for R₂CHADS₂ ($r = 0.197$; $p = 0.0047$) and CHA₂DS₂-VASC ($r = 0.14$; $p = 0.035$).

Patients with a CHADS₂ ≥ 2 had a relative risk (RR) of 2.96 (95%CI 1.80–4.87; $p < 0.0001$) for decompensated HF when compared to a score < 2 . The RR for a CHA₂DS₂-VASC ≥ 2 is 2.18 (95%CI 0.74–6.35; $p = 0.1$), compared to CHA₂DS₂-VASC

< 2 and for R₂CHADS₂ ≥ 2 RR is 2.41 (95%CI 1.39–4.19; $p = 0.001$) compared to a score < 2 .

On logistic regression, CHADS₂ had an OR of 1.52 (95% CI 1.15–2.01) $p = 0.002$ for predicting decompensated HF while for CHA₂DS₂-VASC the OR was 1.23 (95% CI 1.01–1.51) $p = 0.03$ and for R₂CHADS₂ OR 1.31 (95% CI 1.08–1.6) $p = 0.005$. In contrast, for ABC the OR was 1.03 (95% CI 0.63–1.69) $p = 0.88$ and for ATRIA OR 1.03 (95% CI 0.93–1.15) $p = 0.47$.

There are competing conditions considered to be involved in the aetiology of decompensated HF. However, among components of CHADS₂ and CHA₂DS₂-VASC, only congestive HF was found to be associated with decompensated HF (OR 2.29; 95% CI 1.70–3.08; $p < 0.001$).

Among patients baseline characteristics, history of HF and ejection fraction were the only ones that showed a statistically significant difference between groups with and without hospitalisation for acute decompensated HF ($p < 0.0001$ for CHF. $p = 0.01$ for EF).

From patients medication, loop diuretic and digitalis were associated with the risk of hospitalisation

for decompensated HF (furosemide: OR 2.71; 95% CI 1.46–5.03; $p = 0.002$; digoxin: OR 2.28; 95% CI 1.21–4.28; $p = 0.01$). For these two classes of medication there was a significant difference between the groups with and without hospitalisation for HF ($p = 0.014$ for digoxin; $p = 0.022$ for furosemide).

DISCUSSIONS

Stroke risk scores have been developed as combined schemes of the most important cardiovascular risk factors and comorbidities. Thus, the idea that they could also be used for different other estimations, is to some degree intuitive and it is worth pursuing.

Moreover, broadening the utility of a clinical tool that is already used for all AF patients is appealing because it allows the dispense of other time-consuming tools and it gives a better understanding of patient's risks and management strategy.

Simple and dynamic risk assessment should be implemented in clinical practice in order to detect high-risk patients.

Risk prediction for acute decompensated HF is especially important in AF patients since AF is highly associated with HF and also with an adverse prognosis in HF [25, 26].

HF is a complex clinical syndrome that shares common risk factors and pathophysiology with AF [10].

In the Framingham study [27], in patients with AF and HF, 41% had HF first, 38% had AF first and in 21% both conditions occurred simultaneously.

Our study hypothesised that the stroke risk scores could predict acute decompensated HF in AF patients. It is a retrospective, small study which showed that the most widely used thromboembolic risk scores, CHADS₂ and CHADS₂-VASc, as well as R₂CHADS₂, also correlate with hospitalisation for acute decompensated HF.

Although this correlation is modest, it opens the opportunity for future investigations.

Our results are consistent with previous studies that show a correlation for CHADS₂ and CHADS₂-VASc with congestive HF [25] and all-cause cardiovascular hospitalisation [28].

Although the ABC stroke score is more complex and brings more information, our study failed to show an association with decompensated HF. This is in contradiction with recent evidence [29] that show significant higher ABC stroke scores for patients who had acute HF. Our results could be explained by the smaller cohort size with

predominantly low-medium scores, and small number of events.

The ABC score has the disadvantage that the biomarkers predict different clinical events at the same time.

ATRIA stroke model brings supplementary information like glomerular filtration rate, and proteinuria. It also uses a broader range of age categories, which could potentially provide a better insight of the true risk. In the ATRIA study, its discriminatory ability improved when outcome was restricted to severe events [18]. This is an important finding as preventing severe events is more important than preventing minor events and more relevant for patient's management.

For ATRIA, there is also some evidence [30] that in patients with HFpEF, a score ≥ 8 correlates with any hospitalisation as well as hospitalisation for HF.

This is also in contradiction with our findings that failed to show an association between ATRIA and acute decompensated HF. A possible reason is that our outcome is not a major event, for which ATRIA showed its best predictive ability. Also our cohort has a wide range of ejection fraction, with significant difference between the groups with and without decompensated HF.

In our study, independent predictors of decompensated HF were the ejection fraction and history of congestive HF. This suggests that history of HF is an important predictor of the recurrence of HF in AF patients, which is consistent with previous studies and reports [25].

From patients medication, loop diuretics and digitalis correlated with the risk of decompensated HF. Loop diuretics is the cornerstone of congestion management in chronic HF and the fact that its use in outpatient medication prevents future events of decompensated HF is well known. The ESC Guidelines recommend loop diuretics to prevent hospitalization for decompensated HF in patients with congestion [31].

Although it has been previously reported that hypertension is a risk factor for congestive HF [31, 32], in our study there was no correlation.

The modest predictive ability demonstrated by our study and the differences from previously published data, confirm the need for future studies to better describe the potential benefit of using stroke risk scores for predicting acute decompensated HF as well as other outcome.

To this point, the well-known CHADS₂ and CHA₂DS₂-VASc along with the derived R₂CHADS₂

remain the tools with the highest potential for extending their utility beyond their original purpose. The newer scores like the ABC and ATRIA, although more complex, seem not to bring any additional benefit for predicting decompensated HF.

Study limitations

The main limitation of this study is the small cohort size which also influences the number of events.

Another limitation is the retrospective nature of the study, observational data being obtained from patient's hospital chart after admission to Cardiology Department of a tertiary University

Hospital. Being a hospital-based study, one should note that patient's characteristics could differ from those of the general population.

CONCLUSIONS

CHADS₂, CHA₂DS₂-VASc and R₂CHADS₂ have a modest ability to predict hospitalization for decompensated HF in AF patients, while ATRIA and ABC fail to show an association.

These scoring models could be useful in clinical practice to identify patients at increased risk for events but these results need further evaluation on larger and more heterogeneous cohorts.

Introducere. Fibrilația atrială (FA) este cea mai frecventă aritmie care necesită spitalizare. Aceasta asociază un risc crescut de deces, accident vascular cerebral și insuficiență cardiacă (IC). Scorurile de risc pentru accident vascular cerebral (AVC), în special CHA₂DS₂-VASc, au fost aplicate în populații cu patologii diverse. Cu toate acestea, există date limitate cu referire la capacitatea acestor scoruri de a prezice spitalizările pentru IC acut decompensată.

Metode. Am realizat un studiu observațional retrospectiv pe o cohortă de 204 de pacienți internați pentru patologie cardiovasculară la Secția de Cardiologie a Spitalului nostru Universitar terțiar. Am urmărit să determinăm dacă scorurile de risc pentru AVC ar putea prezice internările pentru IC acut decompensată la pacienții cu FA.

Rezultate. Valorile C-statistics pentru CHADS₂ și R₂CHADS₂ au evidențiat o valoare predictivă modestă pentru spitalizare cu IC decompensată (CHADS₂: AUC 0,631 $p = 0,003$; 95% CI 0,560–0,697. R₂CHADS₂: AUC 0,619; 95% CI 0,548–0,686; $p = 0,004$), o corelație marginală pentru CHA₂DS₂-VASc (AUC 0,572 95% CI 0,501–0,641 cu o valoare p de doar 0,09. ABC și ATRIA nu au evidențiat o corelație. Pentru CHADS₂ ≥ 2 RR = 2,96, $p < 0,0001$ pentru IC acut decompensată comparativ cu un scor < 2 . Pentru R₂CHADS₂ ≥ 2 , RR = 2,41, $p = 0,001$ comparativ cu un scor < 2 . Pentru CHA₂DS₂-VASc ≥ 2 RR = 2,18 $p = 0,1$ comparativ cu CHA₂DS₂-VASc < 2 . Coeficientul de corelație a arătat o asociere slabă pentru CHADS₂ ($r = 0,216$; $p = 0,001$), R₂CHADS₂ ($r = 0,197$; $p = 0,0047$ și CHA₂DS₂-VASc ($r = 0,14$; $p = 0,035$).

Concluzii. CHADS₂, R₂CHADS₂ și CHA₂DS₂-VASc se asociază cu riscul de spitalizare pentru IC acut decompensată, în timp ce pentru ABC și ATRIA nu s-a evidențiat o asociere. Cu toate acestea, valoarea predictivă este modestă, iar utilitatea clinică pentru acest obiectiv necesită studii suplimentare.

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Acknowledgements: none to declare

Conflict of interest disclosure: The authors declare that there are no conflicts of interest.

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Received 15th September 2020