Predictive Power of Brown Esus-Af Score for Detection of Post Stroke Atrial Fibrillation: A Brief Report from Real World

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ABSTRACT

Introduction: Searching paroxysmal atrial fibrillation (PAF) is the cornerstone in post embolic stroke of undetermined source (ESUS) patients. The Brown ESUS-AF score was proposed as a simple and good prognosticator of poststroke PAF detection. Age ($\geq$ 75 years 2 points, 65-74 years 1 point) and moderate-severe left atrial enlargement (LAE, 2 points) are the variables enclosed in the score. External validation of Brown ESUS-AF score was the aim of the present study.

Materials and Methods: We analyzed demographic, clinical, trans-thoracic echocardiography and brain computer tomography characteristics of patients with ESUS undergone to two weeks external ECG monitoring after hospital discharge. PAF was considered detected when any evidence of AF and/or atrial flutter occurred at monitoring.

Results: Eighty-two consecutive ESUS patients with mean age $\pm$ SD 72 $\pm$ 10 years were the study population. PAF detection increased from 18.75% of patients with Brown ESUS-AF score 0 to 54.3% of patients with Brown ESUS-AF score $\geq$ 2. AUC of Brown ESUS-AF score in predicting AF detection was 0.642 (95% CI: 0.528-0.745). No difference between predictive power of Brown ESUS-AF score and CHA_2DS_2-VASc score was found.

Conclusion: Brown ESUS-AF score could be used as a screening tool for selecting ESUS patients requiring prolonged ECG monitoring aimed to detect PAF. However, in our study the predictive power of Brown ESUS-AF score was not superior to that of CHA_2DS_2-VASc score.

Keywords
ESUS; Stroke; Atrial fibrillation; Score; ECG monitoring.

Introduction

Occult paroxysmal atrial fibrillation (PAF) represents one of the main causes of embolic stroke of undetermined source (ESUS). Therefore, searching PAF is fundamental in the diagnostic work-up of ESUS. In 2018, Ricci B. et al proposed a new simple score named Brown ESUS-AF score aimed at predicting PAF detection on prolonged electrocardiographic (ECG) monitoring in post ESUS outpatients [1]. The protocol by Ricci B. and colleagues consisted of a 30-day external ECG monitoring followed by an implantable device if the first monitoring was negative. PAF was considered detected when any evidence of PAF or atrial flutter including brief episodes occurred at ECG monitoring. Age ≥ 75 years (2 points), age 65-74 years (1 point), moderate-severe left atrial enlargement (2 points) were the variables they found as independent predictors of AF detection. The predictive power of the Brown ESUS-AF score was good with an area under the receiver operating characteristic (ROC) curve (AUC) of 0.725. PAF detection increased from 4.2% in patients with Brown ESUS-AF score of 0 to 55.6% in patients with a score of 4. In a study comparing 68 patients with first ever AF with 123 patients with cryptogenic stroke, Muscari A et al found an AUC of 0.70 (95% CI: 0.62-0.78) for the Brown ESUS-AF score [2]. Recently Mendez B. et al. showed that the Brown ESUS-AF score is also a good prognosticator of stroke recurrence in ESUS patients [3]. Despite the Brown ESUS-AF score is a very simple and interesting tool, external validations lack. Thus, the aim of our study was the external validation of the Brown ESUS-AF score.

Materials and Methods

We retrospectively analyzed the predictive power of the Brown ESUS-AF score in a cohort of 82 consecutive ESUS patients (48 females) defined according to standardized criteria [4], admitted to our Stroke Unit, and undergone to 15-day external ECG monitoring by using an event recorder (Spider Flash-t™, Sorin Group) after hospital discharge. For all the patients demographic characteristics (age, sex), modified Rankin scale (mRS) at hospital discharge, risk factors for AF and the CHA_2DS_2-VASc score, National Institute of Health Stroke Scale (NIHSS) at stroke onset, brain infarct size (<2.5 or >2.5 cm), location (cortical, cortical-subcortical, subcortical, supra- or sub-tentorial) and number (single or multiple) of the ischemic lesions, left atrium size (with left atrial enlargement, defined as diameter ≥40 mm or area ≥20 cm²), were analyzed. For statistical analysis continuous variables were reported as mean ± standard deviation (SD) or as median and interquartile range (IQR) as appropriate. Categorical variables were analyzed using the χ^2 test and Fisher's exact test when appropriate. Multivariate logistic regression analysis was used to estimate the risk factors for AF detection; ORs and their 95th percentile confidence intervals (CI) were reported. To evaluate the predictive power of the new score, the area under the curve (AUC) of the Receiver Operating Characteristic (ROC) curve was calculated. A p value of <0.05 was considered statistically significant. All analyses were performed using MEDCALC statistical software (MedCalc Software Ltd, Acacialaan 22, B-8400 Ostend, Belgium).

Results

General characteristics of patients are shown in Table 1. Mean age ± SD was 72 ± 10 years. Fourty-one patients (50%) were 75 years old and older, 24 (29.3%) were 65-74 years old, and 37 patients (45.1%) had left atrial enlargement defined as left atrial diameter > 40 mm or left atrial area > 20 cm². PAF was detected in 36 patients (43.9%). Median CHA_2DS_2-VASc score in patients with PAF detection was significantly higher compared with patients without PAF detection (4 vs 3, p=0.02). In patients in whom PAF was detected, median Brown ESUS-AF score was 2 (IQR, 1-2) while in those without AF detection was 1 (IQR 0-2). PAF detection increased from 18.75% in patients with Brown ESUS-AF score 0 to 54.3% in patients with Brown ESUS-AF score ≥ 2. The AUC of Brown ESUS-AF score in predicting AF detection was 0.642 (95% CI: 0.528-0.745, specificity 54.3%, sensitivity 69.4% for Brown ESUS-AF score > 1). No difference between predictive power of Brown ESUS-AF score and CHA2DS2-VASc score (AUC 0.671, 95% CI: 0.559-0.771, difference between AUCs 0.0296, p=0.62)) was found (Figure 1).

Table 1: General characteristics of study patients.

	AF detected	AF not detected	p
Number	36	46	
Median age (IQR), years	**77.5 (72-82)**	**71 (63-77)**	**0.04**
Median CHA_2DS_2-VASc (IQR)	**4 (3-5)**	**3 (2-4)**	**0.02**
Age ≥ 75 years, n (%)	**23 (63.8)**	**18 (39.1)**	**0.04**
Age 65-74 years, n (%)	10 (27.7)	14 (30.4)	0.81
Age ≤ 64 years, n (%)	**3 (8.3)**	**14 (30.4)**	**0.01**
Female sex, n (%)	25 (69.4)	23 (50)	0.11
Blood hypertension, n (%)	**33 (91.6)**	**30 (65.2)**	**0.007**
Heart failure (EF <40%), n (%)	0 (0)	0 (0)	1
Diabetes, n (%)	10 (27.7)	11 (23.9)	0.80
Vascular disease, n (%)	11 (30.5)	10 (21.7)	0.80
Previous TIA/stroke, n (%)	5 (13.8)	9 (19.5)	0.56
Left atrial enlargement, n (%)	19 (52.7)	18 (39.1)	0.26
Brain infarct size ≥ 2.5 cm, n (%)	17 (47.2)	17 (36.9)	0.37
Brain cortical and/or cortical/subcortical infarct, n (%)	28 (77.7)	34 (73.9)	0.26
Multiple brain infarcts, n (%)	21 (58.3)	23 (50)	0.50
Bilateral brain infarcts, n (%)	8 (22.2)	6 (13.0)	0.37
Posterior brain infarcts, n (%)	17 (47.2)	14 (30.5)	0.16
NIHSS ≥ 5 at admission	7 (19.4)	11 (23.9)	0.78
mRS ≥ 3 at discharge	17 (47.2)	16 (34.7)	0.26

AF=atrial fibrillation; IQR=interquartile range; CHA_2DS_2-VASc=congestive heart failure/EF <40%, hypertension, age ≥ 75 years, diabetes, previous TIA/stroke/systemic embolism, vascular disease, age 65-74 years, sex category; EF=ejection fraction; TIA=transient ischemic attack.; NIHSS=National Institute of Health Stroke Scale; mRS=modified Rankin Scale.

Discussion

Identifying predictors of PAF detection in post ESUS patients is of the main importance to choose the appropriate treatment and reduce the risk of stroke recurrence. Systematic reviews showed
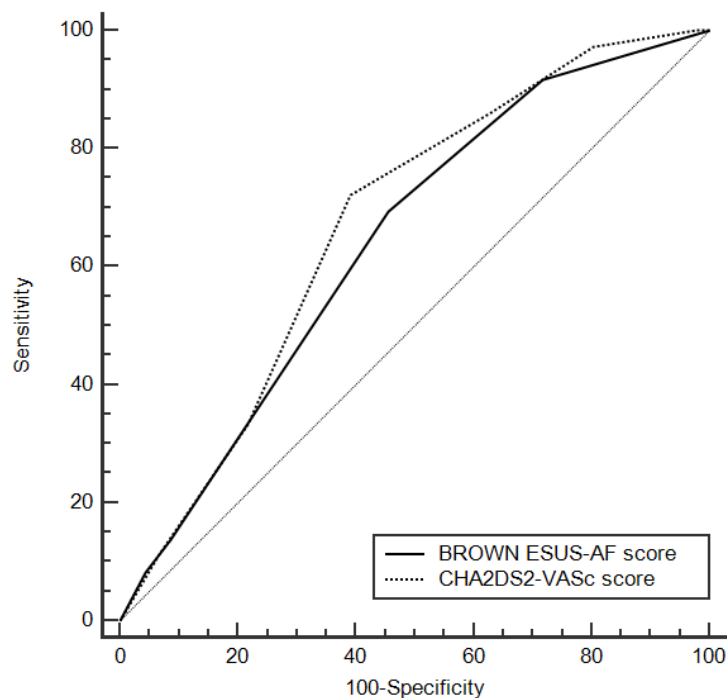
Figure 1: Comparison between AUROCs of Brown ESUS-AF score and CHA2DS2-VASc score in predicting AF detection on external ECG monitoring.

that the rate of stroke recurrence in ESUS patients is 4.5% [5]. Randomized clinical trials found no advantage in the use of direct oral anticoagulants compared with antiplatelets in preventing stroke recurrence [6,7], while in AF-related strokes direct oral anticoagulants are now recognized as the first choice in secondary prevention due to the best efficacy/safety profile compared with vitamin K antagonists or antiplatelets [8].

Our study confirms that the Brown ESUS-AF score could be used as a screening tool for identifying ESUS patients in whom stroke could be more probably related to PAF, and therefore, it may be useful to select patients with priority for searching PAF by prolonged ECG monitoring. However, in our study population, the Brown ESUS-AF score did not show advantage in predict PAF detection compared with CHA_2DS_2-VASc score.

We recognized that our study has limitations, mainly due to its retrospective design and difference in length of ECG monitoring (two weeks in our study, one month in the study of Ricci B. et al) [1].

Conclusion

Brown ESUS-AF score could be used as a screening tool for selecting ESUS patients requiring prolonged ECG monitoring aimed to detect PAF. However, in our study the Brown ESUS-AF seems to bring no advantage compared with CHA_2DS_2-VASc score as PAF prognosticator.

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