

Comparison Between 3 Bleeding Scoring Systems in Nonvalvular Atrial Fibrillation Patients. What Can the New ORBIT Score Provide?



Comparación entre tres sistemas de puntuación de hemorragia en pacientes con fibrilación auricular no valvular. ¿Qué puede ofrecer la nueva puntuación ORBIT?

To the Editor,

Atrial fibrillation (AF) is a health problem of increasing concern at the national level in Spain.¹ Bleeding risk assessment is a key step in AF patient management for a safer use of oral anticoagulants. Current European Society of Cardiology guidelines recommend the use of the HAS-BLED classification system for bleeding risk assessment in nonvalvular AF (NVAF) patients.² However, HAS-BLED has been criticized for the requirement of data on INR (international normalized ratio) monitoring, which are not usually available at the moment of decision-making for anticoagulant-naïve NVAF patients.

The new ORBIT bleeding risk score (Table 1 of the supplementary material) was found to have the advantage of providing similar discrimination and even better calibration than the HAS-BLED and ATRIA bleeding scores (Table 2 of the supplementary material), despite not requiring information on the time in therapeutic range (ie, labile INR) for its calculation.³

However, in a recent validation study,⁴ the new ORBIT score did not outperform HAS-BLED, albeit that study was a clinical trial excluding patients with a history of major bleeding.

In this study, we aimed to explore in a real word cohort of outpatients, whether, as recently suggested,³ there is an incremental prognostic value of the new ORBIT score over HAS-BLED and ATRIA.

The details of this study have been published elsewhere.⁵ Briefly, between January 2011 and February 2013, we studied 911 consecutive NVAF patients recently started on vitamin K antagonists (VKA). Major bleeding was defined using the definition of the International Society on Thrombosis and Haemostasis (ISHT) 2005.

We had insufficient data on the INR values before patient enrollment in the study. However, given the major importance of the labile INR variable, we used each patient's INR measurements during the follow-up to calculate the time in therapeutic range (after excluding the INR values registered during the first month after VKA initiation). According to the study design, we excluded patients with interrupted VKA > 3 days (n = 73 patients) and, in a group of these patients, the reason for VKA interruption was nonmajor bleeding.⁵

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

The median age was 75 years (interquartile range [IQR]: 66-81 years); 34.6% were female. A total of 84.7% had a CHA₂DS₂-VASc ≥ 2 points, and 12.6% had prior bleeding. The median number of INR controls was 15 [14-15]. Time in therapeutic range by Roosendaal was 66% [54-77%]. The median HAS-BLED, ATRIA, and ORBIT scores was 2 [2-3] points, 3 [1-3] points, and 1 [0-2] point.

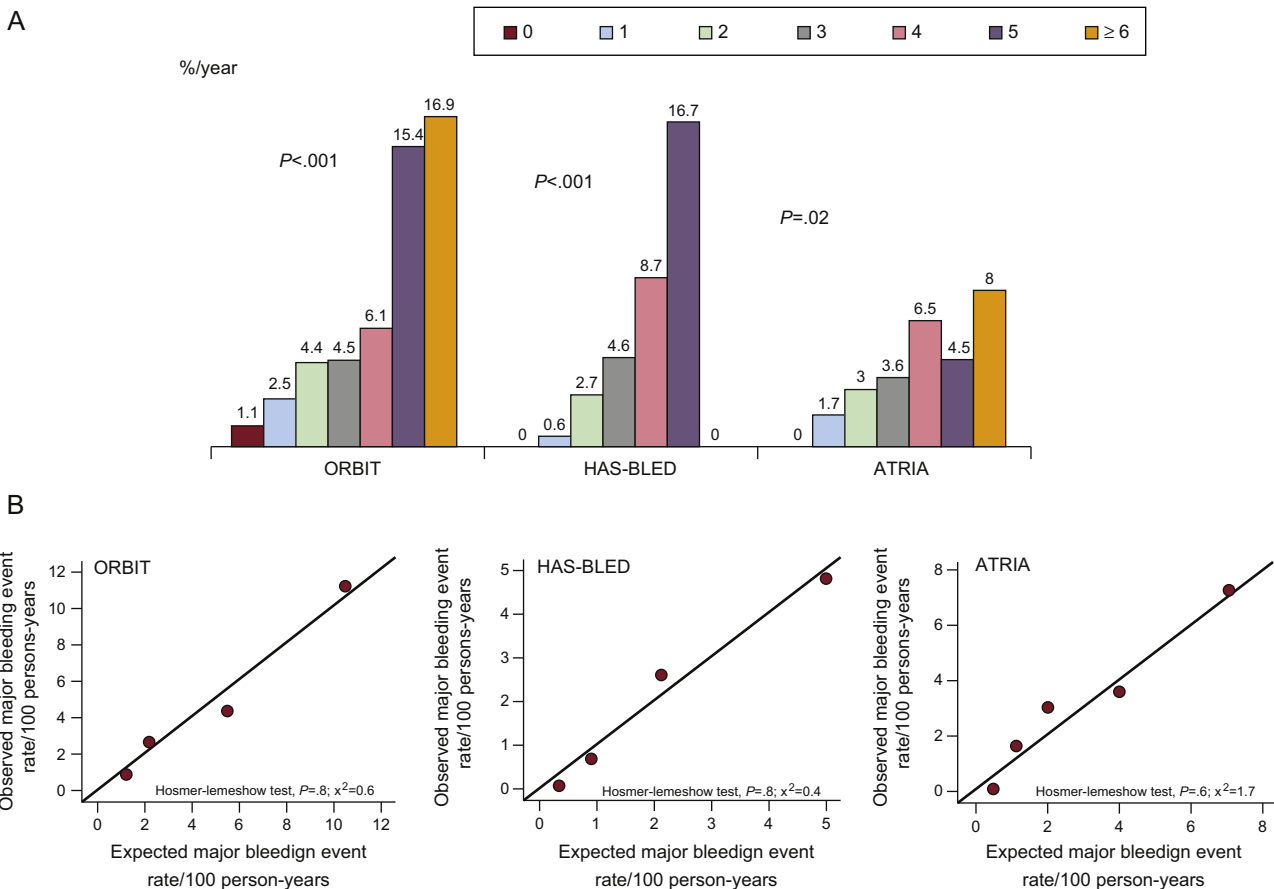


Figure. A: Rate of major bleeding events according to the ORBIT, HAS-BLED and ATRIA scores; B: Calibration for the probability of major bleeding event/100 persons-years by ORBIT, HAS-BLED and ATRIA scores.

Table

Association Between HAS-BLED, ATRIA, and ORBIT Risk Scores and Major Bleeding, and the Discrimination Ability of the 3 Scores

Risk score	sHR ^a	95%CI	P-value	c-statistic for ISHT major bleeding, 95%CI
HAS-BLED^b				
Continuous	1.69	1.39-2.07	< .001	0.68 (0.64-0.71)
Categorical				0.64 (0.60-0.67)
Low-risk ^c	0.2	0.10-0.44	< .001	
High-risk	4.6	2.3-9.6	< .001	
ATRIA^d				
Continuous	1.30	1.18-1.44	< .001	0.71 (0.68-0.74)
Categorical				0.61 (0.57-0.64)
Low-risk ^e	0.3	0.13-0.58	.001	
High-risk	3.6	1.7-7.4	.001	
ORBIT^f				
Continuous	1.4	1.27-1.62	< .001	0.74 (0.71-0.77)
Categorical				0.66 (0.63-0.69)
Low-risk ^g	0.2	0.08-0.34	< .001	
Medium-risk ^h	3.1	1.01-9.6	.048	
High-risk	5.9	2.8-12.4	< .001	
ORBIT				
Categorical				0.66 (0.63-0.69)
Low-risk	0.2	0.08-0.34	< .001	
Medium-high risk	6.0	2.98-12.2	< .001	

95%CI, 95% confidence interval; ATRIA: anticoagulation and risk factors in atrial fibrillation; ISHT: International Society on Thrombosis and Haemostasis; sHR, subhazard ratio.

^a sHR (calculated using competing risks regression analysis by the method of Fine-Gray; death was considered as a competing event for major bleeding).

^b HAS-BLED is comprised by: hypertension [1 point], abnormal renal/liver function [1 point each], stroke, bleeding history or predisposition [1 point], labile INR [1 point], elderly [eg, age > 65 years; 1 point], drugs/alcohol concomitantly [1 point each].

^c Indicates < 3 points.

^d ATRIA bleeding risk score is comprised by: anemia [3 points]; severe renal dysfunction [eg, estimated glomerular filtration rate < 30 ml/min/1.73 m² or dialysis; 3 points], age ≥ years [2 points], prior bleeding [1 point], hypertension [1 point].

^e Indicates < 5 points.

^f Is comprised by: age older than 74 years [1 point], reduced hemoglobin [less than 13 g/dL and 12 g/dL in men and women, respectively; 2 points], bleeding history [2 points], insufficient kidney function [estimated glomerular filtration rate < 60 mL/min/1.73m² [1 point], treatment with antiplatelet [1 point]].

^g Indicates < 2 points.

^h < 4 points.

During 11 [9-12] months of follow-up, 30 patients (incidence rate = 4.0 per 100 person-years; 95% confidence interval [95%CI] had major bleeding; 9 patients had intracranial bleeding (1.3 per 100 person-years; 95%CI, 0.7-2.5) and 60 patients died (8.0 per 100 person-years; 95%CI, 6.2-10.3).

The incidence of major bleeding patients—accounting for death as a competing event—increased steeply with increasing risk points for ORBIT and HAS-BLED compared with ATRIA. However, HAS-BLED might identify better the patients at truly low risk of bleeding (Figure A).

The 3 risk scores, either as continuous or categorical variables, were significantly associated—after adjustment for death as a competing episode—with major bleeding (Table).

ORBIT exhibited the highest discrimination as a continuous and categorical variable (c-statistic = 0.74 and 0.66, respectively) (Table), although there were no significant differences between each pairwise comparisons among the scores ($P \geq .3$).

There were no significant differences between the scores in their discriminatory ability using the net reclassification improvement (NRI) method (ORBIT vs HAS-BLED: NRI = -1.85%; $P = .9$); ORBIT vs ATRIA: NRI = 8.1%; $P = .5$; ATRIA vs HAS-BLED: NRI = 5.9%; $P = .5$).

In patients with labile INR (ie, time in therapeutic range < 60%; $n = 325$ (35.7%) with 13 major bleeding events), ORBIT also exhibited the highest c-statistic values for major bleeding prediction: 0.74 (95%CI, 0.70-0.76) compared with HAS-BLED (c-statistic = 0.67; 95%CI, 0.64-0.70), and ATRIA (c-statistic = 0.71; 95%CI, 0.66-0.73) ($P \geq .2$ for each pairwise comparisons).

For predicting intracranial bleeding, ORBIT and HAS-BLED showed a slightly better association in terms of subhazard ratio (sHR) compared with ATRIA (ORBIT: sHR = 1.3; 95%CI, 1.0-1.66; $P = .05$; HAS-BLED: sHR = 1.4; 95%CI, 0.97-2.01; $P = .07$; ATRIA: sHR = 1.2; 95%CI, 0.96-1.45; $P = .11$). The discrimination was similarly weak: c-statistic of 0.59 (95%CI, 0.56-0.62), 0.58 (95%CI, 0.55-0.61), and 0.61 (95%CI, 0.58-0.65), for ORBIT, HAS-BLED, and ATRIA, respectively (P -value > .2 for all comparisons).

In the entire cohort, the 3 risk scores offered good calibration for major bleeding events (Figure B).

In this study, we found that the new major bleeding ORBIT risk score performs as well as HAS-BLED. On the other hand, our data from the real world indicate conserved discrimination for ORBIT in patients with labile INR and refute the recent findings by Senoo K et al.⁴

In our analysis, we had insufficient data on the quality of INR control before patient enrollment, which may be a potential limitation of our study regarding the calculation of the 'labile INR' variable of the HAS-BLED score.

It is known that HAS-BLED has advantages: it is easy to remember, simple to calculate and pays more attention to modifiable risk factors. In this regard, the results obtained from the analysis of our cohort show that the performance of ORBIT might be comparable to that of the HAS-BLED score. However, future large cohort studies are needed to confirm or refute our findings.

CONFLICTS OF INTEREST

E. Abu-Assi is Associate Editor of *Revista Española de Cardiología*.

SUPPLEMENTARY MATERIAL

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.rec.2016.05.022.

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Atypical Atrial Flutter and Ablation of Recipient-to-Donor Atrioatrial Conduction After Orthotopic Heart Transplant



Aleteo auricular atípico y ablación de la conducción transauricular receptor-donante tras trasplante cardíaco ortotópico

To the Editor,

In orthotopic heart transplant, the biatrial anastomosis technique introduced by Lower and Shumway is widely used.¹ This technique distorts the right atrial geometry and hemodynamics, leading to increased mean atrial pressure, tricuspid and mitral regurgitation, electrical asynchrony, and an increased incidence of atrial flutter.² In the literature, the most commonly described type is cavotricuspid isthmus-dependent flutter, in which the posterior barrier of the circuit is the atrioatrial suture line rather than the crista terminalis. However, when there is electrical conduction between the recipient atrium (A_R) and the donor atrium (A_D) across the atrial anastomosis, either by electrotonic transmission mechanisms or by direct conduction,³ the A_R can contribute to the development of arrhythmias in the donor heart.⁴

We present 4 patients who underwent orthotopic heart transplant with the biatrial anastomosis technique and developed atypical atrial flutter long after surgery (median, 5.5 years [range,

3–10 years]). All reported palpitations, with no signs or symptoms of heart failure, and electrocardiogram showed atrial flutter with variable atrioventricular conduction (Figure 1). Once rejection had been excluded as an acute cause, a guided ablation procedure was performed with endomyocardial biopsy using a 3-dimensional navigation system (CARTO: ThermoCool SmartTouch ablation catheter, Biosense Webster).

In all patients, endocardial mapping showed a macroreentrant tachycardia with a variable relationship between the A_R and A_D . There was a frequency gradient from the A_R , which had a shorter, regular cycle length, to the A_D , which had a longer cycle length (Figure 2A). The A_D cycle length was also variable in 2 patients, with a Wenckebach-type periodicity. Guided by the presence of double potentials, we proceeded to anatomical delineation of the biatrial suture (A_R - A_D) and performed activation mapping of the A_D to determine early activation sites around the suture (Figure 2B). In 3 patients, an earliest activation site was found in the lateral wall of the right atrium (9–10 o'clock position of the suture line in an anteroposterior view), and in 1 patient, 2 earliest activation sites were found (at the 10 o'clock and 12 o'clock positions). A_R entrainment maneuvers demonstrated an increased variability and prolonged mean cycle length in the A_D in all patients and short return cycles in the right A_R in 1 patient. Electrocardiograms of the earliest activation sites in the right A_D showed features of atrioatrial continuity; radiofrequency ablation of these areas achieved A_R - A_D electrical dissociation. Thereafter, the A_R remained in atrial flutter, and the A_D in sinus

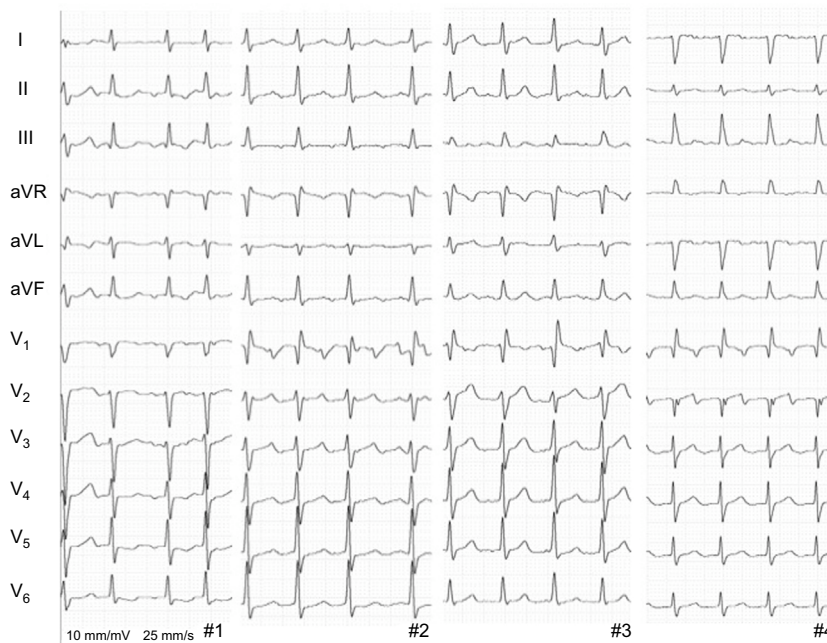


Figure 1. 12-lead electrocardiogram of atypical atrial flutter in the 4 patients.