



## Is the ORBIT Bleeding Risk Score Superior to the HAS-BLED Score in Anticoagulated Atrial Fibrillation Patients?

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**Background:** Several bleeding risk scores have been validated in patients with atrial fibrillation (AF). The ORBIT score has been recently proposed as a simple score with the best ability to predict major bleeding. The present study aimed to test the hypothesis that the ORBIT score was superior to the HAS-BLED score for predicting major bleeding and death in “real world” anticoagulated AF patients.

**Methods and Results:** We analyzed the predictive performance for bleeding and death of 406 AF patients who underwent 571 electrical cardioversion procedures and 1,276 patients with permanent/persistent AF from the FANTASIA registry. In the cardioversion population, 21 patients had major bleeding events and 26 patients died. The predictive performance for major bleeding of HAS-BLED and ORBIT were not significantly different (c-statistics 0.77 (95% CI 0.66–0.88) and 0.82 (95% CI 0.77–0.93), respectively;  $P=0.080$ ). For the FANTASIA population, 46 patients had major bleeding events and 50 patients died. The predictive performances for major bleeding of HAS-BLED and ORBIT were not significantly different (c-statistics 0.63 (95% CI 0.56–0.71) and 0.70 (95% CI 0.62–0.77), respectively;  $P=0.116$ ). For death, the predictive performances of HAS-BLED and ORBIT were not significantly different in both populations. The ORBIT score categorized most patients as “low risk”.

**Conclusions:** Despite the original claims in its derivation paper, the ORBIT score was not superior to HAS-BLED for predicting major bleeding and death in a “real world” oral anticoagulated AF population. (*Circ J* 2016; **80**: 2102–2108)

**Key Words:** Acenocoumarol; Atrial fibrillation; Bleeding risk scores; Electrical cardioversion; ORBIT

Decision-making for anticoagulation therapy for patients with atrial fibrillation (AF) depends on assessment of both thromboembolic and bleeding risks. Recent studies show that bleeding events not only require hospitalization, transfusion or procedures to stop bleeding but there is a large group of patients in whom major hemorrhages lead to death within 30 days after the event.<sup>1,2</sup> Indeed, international

guidelines recommend that antithrombotic therapy should be individualized after discussion of absolute and relative bleeding and ischemic risks.<sup>3,4</sup>

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In recent years, several risk scores have been validated in

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patients with AF to aid clinicians in assessing bleeding risk; some of them are quite complex. The European Society of Cardiology<sup>5</sup> recommends formal assessment of bleeding risk by the HAS-BLED score (Class I, level of evidence C; detailed explanation of acronym in Methods). The HAS-BLED score was developed in 2010 in 3,978 patients from the Euro Heart Survey population,<sup>6</sup> and had better predictive ability (c-statistic 0.72 [95% confidence interval (CI) 0.65–0.79]) than older, complex schemes such as HEMORR<sub>2</sub>HAGES.<sup>7</sup> Moreover, the HAS-BLED score has been validated in populations receiving non-warfarin anticoagulation treatment, as well as in both AF and non-AF populations.<sup>8–10</sup> The HAS-BLED score has been validated in different races. Caucasian patients with HAS-BLED  $\geq 3$  have been shown to have a high risk for major bleeding, irrespective of antithrombotic treatment. Also, in the Japanese population, patients with a HAS-BLED score  $\geq 3$  are at high risk for major bleeding irrespective of warfarin or non-warfarin treatment.<sup>11,12</sup>

Recently, O'Brien et al<sup>13</sup> developed and validated a new scheme for predicting bleeding risk, the ORBIT score. It was proposed as a simple bedside score to be used for both vitamin K antagonists and direct oral anticoagulants. The score was derived from the ORBIT-AF population,<sup>14</sup> with 10,098 voluntary AF outpatients treated with warfarin and dabigatran, and validated in the ROCKET-AF trial population (treated with warfarin or rivaroxaban). Thus, the ORBIT score has not been validated in an AF population treated with acenocoumarol. This bleeding score is claimed to have a statistically superior ability in predicting major bleeding in anticoagulated AF patients, when compared with the HAS-BLED and ATRIA bleeding risk scores.<sup>13</sup>

Our objective was to test the hypothesis that the ORBIT score is superior to the HAS-BLED score for predicting major bleeding and death in “real world” AF patients who were anticoagulated with acenocoumarol. Second, we analyzed if the HAS-BLED score performed better in identifying AF patients who are at low risk of bleeding. We investigated 2 patient populations: (1) anticoagulated AF patients undergoing electrical cardioversion (ECV); and (2) chronic anticoagulated AF patients in the FANTASIIA registry.

## Methods

Between January 2008 and June 2012, we recruited patients with persistent nonvalvular AF who underwent one or more programmed ECV procedures in the General Hospital of Alicante, Spain. ECV was performed using a biphasic defibrillator (Medtronic Lifepack 20). To undergo ECV, when arrhythmia duration was  $>48$  h, INR (international normalized ratio)  $>2$  were required in the previous 3 weeks or transesophageal echocardiography to assess absence of thrombus in the left atrial appendage. If AF duration was  $<48$  h, no anticoagulation therapy was required before ECV. Also, anticoagulation therapy was maintained for at least 4 weeks after ECV except when AF duration was  $<48$  h and no embolic risk factors were present. We included in the study patients who were anticoagulated with vitamin K antagonists (VKA: mostly with acenocoumarol, being the anticoagulant drug most widely used in Spain), as well as those taking direct oral anticoagulants (DOACs). For patients who were anticoagulated with acenocoumarol, INR data were collected after the ECV. We calculated time in the therapeutic range (TTR) through a percentage of INRs in the therapeutic range method, which utilizes the number of visits where the INR was in the therapeutic range (ie, INR between 2 and 3) over the total number of tests (at

least 6 consecutive controls were required). TTR  $<60\%$  was considered poor anticoagulation quality (ie, “labile INR”). Data on baseline clinical characteristics were obtained from hospital medical records. Follow-up started the day of performing ECV and ended on June 2013.

We also recruited patients with chronic AF included in the FANTASIIA (Spanish acronym for “Fibrilación Auricular: influencia del Nivel y Tipo de Anticoagulación Sobre la Incidencia de Ictus y Accidentes hemorrágicos”) registry. FANTASIIA is an observational, multicenter, national and prospective study of the general characteristics and current situation of a Spanish population of nonvalvular AF patients between June 2013 and March 2014. We studied 1,276 consecutive patients, followed in 50 outpatient clinics by 81 investigators (81% cardiologists, 11% primary care physicians and 8% internists). Patients included in the registry had been receiving anticoagulant therapy (VKA or DOAC) for at least 6 months before enrolment. By design, each investigator enrolled 16 patients treated with VKAs and 4 patients treated with DOACs. Coagulation status was determined by the INR values of the 6 months prior to the study entry. The estimated time spent in the TTR was assessed by the Rosendaal method. Poor anticoagulation control (labile INR) was defined as an estimated TTR  $<65\%$ . The FANTASIIA registry is designed as an initial enrolment visit and 3 follow-up visits at 1, 2 and 3 years. At each visit, clinical and laboratory data were collected from patients.

For both populations, we considered nonvalvular AF as the exclusion of rheumatic valve disease, severe valve disease, prosthetic valve or mitral valve repair surgery. CHA<sub>2</sub>DS<sub>2</sub>-VASc, HAS-BLED and ORBIT scores were calculated for all patients included in the study using established definitions of the different risk factors as previously described (Table S1).

HAS-BLED is an acronym for Hypertension (uncontrolled systolic blood pressure  $>160$  mmHg), Abnormal renal and/or liver function, previous Stroke, Bleeding history or predisposition (anemia), Labile INR (only applies to a VKA user; not applicable for a non-VKA user), Elderly (age  $\geq 65$  years), and concomitant Drugs (antiplatelet or nonsteroidal anti-inflammatory drugs) and/or alcohol excess. A HAS-BLED score of 0–1 is categorized as “low risk”, a score of 2 is “moderate/intermediate risk” and a score  $\geq 3$  is “high risk”.

ORBIT-AF is an acronym for: age Older than 74, Reduced hemoglobin or presence of anemia or abnormal hemoglobin (Hb)/hematocrit (Hct) (Hb  $<13$  g/dl or Hct  $<40\%$  for males and Hb  $<12$  g/dl or Hct  $<36\%$  for females), Bleeding history, Insufficient kidney function (estimated glomerular filtration rate  $<60$  ml/min/1.73 m<sup>2</sup>) or Treatment with any antiplatelet drug. An ORBIT score of 0–2 is classified as “low risk”, while “moderate/intermediate risk” is a score of 3 and a score  $\geq 4$  is “high risk”.

## Definitions of Endpoints

Major bleeding events were defined according to the 2005 International Society of Thrombosis and Haemostasis criteria:<sup>15</sup> fatal bleeding or symptomatic bleeding in a critical anatomical site (intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial or intramuscular with compartment syndrome) and/or bleeding causing a fall in Hb  $\geq 20$  g/L, or transfusion of  $\geq 2$  units of packed red blood cells.

For the ECV population, death was classified as being vascular (cardiac, stroke, pulmonary embolism) or nonvascular (neoplasm, trauma or respiratory disease) origin. For the FANTASIIA population, death was classified as a cardiovascular event (acute coronary syndrome, heart failure, lethal

| Table 1. Demographic and Clinical Baseline Characteristics of Both the ECV and FANTASIIA Populations |                        |                                |
|--|------------------------|--------------------------------|
| Patients   | ECV population (n=406) | FANTASIIA population (n=1,276) |
| Age (years)  | 66.9±10.9              | 73.9±9.4                       |
| Sex (male)   | 281 (69.2)             | 566 (44.3)                     |
| Hypertension   | 324 (80.0)             | 1,028 (80.6)                   |
| Heart failure  | 110 (27.2)             | 383 (30.1)                     |
| Diabetes mellitus  | 117 (28.9)             | 374 (29.3)                     |
| Vascular disease   | 90 (22.2)              | 85 (6.6)                       |
| Previous embolism  | 23 (5.7)               | 164 (12.9)                     |
| Previous bleeding  | 18 (4.4)               | 49 (3.8)                       |
| Renal impairment   | 20 (4.9)               | 256 (10.1)                     |
| Liver impairment   | 3 (0.7)                | 16 (1.3)                       |
| Concomitant drugs*   | 67 (16.5)              | 140 (10.9)                     |
| Alcohol abuse  | 28 (6.9)               | 48 (3.8)                       |
| Oral anticoagulant therapy**   |                        |                                |
| Vitamin K antagonists  | 382 (95.0)             | 987 (77.4)                     |
| Direct oral anticoagulants   | 20 (5.0)               | 289 (22.6)                     |
| CHADS <sub>2</sub> score   | 2 (1–2)                | 2.2±1.22                       |
| CHA <sub>2</sub> DS <sub>2</sub> -VASc score <sup>a</sup>  | 3 (2–4)                | 3.7±1.5                        |
| Low risk   | 35 (8.6)               | 14 (1.1)                       |
| Moderate/intermediate risk   | 60 (14.8)              | 74 (5.8)                       |
| High risk  | 311 (76.6)             | 1,188 (93.1)                   |
| HAS-BLED score <sup>b,***</sup>  | 2 (1–3)                | 2.0±1.1                        |
| Low risk   | 110 (28.7)             | 401 (31.5)                     |
| Moderate/intermediate risk   | 104 (27.1)             | 493 (38.6)                     |
| High risk  | 170 (44.2)             | 382 (29.9)                     |
| ORBIT score <sup>c</sup>   | 0 (0–1)                | 1.5±1.4                        |
| Low risk   | 360 (88.9)             | 1,012 (79.3)                   |
| Moderate/intermediate risk   | 23 (5.7)               | 117 (9.2)                      |
| High risk  | 22 (5.4)               | 147 (11.5)                     |
| TTR (%)  | 60 (50–68)             | 60.9±24.4                      |

Data are shown as mean ± SD (standard deviation) of median (IQR: interquartile range) and percentage (%). \*Antiplatelet agents, nonsteroidal anti-inflammatory drugs. \*\*n=402 for ECV population: 4 patients not treated with oral anticoagulation. \*\*\*n=384 for ECV population (labile INR data from 540 procedures (384 patients) to calculate HAS-BLED scores. <sup>a</sup>CHA<sub>2</sub>DS<sub>2</sub>-VASc=low risk: males with 0 points, females with 1 point; moderate/intermediate risk: males with 1 point; high risk: ≥2 points. <sup>b</sup>HAS-BLED=Low risk: 0–1 points; moderate/intermediate risk: 2 points; high risk: ≥3 points. <sup>c</sup>ORBIT=Low risk: 0–2 points; moderate/intermediate risk: 3 points; high risk: ≥4 points. ECV, electrical cardioversion; INR, international normalized ratio; TTR: time in therapeutic range.

arrhythmia or sudden death, artery aneurysm rupture or stroke) or another nonvascular death.

### Statistical Analysis

We tested normal distribution of continuous variables with the Kolmogorov-Smirnov method. Quantitative variables were described using the mean ± standard deviation or median [interquartile range]. Categorical variables are expressed as percentages. Statistical significance was defined as  $P < 0.05$ . Bleeding outcomes by each bleeding risk score were calculated as the overall rate of adverse events per 100 patient-years. Receiver-operating characteristic curves and the c-statistics were compiled for the HAS-BLED and ORBIT scores, according to major bleeding and death outcomes, in order to evaluate their predictive ability using the area under the curve (AUC) method (a measure of their c-index). To compare the ability of the 2 scores to predict thromboembolic events, we calculated the statistical significance of the difference between the areas under the 2 receiver-operating curves with the method of DeLong et al.<sup>16</sup> Statistical analyses were performed with SPSS statistical package version 20.0 for Windows (SPSS Inc,

Chicago, IL, USA) and the MedCalc statistical software for Windows (Version 14.8.1).

### Results

Baseline characteristics of both the ECV and FANTASIIA populations are shown in [Table 1](#).

For the ECV population, we analyzed 406 patients (69.2% male, mean age: 66.9±10.9 years) who underwent 571 procedures. Anticoagulant therapy remained unchanged after 567 (99.3%) procedures: 519 (91.6%) with acenocoumarol, 13 (2.2%) with warfarin and 35 (6.2%) with DOACs. Data on INR control during follow-up were available after 542 procedures. Of these, 159 (39.2%) patients were outside the TTR <60% and were classified as having “labile INR”. Median of TTR with percentage of INRs in the therapeutic range method was 60 (50–68). Only after 4 procedures (0.7%) did physicians not prescribe oral anticoagulation, such as when the arrhythmia duration was <48 h and the patient did not have thromboembolic risk factors. In addition, anticoagulant therapy was stopped after 63 ECV procedures (11.1%) during the follow-

**Table 2. C-Statistics for Major Bleeding and Death With HAS-BLED and ORBIT Risk Scores in ECV and FANTASIIA Populations**

| Risk score                     | Major bleeding |             |             | Death   |             |             |
|--------------------------------|----------------|-------------|-------------|---------|-------------|-------------|
|                                | c-index        | 95% CI      | P value AUC | c-index | 95% CI      | P value AUC |
| <b>A. ECV population</b>       |                |             |             |         |             |             |
| HAS-BLED score                 | 0.77           | 0.66–0.88*  | 0.080       | 0.83    | 0.74–0.91*  | 0.104       |
| ORBIT score                    | 0.82           | 0.77–0.93** |             | 0.78    | 0.69–0.88** |             |
| <b>B. FANTASIIA population</b> |                |             |             |         |             |             |
| HAS-BLED score                 | 0.63           | 0.56–0.71*  | 0.116       | 0.68    | 0.61–0.75*  | 0.415       |
| ORBIT score                    | 0.70           | 0.62–0.77** |             | 0.71    | 0.64–0.78** |             |

\*P value AUC for HAS-BLED score: P<0.001. \*\*P value AUC for ORBIT score: P<0.001. AUC, area under the curve; CI, confidence interval; ECV, electrical cardioversion.

**Table 3. Annual Incidence of Major Bleeding and Death Depending on HAS-BLED and ORBIT Category in Both ECV and FANTASIIA Populations**

| Bleeding risk scores    | Patients undergoing ECV |                      |                |                      | Patients from FANTASIIA registry |                      |                |                      |
|-------------------------|-------------------------|----------------------|----------------|----------------------|----------------------------------|----------------------|----------------|----------------------|
|                         | Major bleeding          |                      | Death          |                      | Major bleeding                   |                      | Death          |                      |
|                         | No. of bleeding events* | Annual incidence (%) | No. of deaths* | Annual incidence (%) | No. of bleeding events           | Annual incidence (%) | No. of deaths* | Annual incidence (%) |
| <b>HAS-BLED score**</b> |                         |                      |                |                      |                                  |                      |                |                      |
| Low                     | 1/165                   | 0.2                  | 0/165          | 0.0                  | 7/401                            | 1.7                  | 7/401          | 1.7                  |
| Moderate/intermediate   | 4/151                   | 0.9                  | 3/151          | 0.7                  | 16/493                           | 3.2                  | 12/493         | 2.4                  |
| High                    | 16/224                  | 2.4                  | 18/224         | 2.9                  | 23/382                           | 6.2                  | 31/382         | 8.2                  |
| <b>ORBIT score</b>      |                         |                      |                |                      |                                  |                      |                |                      |
| Low                     | 10/508                  | 0.3                  | 15/508         | 1.1                  | 20/1,012                         | 1.9                  | 20/1,012       | 1.9                  |
| Moderate/intermediate   | 4/34                    | 4.3                  | 2/34           | 2.1                  | 7/117                            | 6.2                  | 10/117         | 8.6                  |
| High                    | 7/27                    | 9.4                  | 9/27           | 12.1                 | 19/147                           | 14.1                 | 20/147         | 14.0                 |

\*Number of bleeding events or deaths/number of patients in each category. \*\*HAS-BLED could not be calculated in 2 ECV patients with major bleeding and in 4 patients who died (only had data on INR control for 540 procedures). Abbreviations as in Table 1.

up period. The cessation of anticoagulation treatment was according to the decision of the attending physician. The main reason for cessation of oral therapy was cited as a return to sinus rhythm (39 patients; 62.0%).

After a median follow-up of 1,005 (interquartile range, 619–1,489) days, 21 patients (4.9%) had major bleeding events (2 patients with more than 1 bleeding event: total 23 bleeding events) and 26 patients died (6.4%). The distribution of bleeding events was as follows: 12 (52.3%) gastrointestinal, 5 (21.7%) neurologic, 4 (17.4%) urologic and 2 (8.6%) other anatomic bleeding. Of these bleeding events, 4 (3 intracranial and 1 gastrointestinal bleeding) were the leading cause of death. The main causes of death were vascular in 14 (54.0%) patients, nonvascular in 10 (38.0%) and unknown in 2 (8.0%). Deaths from vascular causes were as follows: 4 heart failure, 3 hemorrhagic strokes, 2 ischemic strokes, 3 sudden deaths, 1 gastrointestinal bleeding and 1 aortic aneurysm rupture. Mortality rate of intracranial bleeding was 60%.

For the FANTASIIA population, we analyzed 1,276 patients (57.5% male, mean age: 73.8±9.4 years). Of those, 987 patients received VKAs (77.4%) and 289 received DOACs (22.6%). Data for the analysis of quality of anticoagulation and labile INR were collected for all patients receiving VKAs. Mean TTR with the Rosendaal method was 60.89±24.44. The prevalence of poor anticoagulation control was 54% (515 patients with TTR <65%). After follow-up of 1 year, 46 patients (3.6%) had major bleeding events and 50 patients (3.9%) died. The

distribution of bleeding events was as follows: 20 (43.5%) gastrointestinal, 10 (21.7%) intracranial, 7 (15.2%) urologic and 9 (19.6%) other anatomic bleeding. The main causes of death were: 3 (6.0%) acute coronary syndrome, 10 (20.0%) heart failure, 3 (6.0%) arrhythmia or sudden death, 3 (6.0%) bleeding events, 5 (10.0%) ischemic strokes and 26 (52.0%) other nonvascular causes.

**Table 1** shows how the ECV and FANTASIIA populations were distributed according to low, intermediate/moderate or high strata of HAS-BLED and ORBIT scores. For the ORBIT score, most of the population was classified as “low risk” for bleeding. For the ECV population, 30.6% of the total patients were classified as low risk by HAS-BLED score, whereas with the ORBIT score that percentage of patients at low risk increased to 89.3%. Similar findings were shown for the FANTASIIA population.

### Predictive Performance and Comparisons of Bleeding Scores

For the ECV population, the predictive performance of HAS-BLED reflected by c-indexes was 0.77 (95% CI 0.66–0.88) and 0.83 (95% CI 0.74–0.91) for major bleeding and death, respectively, both P<0.001. For the ORBIT score, c-indexes were 0.82 (95% CI 0.77–0.93) and 0.78 (95% CI 0.69–0.88) for major bleeding and death, respectively, both P<0.001. When we compared bleeding scores, the AUC difference for both scores was not significantly different for predicting both major

bleeding events and death (Table 2A).

For the FANTASIIA population, the predictive performance of HAS-BLED and ORBIT was only modest. For the HAS-BLED score, c-indexes were 0.63 (95% CI 0.56–0.71) and 0.68 (95% CI 0.61–0.75) for major bleeding and death, respectively, both  $P < 0.001$ . In the same way for the ORBIT score, c-indexes were 0.70 (95% CI 0.62–0.77) and 0.71 (95% CI 0.64–0.78) for major bleeding and death, respectively, both  $P < 0.001$ . When we compared both bleeding scores, the AUCs for HAS-BLED and ORBIT scores were similar for major bleeding ( $P = 0.116$ ) and for death ( $P = 0.415$ ) (Table 2B).

### Incidence of Bleeding Events and Death Depending on Risk Score

After classifying patients into low (HAS-BLED 0–1, ORBIT 0–2), intermediate/moderate (HAS-BLED 2, ORBIT 3) and high (HAS-BLED  $\geq 3$ , ORBIT  $\geq 4$ ) risk categories, we analyzed major bleeding and mortality rates within the estimated risk groups for the ECV and FANTASIIA populations (Table 3). The ORBIT score categorized most patients as “low risk” but major bleeding and mortality rates in this group were higher than observed for HAS-BLED.

## Discussion

In this study, we were not able to confirm that the new proposed ORBIT score works better than the more established HAS-BLED score for predicting major bleeding and death in patients with AF. Second, the HAS-BLED score seems to better classify low-risk patients than the ORBIT score, as shown by the lower annual incidence rates of major bleeding and death.

The risk of bleeding while on anticoagulation treatment is not homogeneous and various clinical factors have been associated with incremental bleeding risks such as increasing age, heart failure, renal or liver disease, concurrent use of aspirin or intensity of anticoagulation treatment.<sup>17</sup> Multiple scoring systems have been proposed to predict the real risk of major bleeding in AF patients on anticoagulation treatment. Moreover, net benefit analysis showed that optimal thromboprophylaxis is clearly positive, even in patients with a high bleeding risk, and optimal quality of anticoagulation treatment is only evaluated by the HAS-BLED score.<sup>18</sup>

As shown in the present study, in the FANTASIIA population the HAS-BLED and ORBIT scores showed modest discriminatory capacity for bleeding and mortality events. These findings are consistent with previous large validations [AMADEUS<sup>7</sup> or SPORTIF registry<sup>8</sup>]. However, in our population, the ORBIT score did not perform better than the HAS-BLED score for major bleeding events and death in AF patients treated with acenocoumarol or DOACs.

The ORBIT score was derived from the ORBIT-AF population<sup>14</sup> and validated in the ROCKET-AF trial population.<sup>19</sup> Both populations had similar median ages (75 (67–81) years old for ORBIT-AF vs. 73 (65–78) years old for ROCKET-AF) and high presence of comorbidities such as hypertension (88% for ORBIT-AF vs. 90% for ROCKET-AF), chronic kidney disease or anemia. We applied the ORBIT score to a younger population with fewer risk factors (ECV population) and no statistically significant differences were obtained between the ORBIT and HAS-BLED scores. Moreover, not all populations have the same risk of bleeding. In recent meta-analysis on the incidence of hemorrhagic stroke and major bleeding, the incidence was 2-fold higher in the Asian population compared with non-Asian patients,<sup>20</sup> and the mean of INR between 2 and

3 in Japanese patients was 51.8% in the J-ROCKET trial.<sup>21</sup> These results also suggest that the Japanese population were patients with high bleeding risk and they are not receiving optimal anticoagulation treatment. Major bleeding and intracranial bleeding rates with rivaroxaban in the Japanese population subanalysis of ROCKET-AF tended to be lower compared with the warfarin group but the difference was less than in the Caucasian population<sup>22</sup> and the benefit of rivaroxaban in the Japanese elderly population is unclear.<sup>23</sup> The HAS-BLED score has been validated in Caucasian and Japanese populations,<sup>11,12</sup> and also in younger patients undergoing ECV.<sup>24</sup> The HAS-BLED score has proven useful in different scenarios whereas external validation of the ORBIT score was limited by the characteristics of the ROCKET population. In addition, some variables in the ORBIT score can overlap in the same elderly population, which remains an important limitation of this score. For example, many older people have anemia and a bleeding history, which for the ORBIT-AF score would be a high risk patient while for the HAS-BLED score would be moderate bleeding risk patient.

Approximately 90% of the present ECV population and 80% of the FANTASIIA population were classified as “low risk” by the ORBIT score, while only 30% of both populations were classified as low risk by the HAS-BLED score. In the ORBIT score validation study,<sup>13</sup> the distribution was 58.6% for the low-risk group, 18.2% for moderate risk and 23.2% for high risk. Moreover, a “low risk” ORBIT score had annual rates for major bleeding (bleeds per 100 patient-years) of 2.4% for low risk, 4.7% for moderate risk and 8.1% for high risk. In the validation of HAS-BLED using the SPORTIF trial population,<sup>8</sup> a “low risk” HAS-BLED score had respective annual rates for major bleeding of 0.9%, 3.7% and 6.7%. Similar data obtained by our group in AF patients treated mainly with acenocoumarol, reported annual rates of bleeding of 0.8%, 1.88% and 5.72% for low, moderate and high risk HAS-BLED categories, respectively.<sup>25</sup> Thus, patients classified as low risk by HAS-BLED score typically have a low risk of bleeding ( $< 1\%$ ). In our population, major bleeding and mortality rates were lower for patients classified as low risk according to HAS-BLED score than for those classified as low risk with the ORBIT score, but the difference was small. However, in our population, major bleeding rates were also higher for patients classified as a high risk by ORBIT score for both the ECV population (2.4% vs. 9.4%) and FANTASIIA population (6.2% vs. 14.1%). The annual incidence of major bleeding in high-risk patients was similar to clinical trials that have evaluated the HAS-BLED score, but for the ORBIT score the rate was higher than in the study by O’Brien et al.<sup>13</sup> One reason could be the low number of patients in our study classified as high risk by the ORBIT score. In the current era of electronic health alerts on computerized systems, a “low risk” categorization would trigger “no action”, whereas a high risk “flag” would trigger an alert to review the patient, and thus address the potentially correctable bleeding risk factors.<sup>26,27</sup>

The new bleeding ORBIT score excludes Labile INR (“L” in HAS-BLED), one of the most powerful predictors of bleeding when on a VKA.<sup>26</sup> The risk of ischemic events is significantly higher for INR values  $< 2.0$  and serious bleeds (ie, intracranial hemorrhage) are common at INRs  $> 3.5$ .<sup>28</sup> In report by O’Brien et al, the ORBIT score was considered a simple score to be used for all types of AF patients and they highlighted that “labile INR is difficult to measure and not relevant to patients taking novel oral anticoagulants”.<sup>13</sup> This comment is not supported by recent European “real world” data. For example, the PREFER in AF registry<sup>29</sup> enrolled 7,243 patients

with AF from 461 European centers, and only 6.1% (n=442) patients received DOACs. In the Spanish population, this rate was 11%.<sup>30</sup> Thus, it is still important to assess the quality of anticoagulation control.<sup>31,32</sup> Currently, the HAS-BLED score is one of few scores that considers the quality of anticoagulation control when assessing bleeding risk.<sup>33</sup> Moreover, recent clinical trials have shown moderate predictive value for bleeding by HAS-BLED score in patients treated with DOACs.<sup>34,35</sup> These data still confirm the usefulness of the HAS-BLED score despite the exclusion of acronym “L” for Labile INR.<sup>36,37</sup>

In addition, the ORBIT score is a more static scheme and physicians have little capacity to correct for reversible bleeding risk factors. In contrast, the HAS-BLED score is a dynamic scheme that makes clinicians take into account (and thus avoid) potentially reversible risk factors. It is possible that a static score is simpler and easier for daily clinical practise, but the dynamic nature of the HAS-BLED score only reflects the variability and dynamism of the hemostasis system. A high HAS-BLED score is not an excuse to avoid oral anticoagulation but rather to “flag” for more careful review those patients potentially at risk of bleeding.<sup>38</sup> It also helps identify correctable bleeding factors such as uncontrolled blood pressure, labile INR or concomitant aspirin/nonsteroidal anti-inflammatory drug use.<sup>39</sup>

### Study Limitations

First, in the ECV population, not all components of the HAS-BLED score were available for all patients (eg, incomplete data on INR). Also, the ECV population was at relatively low risk for bleeding events and death compared with AF patients in daily clinical practice.

### Conclusions

Despite the original claims in its derivation paper, the ORBIT score was not superior to HAS-BLED for predicting major bleeding and death in a “real world” population of AF patients treated with oral anticoagulation.

### What Is Known About This Topic?

- Oral anticoagulation treatment of atrial fibrillation patients is associated with high risk of bleeding events. Antithrombotic therapy should be individualized.
- Several bleeding scores had been proposed such as HEMORR<sub>2</sub>HAGES, ATRIA and HAS-BLED.
- More recently, the ORBIT risk score has been developed as simple score for predicting bleeding risk and with a claim of better predictive performance for bleeding than the HAS-BLED score in any anticoagulated AF patient.

### What Does This Paper Add?

- The HAS-BLED score exhibits similar performance to the ORBIT score for major bleeding and mortality in a “real world” AF population anticoagulated with acenocoumarol.
- HAS-BLED could better identify patients at “truly low risk” of bleeding compared to the ORBIT score, as the latter categorizes a large proportion of patients to be at “low risk”.

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### Supplementary Files

#### Supplementary File 1

**Table S1.** Definition of HAS-BLED and ORBIT scores

Please find supplementary file(s):  
<http://dx.doi.org/10.1253/circj.CJ-16-0471>