

External Validation of HASBLED and ORBIT bleeding risk scores in Wales-AF population

FATEME Torabi¹, D. Harris¹, A. Lacey¹, A. Akbari¹, M. Gravenor¹, J. Halcox¹

¹Swansea University, Swansea, United Kingdom of Great Britain & Northern Ireland

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Background: Anticoagulant therapy (AC) is recommended for Atrial Fibrillation (AF) patients when formal assessment of thromboembolic and bleeding risk suggests a net benefit of AC treatment. Recent UK National Institute of Health and Care Excellence guidelines consider that the ORBIT bleeding risk score(1) provides a more accurate assessment of bleeding risk with AC than the HASBLED score(2) and is recommended for routine clinical use in the UK.

Purpose: To compare the performance of HASBLED and ORBIT scores to predict hospitalisations for bleeding (HB) in a large population of UK patients with AF receiving AC.

Methods: We conducted a retrospective longitudinal analysis using linked primary and secondary care health records in the All-Wales SAIL databank. Patients with a diagnosis of AF treated with AC were identified between 2012 and 2018. Both HASBLED and ORBIT scores were calculated for each patient annually based on identified comorbidities, demographics and prescription data. All HB were evaluated. Logistic regression models were used to compare sensitivity and specificity of each score for HB prediction. The Area Under Curve for the Receiver operating Characteristic plot (AUC) was generated for each score to illustrate the risk discrimination ability of each prediction schemes.

Results: A total of 107,137 (45% female, mean age=74) AF patients were evaluated over the study period. The number of anticoagulated AF patients increased from 27,959 in 2012 (49.3% of cohort) to 48,595 in 2018 (66.8%), providing a total of 265,410 patient years of AC therapy for analysis. There were 710 HB (2.5% of AC patients) in 2012 increasing to 1,146 (2.4%) in 2018. The predictive power of HASBLED and ORBIT increased slightly over the period of study: with observed HASBLED AUC of 60.8 and ORBIT AUC of 64.8 in 2018 (Figure 1). Over the period of study, the observed HB rates for AC AF patients with HAS BLED scores of 0-3 and ORBIT scores of 0-5 were similar to those observed in the original studies, but observed HB for patients with higher HASBLED and ORBIT scores were less consistent (Fig. 2)

Conclusion: Our findings demonstrated that HASBLED and ORBIT were relatively limited in their predictive performance for HB in a large, real-world AC AF population, with ORBIT providing more accurate prediction across the overall risk range. This highlights the need to develop and validate new bleeding risk scores from the wide range of clinical and demographic factors in AF patients to improve effectiveness of risk communication and AC prescribing in AF.

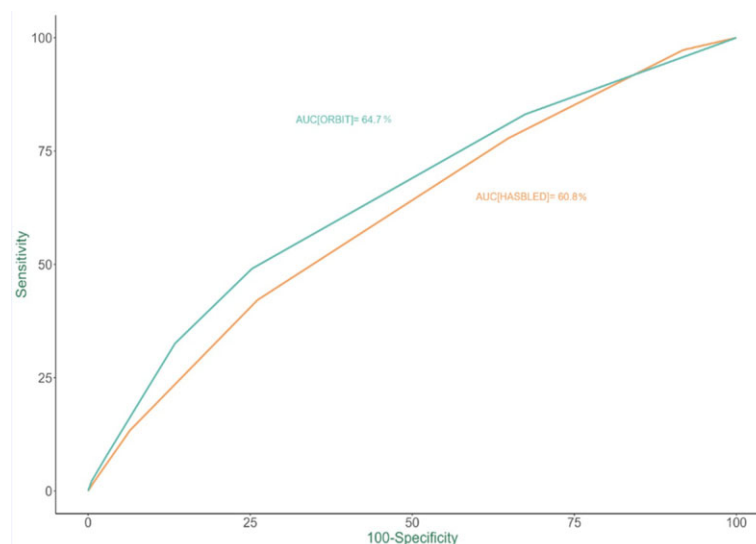


Figure 1- Area Under receiver operation Curve (AUC) of HASBLED and ORBIT for prediction of major bleeding events during 2018.

Figure 1

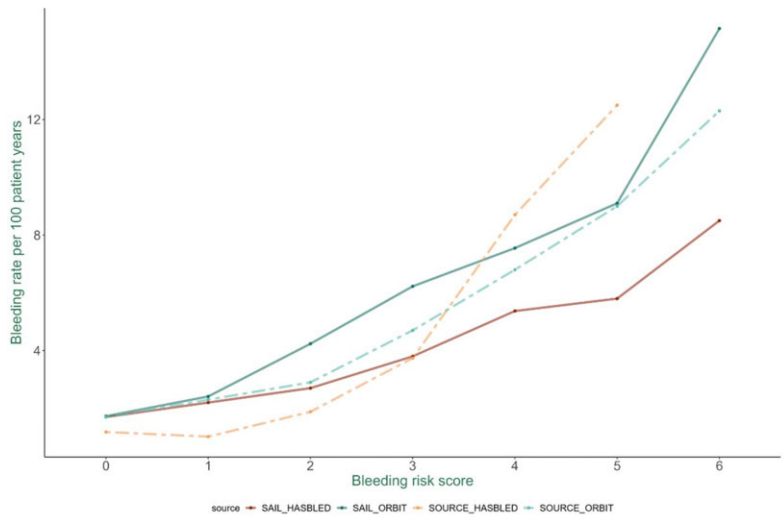


Figure 2 – comparison of observed bleeding event rates per 100 patient years for SAIL (All-Wales) AC AF patients vs original HASBLED and ORBIT cohort bleeding rates according to respective risk scores.

Figure 2



Patients on ENTRESTO experience fewer hospitalisations, reduced risk of CV death and improved QoL versus ACEi (enalapril)^{*3-7}

QoL based on post hoc analysis^{6,7}

Current, expert-led ESC guidelines recommend ENTRESTO as a first-line treatment option for eligible patients with symptomatic chronic HFrEF in combination with a BB, SGLT2i and MRA⁸

Explore
ENTRESTO
further

~2% of the NHS budget is spent on HF^{†9,10}

~70% of the cost of HF to the NHS is due to hospitalisation⁹

Versus ACEi (enalapril), at a median follow-up of 27 months, **ENTRESTO** significantly reduced the risk of:^{‡3}

Composite of death from CV causes or first hospitalisation for worsening HF
20% RRR (ARR=4.7%; p<0.001)

Death from CV causes
20% RRR (ARR=3.1%; p<0.001)

First hospitalisation for worsening HF
21% RRR (ARR=2.8%; p<0.001)

Starting ENTRESTO first-line could add 1 to 2 years to patients' lives vs ACEi⁴

Based on actuarial estimates from the PARADIGM-HF trial, and assuming that protective effects of ENTRESTO remain consistent with long-term use; extrapolated from available short-term follow-up data. Results were found in patients who were 45–75 years of age.⁴

The most commonly reported adverse reactions with ENTRESTO were hypotension (17.6%), hyperkalaemia (11.6%) and renal impairment (10.1%); angioedema was reported in patients treated with ENTRESTO (0.5%; uncommon).^{1,2}

For further safety information, please refer to the Summary of Product Characteristics^{1,2}

ACEi, angiotensin converting enzyme inhibitor; ARR, absolute risk reduction; BB, beta blocker; CV, cardiovascular; DHSC, Department of Health and Social Care; EF, ejection fraction; ESC, European Society of Cardiology; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor agonist; QoL, quality of life; RCT, randomised controlled trial; RR, risk reduction; SGLT2i, sodium-glucose cotransporter 2.

*PARADIGM HF (N=8,442) was a double-blind RCT of patients with class II, III or IV HF and an EF of ≤40% randomised to receive either ENTRESTO (200 mg twice daily) or enalapril (10 mg twice daily) in addition to recommended therapy. Primary outcome was a composite of death from CV causes or hospitalisation for HF¹; [†]NHS budget 2020–2021 based on DHSC departmental expenditure limit of £130.38 billion¹⁰; [‡]N=8,399.

References: **1.** ENTRESTO GB Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/7751/smpc> [Accessed September 2023]; **2.** ENTRESTO NI Summary of Product Characteristics. Available at: <https://www.emcmedicines.com/en-gb/northernireland/medicine?id=a1393009-6872-4eb0-9aaf-e19f456e9dff&type=smpc> [Accessed September 2023]; **3.** McMurray JJV, et al. *N Engl J Med* 2014;371(11):993–1004; **4.** Claggett B, et al. *N Engl J Med* 2015;373(23):2289–2290; **5.** Solomon SD, et al. *JACC Heart Fail* 2016;4(10):816–822; **6.** Lewis EF, et al. *Circ Heart Fail* 2017;10(8):e003430; **7.** Chandra A, et al. *JAMA Cardiol* 2018;3(6):498–505; **8.** McDonagh TE, et al. *Eur Heart J* 2021;42(36):3599–3726; **9.** National Institute for Health and Care Excellence. NG106: Chronic heart failure in adults: diagnosis and management. Available at: <https://www.nice.org.uk/guidance/ng106> [Accessed September 2023]; **10.** Department of Health and Social Care. DHSC annual report and accounts: 2018 to 2019. Available at: <https://www.gov.uk/government/publications/dhsc-annual-report-and-accounts-2018-to-2019> [Accessed September 2023].

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