Background: The optimal duration of anticoagulant therapy after the first episode of unprovoked venous thromboembolism (VTE) is controversial. Several clinical prediction rules (CPR) have been developed, but few have been externally validated in an independent cohort.

Aims: We aimed at validating the DASH prediction model, in which a score ≤1 would indicate an annual recurrence risk < 5%, therefore potentially excluding the need of prolonged treatment. We were also willing to evaluate the DASH score in a predefined patient subgroup (elderly vs. younger patients).

Methods: Patients with a proximal unprovoked DVT or PE, who received a full course of VKA or DOAC (>3 months) and having D-dimer measured after treatment withdrawal were eligible. The DASH score was computed based on D-dimer after therapy withdrawal (considered positive when values exceeded a cut-off of 250 ng/ml DDU or 500 FEU), age< 50 at index event, male sex and hormone use at index event. Recurrent VTE events were symptomatic proximal or distal DVT/PE, and were analyzed with a time-dependent analysis. Observed 12 and 24-months recurrence rates were compared to recurrence rates predicted by the DASH model.

Results: We analyzed a total of 827 patients, of whom 100 (12.1 %) had an objectively documented recurrence. On average, recurrence risk factors were less represented than in the original DASH cohort, with a greater proportion of subjects having a „low-risk" (< =1) DASH score (66.3% vs. 51.6%, p< 0.001).

Figure 1, Panel A shows the observed vs. expected cumulative incidence at 2-years for all enrolled subjects, with a slope equal to 0.71 (95% CI 0.51- 1.45). Panel B shows the same data subjects >65 years (dotted line) vs. younger (continuous); c-statistic was lower for subjects >65 years (0.54) vs. younger ones (0.72).

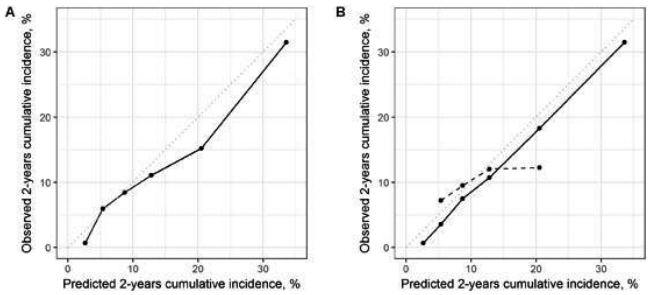

FIGURE 1 Panel A, all data; Panel B, stratified by age

Conclusions: These results confirm the validity of DASH prediction model, particularly in young subjects. The recurrence risk in elderly patients (>65 years) is >5% even with the lowest DASH scores.

OC 39.3 | Extended Anticoagulation with Two Doses of Rivaroxaban (20 mg and 10 mg) for Preventing Recurrent Venous Thromboembolism: A Benefit-risk Analysis of EINSTEIN CHOICE

J.I. Weitz[1], A.W.A. Lensing[2], P.S. Wells[3], M. Gebel[2], A.F. Pap[2], M. Homering[2], J. Beyer-Westendorf[4], H. Bounameaux[5], P. Prandoni[6], M.H. Prins[7]

[1]*Thrombosis and Atherosclerosis Research Institute and McMaster University, Hamilton, Canada,* [2]*Bayer AG, Wuppertal, Germany,* [3]*University of Ottawa and the Ottawa Hospital Research Institute, Department of Medicine, Ottawa, Canada,* [4]*University Hospital ‚Carl-Gustav Carus', Department of Vascular Medicine, Dresden, Germany,* [5]*University Hospitals of Geneva and Faculty of Medicine, Geneva, Switzerland,* [6]*University of Padua, Department of Cardiothoracic & Vascular Sciences, Padua, Italy,* [7]*University of Maastricht, Department of Epidemiology and Technology Assessment, Maastricht, The Netherlands*

Background: Most patients with unprovoked venous thromboembolism (VTE) or with ongoing risk factors receive 6 to 12 months of anticoagulant therapy. The decision to extend therapy depends on the balance between the risk of recurrent VTE if treatment stops and the risk of bleeding if treatment continues. Information on this benefit-risk balance is limited.

Aims: The benefit-risk tradeoff of extended treatment with 20 mg or 10 mg of once daily rivaroxaban was assessed in patients with symptomatic VTE who had completed 6-12 months of anticoagulation and for whom there was equipoise regarding the need for extended anticoagulation.

Methods: One-year cumulative incidences were estimated for recurrent VTE and major bleeding with the Kaplan-Meier method. Benefits and risks were presented using the differences between treatment groups in a hypothetical population of 10,000 VTE patients followed for 1 year.

Results: A total of 1107 patients were treated with rivaroxaban 20 mg, 1127 with rivaroxaban 10 mg, and 1131 with aspirin. The cumulative incidence of recurrent VTE was 1.9% in patients in the rivaroxaban 20 mg group, 1.6% in patients in the rivaroxaban 10 mg group, and 5.0% in patients in the aspirin group. The cumulative incidences of major bleeding were 0.7%, 0.4% and 0.5% in the rivaroxaban 20 mg, rivaroxaban 10 mg, and aspirin groups, respectively. Compared with aspirin in a hypothetical population of 10,000 VTE patients followed for 1 year, treatment with 20 mg or 10 mg of rivaroxaban would result in 312 (95% confidence interval [CI], 145 to 479) and 341 (95% CI, 175 to 507) fewer recurrent VTE events (NNT=33 and 30, respectively) and in 28 (95% CI, -43 to 99) and 0 (95% CI, -60 to 59) more major bleeding events (NNH=356 and >10,000, respectively).

Conclusions: Extended anticoagulation with once daily rivaroxaban (20 mg or 10 mg) provides a clinically important benefit in terms of reduction in recurrent VTE, and both regimens have favorable benefit-risk profiles.

OC 39.4 | Prediction of Major Bleeding (MB) Risk in 2514 High Recurrence Risk Venous Thromboembolism Patients Treated Beyond 3 to 6 Months with Oral Anticoagulation Therapy (OAT)

P. Wells[1], M. Rodger[1], M. Kovacs[2], D. Anderson[3], S. Kahn[4], S. Solymoss[4], C. Kearon[5], V. Shah[6], D. Keeling[7], I. Chagnon[8], R. Zide[9], M. Carrier[1], R. Mallick[1], D. Corsi[1], G. Le Gal[1], S. Schulman[10], S. Kaatz[6]

[1]*University of Ottawa and the Ottawa Hospital Research Institute, Medicine, Ottawa, Canada,* [2]*University of Western Ontario, Medicine, Ottawa, Canada,* [3]*Dalhousie University, Medicine, Halifax, Canada,* [4]*McGill University, Medicine, Montreal, Canada,* [5]*McMaster University, Medicine, Hamilton, Canada,* [6]*Henry Ford Hospital, Medicine, Detroit, United States,* [7]*Oxford University Hospitals*

NHS Foundation Trust, Medicine, Headington, United Kingdom, [8]Universite de Montreal, Medicine, Montreal, Canada, [9]Lahey Hospital and Medical Center, Medicine, Burlington, United States, [10]McMaster University and Thrombosis and Atherosclerosis Research Institute, Medicine, Hamilton, Canada

Background: A tool to predict the risk of MB in patients on extended OAT for venous thromboembolism (VTE), has not been developed. Identifying those with an annual MB rate over 3% is the target at which the risk of continued OAT exceeds benefit.

Aims: To develop a prediction rule for major bleeding that selects a clinically meaningful proportion of patients with a MB risk over 3%.

Methods: a multicentre, multinational prospective cohort study of extended OAT for unprovoked VTE, or provoked VTE with prior VTE. Cancer patients were excluded. Enrollment was after at least 3 months of OAT. All bleeding events were adjudicated. Univariate Cox proportional hazards analysis was used to determine the strength of association between each variable and risk of MB to permit selection of a subset of variables for the subsequent multivariate analysis. Of the 24 variables analysed 10 were found to be strongly associated with MB risk (P< 0.05) (Table 1). A multivariable Cox regression model was built using clinically important, easily measurable variables.

Results: 2514 patients enrolled with > 7100 years of observation. The mean age was 60 years, 64% were male, 92% Caucasian, mean BMI was 31, and 9% were on antiplatelet agents. Patients were followed for a mean of 2.8 years. 90% were on VKAs.121 patients (4.8%) experienced at least one MB episode. The annual rate of MB was 1.7 per 100 patient years of observation (rate constant). All variables in the derived model scored one except anemia (2) [Table 2]. 21% had a score of 2 (MB rate 3.1%, 95% CI=2.3 to 4.2%), 7% scored 3 (MB rate 4.5%, 95% CI=2.7 to 7.1%), and 1% scored ≥ 4 (MB 7.9%%, 95% CI=2.6 to 18.6%). All the fatalities from MB were in these high-risk groups. In the 71% at low risk the MB rate was 1.1%. All differences were statistically significant with p values < 0.0001. The C-index was 0.74.

Conclusions: Almost 30% of patients would score high risk (i.e. >3%) for MB and consider not continuing OAT. If validated (as planned prior to the ISTH) this could change practice.

TABLE 1 One. Significant variables in the univariate analysis

VARIABLE	NO MAJOR BLEED (N)	NO MAJOR BLEED (% OF ALL NO BLEED PATIENTS)	MAJOR BLEED (N)	MAJOR BLEED (% OF ALL MAJOR BLEED PATIENTS)	ABSOLUTE RISK (%)	HAZARD RATIO	LOWER 95% CI	UPPER 95% CI	P-VALUE
AGE > 65	893	37.3	68	57.6	7.1	2.29	1.60	3.28	<0.0001
FEMALE	849	35.4	58	49.2	6.4	1.8	1.26	2.57	0.0013
HYPERTENSION	886	37	61	51.7	6.4	1.74	1.21	2.48	0.0024
CYP2C9 *3 HETERO/ HOMO	239	10.4	21	19.3	8.1	1.93	1.20	3.10	0.0066
DVT AND PE	445	18.6	12	10.2	2.6	0.46	0.25	0.84	0.0112
ANTIPLATELET AGENT	209	8.7	23	19.5	9.9	2.32	1.47	3.65	0.0003
CREATININE CLEARANCE < 50	146	6.6	22	19.6	13.1	3.26	2.05	5.18	<0.0001
HEMOGLOBIN < 100	32	1.4	4	3.4	11.1	2.86	1.06	7.76	0.0389
STATIN USE	636	26.6	48	41	7.0	1.96	1.36	2.82	0.0003

TABLE 2 Two. Major bleeding by score in final model

POINTS	# OF PATIENTS	% OF PATIENT POPULATION	# OF MB EVENTS	MAJOR BLEED RATE PER 100 PT YEARS	LOWER 95% CI	UPPER 95% CI
0 OR 1	1638	71	51	1.07	0.8	1.4
2	485	21	40	3.1	2.2	4.2
3	158	7	19	4.5	2.7	7.1
4	24	1	5	8.0	2.6	18.6
5	5	0	0	0		

VARIABLES USED INCLUDE HEMOGLOBIN < 100, AGE > 65 YEARS, USE OF ANTIPLATELET AGENT, CREATININE CLEARANCE < 50 AND HYPERTENSION