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The American College of Chest Physician score to assess therisk of bleeding during anticoagulation in patients with venous thromboembolism

comment

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Bleeding risk scores in patients receiving anticoagulation for venous thromboembolism: Simplicity and practicality matter

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In patients with venous thromboembolism (VTE), the goal of anticoagulation is to treat the current VTE and to prevent recurrent VTE. However, anticoagulation also imposes an increased risk for bleeding events and this risk must be assessed to determine appropriateness of a given treatment plan for each patient.

The American College of Chest Physicians (ACCP) guidelines for VTE management presented a set of 18 risk factors and scoring system to distinguish patients with a low, moderate, or high risk of bleeding [1]. Having two or more of these risk factors was deemed high risk based on bleeding rate estimates from several studies and the scoring system was used to make recommendations for time-limited or extended treatment courses.

Palareti *et al* utilized the observational START2-Register cohort to apply the ACCP risk score in an observational retrospective study and to evaluate treatment duration in patients with provoked and unprovoked VTE [2]. The authors note that 24% of the cohort had no ACCP risk factors and 52.9% had ≥2 or more and were categorized as 'high risk'. A higher proportion of high risk patients (55.3%) received extended anticoagulation compared to moderate or low risk (44.6% and 40.9%). Among these groups bleeding event counts (48 total) were low, did not allow for stable estimates in the regression, and showed incidence proportions of 2.6%, 2.1%, and 1.1% among high, moderate, and low patient groups.

The work is commendable but brings to question the utility of the ACCP risk factors and scoring system in predicting bleeding events. The 18 risk factors were accumulated from several studies and have not been independently evaluated as a combined risk score. However, the risk factors are similar to prior studies that may provide insight to their applied use. Our group recently evaluated the HAS-BLED score, which has been used for nearly a decade in the atrial fibrillation population [3, 4], in VTE patients in a large, claims-based study [5]. This was the first study to reliably estimate the risk of bleeding associated with individual criteria and high risk cut-points for the HAS-BLED score in VTE, and included over 100,000 VTE patients. Prediction of bleeding events based only on the HAS-BLED score was acceptable, with c-indices from survival regression models ranging from 0.66 to 0.73.

Nearly all risk factors in the HAS-BLED score were included in the ACCP risk score as are the risk factors in the recently developed VTE-BLEED risk score (Table), so we anticipate the ACCP risk score will have slightly improved prediction of bleeding events [6]. However, with 18 risk factors considered in the ACCP score and cutoffs of just a few points, the utility of a risk score that categorizes more than 50% of patients as high risk should be also questioned. An ideal score should be more discriminating at the patient level and allow for clinical assessment of those truly at the highest risk. In our study, a high risk cut-point of ≥4 points provided the best relative discrimination when compared with lower scores. This 'high risk' classification had <5% sensitivity as roughly 5% of the patient population were deemed high risk. In this sense, the low sensitivity for bleeding rates observed in our study is acceptable as long as we can be assured that the relative risk among our stratified patients is actionable, i.e. patients can be flagged for additional follow-up, modified treatment, or intensified evaluation. In order to determine appropriate cut points, the ACCP score should be evaluated in a large enough cohort to assess meaningful, empirically determined cut points that provide informative discrimination within a patient population.

Beyond making initial treatment decisions, practical risk scores should be informative toward reducing the risk for bleeding rather than for assessment alone. Only a few of the considered risk factors are modifiable (e.g., certain medication use, excess alcohol, and uncontrolled hypertension, among others). Limiting focus on modifiable bleeding risk is an inferior strategy for bleeding risk prediction compared to a formal bleeding score such as HAS-BLED [7]; however, developing more complex risk scores necessitate complex assessments that may detract from widespread adoption of risk scores and provide only marginal increases of prediction, all the while providing few actionable data points. Further, while the ACCP risk score was described as a means to plan treatment, clinicians should consider the time-varying risk factors and prospectively adjust treatment strategies rather than relying on a baseline assessment. Indeed, the change in bleeding risk profile is highly predictive of bleeding events, especially in the initial 3 months [8].

Some urge caution in applying bleeding risk scores in the clinical environment, due to the development of these scores based on initial clinical decisions to prescribe anticoagulants which necessitated that the patients were considered lower bleed risk [9]. There is also the perception that bleeding risk scores are inappropriately used to deny patients anticoagulation due to their perceived 'high risk' although bleeding risk is highly dynamic and modifiable, and the reversible risk factors for bleeding should be addressed in all patients rather than just those at high risk [10]. Further, the Palareti study illustrates the apparent counterintuitive assessment of risk factors and scores for treatment decisions as more "high risk" patients received extended anticoagulation despite ACCP recommendations for short-term treatment. This may be attributed to the fact that recurrent VTE and adverse bleeding events share many of the same risk factors captured by the ACCP score; thus, the risk scores capture poorer prognoses in general. As a result, any withholding or shortening of treatment duration based on risk scores could lead to worse net clinical benefit when both effectiveness and safety outcomes are considered.

Current risk scores were assessed in patients receiving vitamin K antagonist therapy or low molecular weight heparins, so existing and newly developed tools should evaluate whether direct-acting oral anticoagulant (DOAC)-related bleeding events have a unique set of risk factors given their rapid uptake. Moving forward, prediction tools will need to be adapted to be both simple and practical at the point of care by incorporating a small number of key, modifiable risk factors that can be targeted throughout care to improve patient outcomes. The net clinical benefit of incorporating not only bleeding but also VTE risk should be considered, as should patient desires and preferences for treatment selection and duration. Lastly, prediction tools should be implemented as longitudinal assessments rather than as standalone baseline assessments to determine the appropriateness of current regimens reflective of new or worsening risk factors or, ideally, improved management of modifiable risk factors.

Addendum

J. Brown and G. Lip conceived this commentary and J. Brown and A. Goodin created the first draft. All authors critically revised the commentary.

Disclosure of Conflict of Interests

G. Lip reports consultancy and speaker fees from Bayer, Bayer/Janssen, BMS/Pfizer, Biotronik, Medtronic, Boehringer Ingelheim, Microlife, Roche, and Daiichi-Sankyo outside the submitted work.

Table: Comparison of risk factors included in existing bleed risk tools			
	ACCP[a]	HAS-BLED[b]	VTE-BLEED[c]
Age >65	X	X	X[d]
Age >75	X		
Previous bleeding	X	X[e]	X
Cancer	X		X
Metastatic Cancer	X		
Renal failure	X	X	X
Liver failure	X	X	
Thrombocytopenia	X		
Previous stroke	X	X	
Diabetes	X		
Anemia	X		X
Antiplatelet therapy	X	X	
Poor anticoagulant control	X	X	
Comorbidity and reduced functional capacity	X	X[f]	X[g]
Recent surgery	X		
Frequent falls	X		
Alcohol abuse	X	X	
NSAID use	X	X	

Abbreviations: ACCP=American College of Chest Physicians; NSAID=non-steroidal anti-inflammatory drugs
[a]ACCP risk factors were derived from published studies. Bleed risk scores are classified as: 0=low, 1=moderate, and ≥2=high risk of bleeding.

[b]HAS-BLED is an acronym for Hypertension, Abnormal liver/renal function, Stroke history, Bleeding predisposition, Labile INR, Elderly, Drug/alcohol usage. Developed in Euro Heart Survey of Atrial Fibrillation patients and recently translated to venous thromboembolism patients. Scores range from 0 to 9, where ≥3 or ≥4 are usually deemed high risk.
[c]Developed in patients with venous thromboembolism randomized to dabigatran in the RE-COVER study.
[d]Age ≥60
[e]HAS-BLED distinguished "Previous bleed or predisposition to bleeding." This has been interpreted broadly and can include risk factors such as cancer, surgery, or other predisposing factors.
[f]HAS-BLED specifically considers only uncontrolled hypertension as a comorbidity. ACCP includes a broader definition.
[g]Considers uncontrolled hypertension only in males.

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