

## The “Risk” of Risk Assessment Models for Venous Thromboembolism in Medical Patients

To the Editor:

We read with interest the derivation and validation of a simple risk assessment model (RAM) by Woller et al<sup>1</sup> for identifying at-risk hospitalized medical patients for venous thromboembolism. As the authors point out, previous RAMs for this group have been complex, with incomplete scoring systems and inadequate validation. The authors derived and validated their 4-factor RAM (which included previous venous thromboembolism, bed rest, cancer, and peripherally inserted central catheter lines) from data using an electronic medical record and query of International Classification of Diseases (ICD)-9 codes attributable to hospitalization, with an excellent receiver operating curve of >0.80. However, 2 issues remain.

First, the ICD-9 codes for venous thromboembolism may lack discrimination and include upper-extremity disease, superficial thrombophlebitis, and chronic deep venous thrombosis, which may explain a ~3- to 5-fold higher-than-expected 90-day rate of clinical venous thromboembolism in the validation cohort (4.5%). Upper extremity disease, in particular, has a different pathophysiology from lower extremity disease, with uncertain effects of using thromboprophylaxis in reducing that risk.<sup>2</sup> Hence, the possibility of confounding exists when upper extremity events are included across smaller subgroups of patients when developing risk scores or prediction rules. This especially holds true with weak risk factors, such as advanced age or immobility.

Second, many of the 86 risk factors used in predicting venous thromboembolism risk were attributable to the hospitalization itself, and not necessarily present at admission, which would be more useful clinically in identifying patients who would benefit from venous thromboembolism

prophylaxis begun near the time of admission, enabling the model to be truly predictive rather than associative of venous thromboembolism risk.

Recently, our group published evidence-derived RAMs from an international 15,156-patient database from the IMPROVE registry of hospitalized medical patients.<sup>3</sup> We developed 2 risk models using Cox multiple regression analysis as shown in the **Table**: a 4-factor predictive model based solely on venous thromboembolism risk factors present at admission, and a 7-factor associative model that included factors present during hospitalization whose timing relative to the venous thromboembolism event could not be completely determined. The final risk scores in both of our models looked very different when we removed upper-extremity disease as an outcome, including elimination of central line catheters as a risk factor.

Lastly, our model was able to incorporate multiple levels of venous thromboembolism risk, as opposed to a binary-risk vs no-risk approach adapted by the model used by Woller et al. All of the RAMs in this patient group need prospective validation to assess whether venous thromboembolism is reduced by use of the scores.

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## References

1. Woller SC, Stevens SM, Jones JP, et al. Derivation and validation of a simple model to identify venous thromboembolism risk in medical patients. *Am J Med.* 2011;124:947-954.
2. Spyropoulos AC. Upper vs lower extremity deep vein thrombosis: outcome definitions of venous thromboembolism for clinical predictor rules or risk factor analyses in hospitalized patients. *J Thromb Haemost.* 2009;7:1041-1042.
3. Spyropoulos AC, Anderson FA, FitzGerald G, et al. Predictive and associative models to identify hospitalized medical patients at risk for VTE. *Chest.* 2011;140(3):706-714.

**Table** Predictive and Associative Models to Identify Hospitalized Medical Patients at Risk for VTE

	Hazard Ratio (95% CI)	Chi-squared	P Value	Points
Predictive model for 3-month VTE and points assigned to each independent risk factor				
VTE risk factor				
Previous VTE	5.0 (3.3-7.8)	53	<.001	3
Known thrombophilia	5.2 (1.3-21.5)	5.2	.02	3
Current cancer	2.0 (1.3-3.1)	11	.001	1
Age >60 years	1.8 (1.2-2.7)	8.5	.004	1
Associative* model for 3-month VTE and points assigned each patient characteristic				
Patient characteristic				
Previous VTE*	4.7 (3.0-7.2)	48	<.001	3
Known thrombophilia	3.5 (1.1-11)	5.2	.04	2
Current lower limb paralysis	3.0 (1.6-5.7)	11	.001	2
Current cancer	2.8 (1.9-4.2)	27	<.001	2
Immobilized ≥7 days†	1.9 (1.3-2.7)	11	.001	1
ICU/CCU stay	1.8 (1.1-2.9)	6.1	.01	1
Age >60 years	1.7 (1.1-2.6)	6.3	.01	1

CCU = critical care unit; CI = confidence interval; ICU = intensive care unit; VTE = venous thromboembolism.

Associative model: Score 0-1: low VTE risk, Score 2-3: moderate VTE risk, Score 4 or more: high VTE risk.

\*Previous VTE and age are both known to have occurred before 3-month VTE; the other patient factors are known to have been present at or during hospital admission.

†Days immobile immediately before and during hospital admission.