

Supplementary material

Validation of the Khorana score for predicting venous thromboembolism in 40,218 cancer patients initiating chemotherapy

Supplementary Table S1 The Khorana score and its components		
	Khorana component	Score
Cancer type	Stomach	+2
	Pancreatic	+2
	Lung	+1
	Lymphoma	+1
	Gynecological	+1
	Bladder	+1
	Testicular	+1
	Other	0
Laboratory values	Hemoglobin level <10 g/dL or use of erythropoiesis stimulating agent	+1
	Pre-chemotherapy platelet count $\geq 350 \times 10^9/L$	+1
	Pre-chemotherapy leukocyte count $> 11 \times 10^9/L$	+1
Anthropometry	Body mass index $\geq 35 \text{ kg/m}^2$	+1
Maximum score		6

Supplementary Table S2 Codes used to define the study population, covariates, and outcomes			
	Code type and source	Codes	
Chemotherapy	ICD-10 codes, treatment, and procedure codes – National Patient Registry	BWHA1-3	
Atrial fibrillation		I48	
Mechanical heart valves		KFCA60 KFGE00 KFKD00 KFJF00 KFMD00 KFDK51 KFMD54	
<i>Khorana components</i>			
Stomach		C16	
Lung		C34	
Pancreatic		C25	
Lymphoma		C81-86	
Gynecologic		C51-58	
Bladder		C679	
Testicular		C62	
Body mass index ≥ 35 kg/m ²		DE660C-DE660H DE662	
Hemoglobin		Treatment code – National Patient Registry & NPU codes - Register of Laboratory Results for Research database	NPU02319 BOHE1
Platelet count	NPU03568		
Leukocyte count	NPU02593		
<i>Cancer types used in stratified analyses</i>			
Gastrointestinal	ICD-10 codes – National Patient Registry	C15-21, C26	
Hepatobiliary or pancreatic		C22-25	
Lung		C34	
Breast		C50	
Renal, bladder or prostate		C61, C64-68	
Gynecologic		C51-58	
Hematologic		C81-88, C91-95	
<i>Medication</i>			
Anticoagulation	ATC codes – National Prescription Registry	B01AA03 B01AF02 B01AA04 B01AE07 B01AF01 B01AF03 B01AB	
<i>Outcomes</i>			
Venous thromboembolism (primary outcome)	ICD-10 codes and procedure codes – National Patient Registry	I26 I801 I802 I803 I808 I809 and imaging code UXUG or UXC	
Venous thromboembolism (broad definition)	ICD-10 codes – National Patient Registry	H348E H348F I26 I636 I676 I801 I802 I803 I808 I809 I81 I822 I823 I828 I829 O223 O225 O229 O871 O879 O873 O882 T817C T817D	
NPU: Nomenclature, Properties and Units ICD: International Classification of Diseases ATC: Anatomical Therapeutic Classification system			

Supplementary Table S3 Number of events and six-month cumulative incidence of venous thromboembolism stratified by cancer type and original Khorana score categories using two different risk estimators with and without competing risk

		No. of events	Cumulative incidence, % (95% confidence interval)		Relative overestimation by Kaplan Meier
			Competing risk estimate*	Kaplan Meier	
Cancer type					
<i>Gastrointestinal cancer</i>	0: Low risk	89	2.2 (1.8-2.7)	2.3 (1.8-2.8)	4.5%
	1-2: Intermediate risk	125	3.0 (2.5-3.6)	3.2 (2.7-3.8)	6.7%
	≥3: High risk	44	5.7 (4.2-7.5)	6.3 (4.7-8.4)	10.5%
<i>Hepatobiliary or pancreatic cancer</i>	0: Low risk	15	4.4 (2.6-6.9)	4.7 (2.8-7.6)	6.8%
	1-2: Intermediate risk	62	5.6 (4.3-7.1)	6.1 (4.8-7.8)	8.9%
	≥3: High risk	34	4.0 (2.9-5.5)	4.7 (3.4-6.6)	17.5%
<i>Lung cancer</i>	1-2: Intermediate risk	91	3.2 (2.7-3.7)	3.4 (3.0-4.0)	6.3%
	≥3: High risk	118	3.3 (2.4-4.3)	3.9 (3.0-5.2)	18.1%
<i>Breast cancer</i>	0: Low risk	38	0.7 (0.5-0.9)	0.7 (0.5-0.9)	0%
	1-2: Intermediate risk	10	0.6 (0.3-1.0)	0.6 (0.3-1.0)	0%
	≥3: High risk	<5	N/A†		
<i>Urologic cancer, incl. prostate</i>	0: Low risk	25	2.0 (1.3-2.9)	2.0 (1.4-3.0)	0%
	1-2: Intermediate risk	49	4.5 (3.4-5.9)	4.7 (3.6-6.2)	4.4%
	≥3: High risk	10	6.1 (3.1-10.5)	7.5 (4.0-13.6)	23.0%
<i>Gynecologic cancer</i>	1-2: Intermediate risk	52	2.4 (1.8-3.1)	2.4 (1.8-3.2)	0%
	≥3: High risk	27	5.0 (3.4-7.1)	5.3 (3.7-7.7)	6.0%
<i>Hematologic cancer</i>	0: Low risk	<5	0.5 (0.1-1.8)	0.5 (0.1-2.2)	0%
	1-2: Intermediate risk	96	2.4 (2.0-3.0)	2.6 (2.1-3.1)	8.3%
	≥3: High risk	13	2.6 (1.4-4.2)	2.7 (1.6-4.7)	3.8%

Note: For lung and gynecological cancer, all patients are assigned minimum 1 point due to cancer type.

* Considering death as competing risk † Too few events to estimate cumulative incidence.

Supplementary Table S4 Number of events and six-month cumulative incidence of venous thromboembolism in cancer patients initiating chemotherapy using a broad outcome definition*			
	Patients, <i>n</i>	Events, <i>n</i>	Cumulative incidence, % (95% confidence interval†)
Overall	40,221	1,376	3.4 (3.2-3.6)
<i>Original Khorana categories</i>			
0: Low risk	14,258	335	2.4 (2.1-2.6)
1-2: Intermediate risk	21,561	822	3.8 (3.6-4.1)
≥3: High risk	4,402	219	5.0 (4.4-5.6)
<i>Khorana score level</i>			
1	12,860	435	3.4 (3.1-3.7)
2	8,701	387	4.4 (4.0-4.9)
3	3,623	175	4.8 (4.2-5.6)
4	716	39	5.4 (3.9-7.3)
5-6	63	5	7.9 (2.9-16.2)
<i>Guideline threshold</i>			
Score 0-1	27,118	770	2.8 (2.6-3.0)
Score ≥2	13,103	606	4.6 (4.3-5.0)
*Includes pulmonary embolism, deep vein thrombosis, thrombophlebitis and thrombosis located in the retinal, cerebral, portal, caval, or renal vein without requiring imaging procedures in combination with the diagnoses.			
† Based on the cumulative incidence function considering death as competing risk.			