

Supplementary Tables and Figures

Supplementary Table 1. Patient's characteristics according to the use of LMWH-based TP.

Characteristic	Total (N=535)	no LMWH (N=479)	LMWH (N=56)	p value
TE	29 (5.4)	26 (5.4)	3 (5.4)	1.000
Age, median (IQR)	64 (56-72)	63 (55-72)	68 (61 -71)	0.048
Gender, male	277 (51.8)	246 (51.4)	31 (55.4)	0.672
BMI, median (IQR)	24 (21-26)	24 (21-26)	24 (22-26)	0.883
≥35 kg/m ²	7 (1.3)	7 (1.5)	-	1.000
ECOG PS				
0-1	442 (82.6)	409 (85.4)	33 (58.9)	<.001
≥2	93 (17.4)	70 (14.6)	23 (41.1)	
Smoking status				
Never	333 (66.5)	306 (67.7)	27 (55.1)	0.082
Former	110 (22.0)	93 (20.6)	17 (34.7)	
Current	58 (11.5)	53 (11.7)	5 (10.2)	
NA	34	27	7	
Cancer type				
CUP	9 (1.7)	9 (1.9)	-	<.001
Lung	122 (22.8)	96 (20.0)	26 (46.4)	
Breast	44 (8.2)	38 (7.9)	6 (10.7)	
Colorectal	105 (19.6)	104 (21.7)	1 (1.8)	
Pancreatic	37 (6.9)	33 (6.9)	4 (7.1)	
Gastric and GEJ	75 (14.0)	70 (14.6)	5 (8.9)	
Biliary Tract	29 (5.4)	29 (6.1)	-	
Oesophageal	15 (2.8)	15 (3.1)	-	
Renal	8 (1.5)	7 (1.5)	1 (1.8)	
Melanoma	10 (1.9)	8 (1.7)	2 (3.6)	
Anal	23 (4.3)	22 (4.6)	1 (1.8)	
Prostate	8 (1.5)	7 (1.5)	1 (1.8)	
Bladder	3 (0.6)	3 (0.6)	-	
Other	47 (8.8)	38 (7.9)	9 (16.1)	
Stage				
Locally advanced	123 (23.0)	112 (23.4)	11 (19.6)	0.616
Metastatic	412 (77.0)	367 (76.6)	45 (80.4)	
Number of metastatic sites				
≤2	374 (69.9)	341 (71.2)	33 (58.9)	0.059
>2	161 (30.1)	138 (28.8)	23 (41.1)	
Ongoing anticancer treatment				
Platinum-based CT				
no	277 (51.8)	246 (51.4)	31 (55.4)	0.571
yes	258 (48.2)	233 (48.6)	25 (44.6)	
Gemcitabine-based CT				
no	494 (92.3)	445 (92.9)	49 (87.5)	0.150
yes	41 (7.7)	34 (7.1)	7 (12.5)	
Targeted therapy				
no	458 (85.6)	411 (85.8)	47 (83.9)	0.705
yes	77 (14.4)	68 (14.2)	9 (16.1)	
Immune checkpoint inhibitors				
no	498 (93.3)	448 (93.7)	50 (89.3)	0.210
yes	36 (6.7)	30 (6.3)	6 (10.7)	
NA	1	1	-	
Endocrine therapy				
no	514 (96.3)	460 (96.2)	54 (96.4)	1.000
yes	20 (3.7)	18 (3.8)	2 (3.6)	
NA	1	1	-	
Anti-angiogenic therapy				1.000

no	514 (96.3)	460 (96.2)	54 (96.4)	
yes	20 (3.7)	18 (3.8)	2 (3.6)	
NA	1	1	0	
Reason for hospitalization				
Acute Respiratory Insufficiency	5 (0.9)	2 (0.4)	3 (5.4)	
Biopsy	83 (15.5)	76 (15.9)	7 (12.5)	
Cancer Progression/CT Toxicity	23 (4.3)	20 (4.2)	3 (5.4)	
CVC placement	19 (3.6)	16 (3.3)	3 (5.4)	
Diarrhea	4 (0.7)	4 (0.8)	-	
Dysphagia	2 (0.4)	2 (0.4)	-	
Fever / Acute Infection	33 (6.2)	25 (5.2)	8 (14.3)	
Intestinal (sub-)occlusion	6 (1.1)	6 (1.3)	-	0.004
Immune related adverse events	4 (0.7)	3 (0.6)	1 (1.8)	
Malnutrition / Cachexia	10 (1.9)	9 (1.9)	1 (1.8)	
Nausea-Vomiting	3 (0.6)	3 (0.6)	-	
Obstructive jaundice	2 (0.4)	2 (0.4)	-	
Other	13 (2.4)	9 (1.9)	4 (7.1)	
Pleural Effusion	15 (2.8)	11 (2.3)	4 (7.1)	
Refractory Pain	11 (2.1)	10 (2.1)	1 (1.8)	
Treatment Administration	302 (56.4)	281 (58.7)	21 (37.5)	
LOS, median (IQR)	5 (3-8)	5 (3-8)	8 (4-15)	<.001
Fever during hospitalization	56 (10.5)	39 (8.1)	17 (30.4)	<.001
Use of antiplatelet agents	63 (11.8)	60 (12.5)	3 (5.4)	0.129
Khorana Score				
0	153 (28.6)	153 (31.9)	-	
1	155 (29.0)	131 (27.3)	24 (42.9)	<.001
2	139 (26.0)	122 (25.5)	17 (30.4)	
≥3	88 (16.4)	73 (15.2)	15 (26.8)	
Vascular compression	63 (12.1)	51 (10.9)	12 (21.8)	0.019
NA	13	12	1	
Previous TEs	29 (5.4)	23 (4.8)	6 (10.9)	0.059
NA	2	1	1	

Data are presented as n (%) except where otherwise noted. The p value of the χ^2 test, Fisher's exact test or WMW test assessing the association between each characteristic and the occurrence of TE events is indicated in the right column of the table. The p value of the test is indicated in bold numbers when statistically significant.

Abbreviations: BMI: body mass index; CT: chemotherapy; CUP: cancer of unknown primary; CVC: central venous catheter; ECOG PS: Eastern Cooperative Oncology Group Performance Status; GEJ: gastro-esophageal junction; IQR: interquartile range; LMWH: low molecular weight heparin; LOS: length of stay; NA: not available; TE: thromboembolic event.

Supplementary Table 2. Baseline laboratory values in the whole case series and according to the occurrence of thromboembolic events.

	Total (N = 535)	Without TE (N = 506)	With TE (N = 29)	p value
WBCs [/ μ L]				
median (IQR)	7620 (5760 - 10220)	7655 (5762 - 10230)	7250 (5760 - 9270)	0.846
>11000	105 (19.6)	100 (19.8)	5 (17.2)	0.740
Hemoglobin [g/dl]				
median (IQR)	12.3 (11.0 - 13.4)	12.3 (11.1 - 13.4)	11.5 (10.2 - 12.7)	0.009
<10	67 (12.5)	61 (12.1)	6 (20.7)	0.281
Platelets [$\times 10^9$ /L]				
median (IQR)	280 (215 - 366)	280 (217 - 366)	276 (182 - 309)	0.316
≥ 350	152 (28.4)	145 (28.7)	7 (24.1)	0.754
Neutrophils [/ μ L]				
median (IQR)	5200 (3800 - 7650)	5200 (3800 - 7600)	5200 (4000 - 8000)	0.730
Monocytes [/ μ L]				
median (IQR)	400 (300 - 600)	400 (300 - 600)	500 (300 - 600)	0.771
Albumin [g/dl]				
median (IQR)	4.0 (3.6 - 4.3)	4.0 (3.7 - 4.3)	3.7 (3.2 - 4.0)	<.001
NA	23	23	-	
CRP [mg/L]				
median (IQR)	11 (2 - 46)	11 (2 - 44)	42 (19 - 117)	0.003
NA	64	60	4	
Fibrinogen [mg/dl]				
median (IQR)	423 (343 - 552)	424 (344 - 552)	416 (315 - 540)	0.557
NA	62	55	7	
LDH [U/L]				
median (IQR)	351 (282 - 483)	346 (281 - 473)	485 (341 - 574)	<.001
NA	30	30	-	

All blood tests were performed at Istituto Nazionale dei Tumori of Milan. Cut-offs for hemoglobin, white blood cells and platelets counts were chosen according to the Khorana Score. The p value is indicated in the right column of the table and in bold numbers when statistically significant.

Abbreviations: CRP: C-reactive protein; IQR: interquartile range; LDH: lactate dehydrogenase; NA: not available; TE: thromboembolic event; WBCs: white blood cells.

Supplementary Table 3. Univariable and multivariable binary logistic regression analyses of association between clinical and biological variables and TEs.

Characteristic		Univariable OR (95 CI, p)	Multivariable OR (95 CI, p)
Age	Continuous	1.02 (0.99-1.05, p=0.299)	-
Gender	Male vs female	2.15 (0.99-5.06, p=0.062)	-
BMI	Continuous	0.98 (0.88-1.07, p=0.640)	-
ECOG PS	≥2 vs 1	2.26 (0.95-5.00, p=0.051)	-
Smoking status	Never	-	-
	Former	2.22 (0.98-4.85, p=0.048)	-
	Current	0.35 (0.02-1.76, p=0.315)	-
Stage	Locally advanced vs metastatic	1.92 (0.73-6.62, p=0.234)	-
Number of metastatic sites	≤2 vs >2	1.69 (0.77-3.60, p=0.177)	-
Platinum-based CT	Yes vs no	1.34 (0.63-2.90, p=0.443)	-
Gemcitabine-based CT	Yes vs no	1.42 (0.33-4.28, p=0.579)	-
Targeted therapy	Yes vs no	0.20 (0.01-0.97, p=0.119)	-
Immune checkpoint inhibitors	Yes vs no	1.65 (0.38-5.02, p=0.429)	-
Endocrine therapy	Yes vs no	2.01 (0.31-7.46, p=0.366)	-
Antiangiogenic therapy	Yes vs no	0.92 (0.05-4.67, p=0.933)	-
Use of antiplatelet agents	Yes vs no	1.21 (0.35-3.26, p=0.729)	-
Use of LMWH	Yes vs no	0.99 (0.23-2.92, p=0.982)	-
Khorana Score	0	-	-
	1	1.29 (0.47-3.68, p=0.627)	-
	2	1.27 (0.45-3.72, p=0.649)	-
	≥3	1.26 (0.36-4.06, p=0.704)	-
Vascular compression	Yes vs no	6.30 (2.79-13.85, p<.001)	5.35 (2.30-12.10, p<.001)
Previous TEs	Yes vs no	3.08 (0.86-8.71, p=0.051)	-
WBC [/ μ L]	Continuous	1.00 (1.00-1.00, p=0.776)	-
Hemoglobin [g/dl]	Continuous	0.75 (0.62-0.90, p=0.002)	-
	< 10 vs ≥10	0.53 (0.22-1.47, p=0.179)	-
Platelets [$\times 10^9$ /L]	Continuous	1.00 (1.00-1.00, p=0.805)	-
Neutrophils [/ μ L]	Continuous	1.00 (1.00-1.00, p=0.774)	-
Monocytes [/ μ L]	Continuous	1.00 (1.00-1.00, p=0.990)	-
Albumin [g/dl]	Continuous	0.29 (0.15-0.57, p<.001)	0.34 (0.17-0.70, p=0.003)
Log(CRP)	Continuous	1.54 (1.19-2.03, p=0.002)	-
Fibrinogen [mg/dl]	Continuous	1.00 (1.00-1.00, p=0.853)	-
Log(LDH)	Continuous	2.29 (1.33-3.79, p=0.002)	1.90 (1.07-3.24, p=0.022)

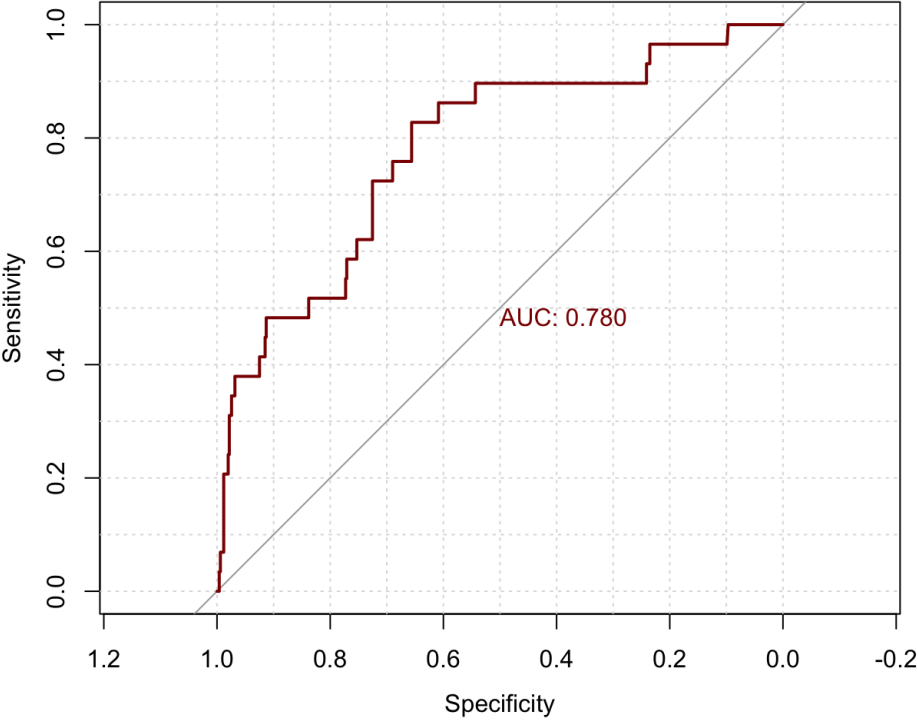
Abbreviations: BMI: body mass index; CRP: C-reactive protein; CT: chemotherapy; LDH: lactate dehydrogenase; ECOG PS: Eastern Cooperative Oncology Group Performance Status; LMWH: low molecular weight heparin; NA: not available; TE: thromboembolic event; WBC: white blood cells.

Supplementary Table 4. Univariate and multivariable binary logistic regression analyses of association between clinical and biological variables and TEs in patients not treated with low-molecular-weight heparin thromboprophylaxis.

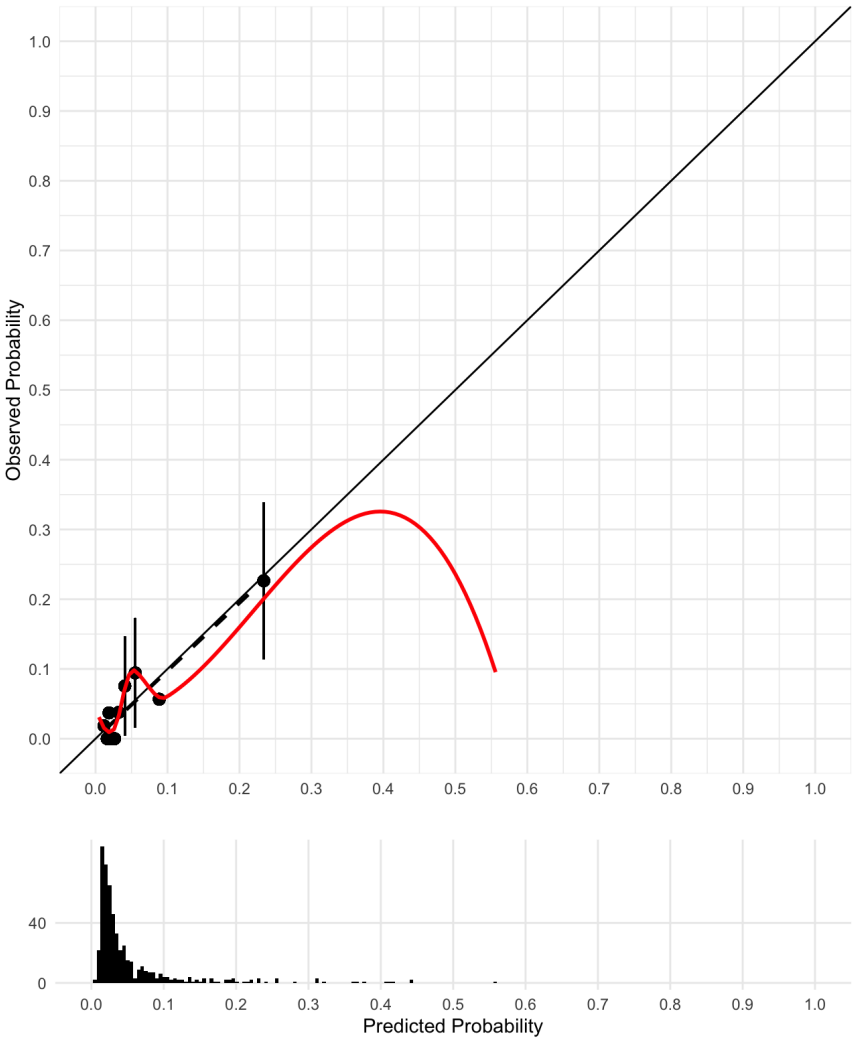
Characteristic		Univariable OR (95 CI, p)	Multivariable OR (95 CI, p)
Age	Continuous	1.03 (1.00-1.07, p=0.113)	-
Gender	Male vs Female	1.85 (0.82-4.42, p=0.147)	-
BMI	Continuous	0.99 (0.89-1.09, p=0.867)	-
ECOG PS	≥2 vs 0-1	2.80 (1.11-6.53, p=0.021)	-
Smoking status	Never	-	-
	Former	2.48 (1.04-5.66, p=0.033)	-
	Current	0.41 (0.02-2.06, p=0.387)	-
Stage	Locally advanced vs metastatic	1.72 (0.64-5.98, p=0.327)	-
Number of metastatic sites	>2 vs ≤2	1.88 (0.82-4.19, p=0.123)	-
Platinum-based CT	Yes vs no	1.25 (0.56-2.80, p=0.586)	-
Targeted-therapy	Yes vs no	0.23 (0.01-1.12, p=0.153)	-
Immune checkpoint inhibitors	Yes vs no	2.06 (0.47-6.40, p=0.263)	-
Endocrine therapy	Yes vs no	2.28 (0.35-8.64, p=0.291)	-
Antiangiogenic therapy	Yes vs no	1.03 (0.06-5.32, p=0.981)	-
Antiplatelet Therapy	Yes vs no	1.29 (0.37-3.52, p=0.651)	-
Khorana Score	0	-	-
	1	1.36 (0.47-3.97, p=0.566)	-
	2	1.27 (0.42-3.81, p=0.664)	-
	≥3	1.21 (0.31-4.14, p=0.768)	-
Vascular compression	Yes vs no	6.28 (2.60-14.58, p<.001)	5.91 (2.33-14.57, p<.001)
Previous TEs	Yes vs no	2.82 (0.63-9.02, p=0.113)	-
WBC [/ μ L]	Continuous	1.00 (1.00-1.00, p=0.606)	-
Hemoglobin [g/dl]	Continuous	0.74 (0.61-0.90, p=0.002)	-
	< 10 vs ≥10	0.40 (0.16-1.15, p=0.064)	-
Platelets [$\times 10^9$ /L]	Continuous	1.00 (1.00-1.00, p=0.895)	-
Neutrophils [/ μ L]	Continuous	1.00 (1.00-1.00, p=0.902)	-
Monocytes [/ μ L]	Continuous	1.00 (1.00-1.00, p=0.946)	-
Albumin [g/dl]	Continuous	0.21 (0.10-0.44, p<.001)	0.22 (0.10-0.49, p<.001)
Log(CRP)	Continuous	1.54 (1.17-2.07, p=0.003)	-
Fibrinogen [mg/dl]	Continuous	1.00 (1.00-1.00, p=0.488)	-
Log(LDH)	Continuous	2.43 (1.38-4.12, p=0.001)	1.85 (1.01-3.27, p=0.038)

Abbreviations: BMI: body mass index; CRP: C-reactive protein; CT: chemotherapy; LDH: lactate dehydrogenase; ECOG PS: Eastern Cooperative Oncology Group Performance Status; NA: not available; TE: thromboembolic event; WBC: white blood cells.

Supplementary Figure 1. Receiver Operator Characteristics (ROC) curve for logistic regression model for thromboembolic events. The Harrell's c-index, corresponding to the area under the ROC was 0.78.



Supplementary Figure 2. Calibration plot of the weighted TE risk score. Cases are grouped in 10 quantiles, with overall distribution plotted below. *Abbreviations:* TE: thromboembolic event.



Supplementary Figure 3. Landmark analysis of Overall Survival according to the occurrence of TEs during or after hospitalization. OS was calculated from the 45th day after discharge until death or last follow up. *Abbreviations:* NA: not available (not reached), OS: Overall survival TEs: thromboembolic events.

