

	Total	Cohort 1	Cohort 2	*p
<u>Demographics and treatment</u>				
Age (years) Mean \pm SD	57.98 \pm 19.39	52.17 \pm 19.60	61.26 \pm 18.54	0.0002
Sex (% male)	39.4	45.1	36.3	0.1644
VTE provoked (%)	53.9	52.9	54.4	0.9013
Recent travel for > 3 hours (%)	12.3	12.7	12.1	0.8532
Trauma or LE fracture within 3 months (%)	9.9	10.8	9.3	0.6838
Bed rest (%)	16.2	8.8	20.3	0.0118
Surgery or anesthesia within 3 months (%)	14.8	9.9	17.6	0.1153
Family history of VTE (%)	22.9	31.4	18.0	0.0121
Active cancer (%)	8.5	2.0	12.1	0.003
Concomitant DVT (%)	47.5	34.3	54.9	0.0009
DVT in lower extremity (%)	33.7	33.3	33.9	1
Time from first symptom to diagnosis (days) Mean \pm SD	13.17 \pm 25.12	11.16 \pm 17.09	14.29 \pm 28.61	0.0409
Diagnosis by CTPA, rather than VQ (%)	72.5	74.5	71.4	0.6778
Initial pulmonary vascular obstruction, mean \pm SD	35.8 \pm 24.1	38.8 \pm 25.9	34.1 \pm 22.9	0.1383
Days of anticoagulation Mean \pm SD	224.7 \pm 145.39	212.5 \pm 82.80	231.8 \pm 171.42	0.91
Extended duration anticoagulation (%)	21.5	16.7	24.2	0.1752
Interval from diagnosis to study VQ scan (days), mean \pm SD	304 \pm 105	258 \pm 75	330 \pm 111	<0.0001
<u>Clinical laboratory</u>				
Factor V _{Leiden} (%)	9.1	15.9	6.2	0.025
Prothrombin 20210a (%)	7.8	13.0	5.6	0.0637
Fibrinogen A α T312A (%)	45.2	57.6	37.3	0.0019
Antithrombin 3 (IU/dL) Mean \pm SD	96.84 \pm 11.74	97.54 \pm 12.95	96.50 \pm 11.13	0.5982
Protein C value (IU/dL) Mean \pm SD	102.40 \pm 21.41	98.45 \pm 24.81	104.10 \pm 19.69	0.0749
Protein S value (IU/dL) Mean \pm SD	89.48 \pm 21.26	89.18 \pm 20.76	89.60 \pm 21.53	0.9643
Fibrinogen (g/L) Mean \pm SD	3.79 \pm 1.05	4.28 \pm 1.13	3.52 \pm 0.89	<0.0001
Platelet (G/l) Mean \pm SD	258.8 \pm 74.09	258.8 \pm 86.43	258.9 \pm 68.48	0.6496
Prothrombin ratio (% control) Mean \pm SD	81.96 \pm 19.81	78.97 \pm 18.52	83.75 \pm 20.38	0.001
Thrombin (%) Mean \pm SD	88.80 \pm 28.91	83.35 \pm 30.13	93.76 \pm 27.03	0.0811
FV (%) Mean \pm SD	104.9 \pm 25.85	106.2 \pm 26.58	103.8 \pm 25.32	0.9201

FVII (%) Mean ± SD	93.14 ± 38.20	86.67 ± 40.75	100.30 ± 34.10	0.1526
<u>Fibrin property</u>				
Aα-chain aphosphorylated (%) Mean ± SD	37.74 ± 9.16	36.32 ± 6.88	38.66 ± 10.28	0.2214
Aα-chain monophosphorylated (%) Mean ± SD	32.20 ± 3.47	31.68 ± 2.33	32.54 ± 4.02	0.0028
Aα-chain diphosphorylated (%) Mean ± SD	30.06 ± 8.04	32.00 ± 5.96	28.80 ± 8.94	0.0048
Phosphorylation per Aα-chain Mean ± SD	0.92 ± 0.17	0.96 ± 0.13	0.90 ± 0.19	0.0533
Bβ-chain monosialylated (%) Mean ± SD	58.45 ± 6.97	58.25 ± 7.38	58.58 ± 6.71	0.836
Bβ-chain hydroxylated (%) Mean ± SD	21.83 ± 9.69	20.94 ± 5.13	22.40 ± 11.72	0.0289
des-gln461 Bβ-chain (%) Mean ± SD	11.24 ± 9.54	5.95 ± 1.69	14.66 ± 10.88	<0.0001
γ-chain monosialylated (%) Mean ± SD	70.63 ± 7.37	71.76 ± 5.90	69.90 ± 8.12	0.1289
γ' (%) Mean ± SD	2.74 ± 1.67	3.47 ± 1.35	2.26 ± 1.69	<0.0001
α-chain crosslinking (%) Mean ± SD	30.38 ± 12.80	34.46 ± 14.72	27.93 ± 10.82	0.0001
Clot permeability (Ks) Mean ± SD	5.2e-10 ± 2.3e-10	6.2e-10 ± 2.3e-10	4.5e-10 ± 2.0e-10	<0.0001
Accessibility of B-knob (ug bound) Mean ± SD	2.23 ± 0.76	2.05 ± 0.85	2.34 ± 0.69	0.0001
Clot turbidity (OD) Mean ± SD	0.21 ± 0.06	0.22 ± 0.05	0.21 ± 0.06	0.0022
Lysis rate (OD/min) Mean ± SD	-0.0015 ± 0.0004	-0.0017 ± 0.0004	-0.0014 ± 0.0004	<0.0001
Corrected lysis rate (ratio/min) Mean ± SD	-0.73 ± 0.20	-0.78 ± 0.19	-0.70 ± 0.20	0.0048
Time to complete lysis (min) Mean ± SD	139.4 ± 34.34	128.0 ± 23.87	146.6 ± 37.88	<0.0001
Fibrinogen mass variants (%)	17.6	13.0	20.6	0.1323
<u>Outcomes</u>				
RPVO ≥ 10%	75 (26.4%)	29 (28.4%)	46 (25.2%)	0.5770
CTEPH (%)	2.8	2.0	3.3	0.7155

Table S1. Comparison of characteristics between cohort 1 and cohort 2. Wilcoxon-Mann-Whitney was used to calculate p-values for continuous variables. Fisher's exact test was used for binary variables.

	Cohort 1			Cohort 2		
	Patients with RPVO <10% (n=73)	Patients with RPVO ≥ 10% (n=29)	p	Patients with RPVO < 10% (n=136)	Patients with RPVO ≥ 10% (n=46)	p
<u>Demographics and treatment</u>						
Age (years) Mean ± SD	49.3 ± 18.1	59.4 ± 21.6	0.02	59.2 ± 19.3	67.4 ± 14.4	0.02
Males	45.2 %	44.8 %	1.00	40.4 %	33.9 %	0.05
Provoked VTE	60.3 %	34.5 %	0.03	55.1 %	52.2 %	0.74
Travel > 3 hours	15.1 %	6.9 %	0.34	12.5 %	10.9 %	1.00
Trauma or LE fracture within 3 months	12.3 %	6.9 %	0.72	10.3 %	6.5 %	0.57
Recent bed rest	12.3 %	0 %	0.06	22.8 %	13 %	0.20
Surgery or general anesthesia within 3 months	11.1 %	6.9 %	0.72	18.4 %	15.2 %	0.82
Active cancer	2.7 %	0.0 %	1.00	13.2 %	8.7 %	0.60
Family history of VTE	32.9 %	27.6 %	0.64	20.5 %	10.9 %	0.18
Concomitant DVT	30.1 %	44.8 %	0.17	52.9 %	60.9 %	0.39
Concomitant lower extremity DVT	28.8 %	44.8 %	0.16	32.8 %	37.2 %	0.71
Concomitant upper extremity DVT	0.0 %	0.0 %	NA	22.1 %	27.9 %	0.53
Interval from symptoms to diagnosis (days) Mean ± SD	8.7 ± 15.5	17.1 ± 19.4	0.001	12.5 ± 25.4	19.8 ± 36.3	0.34
Initial pulmonary vascular obstruction (%) Mean ± SD	32.4 ± 23.2	54.9 ± 25.9	0.0001	30.7 ± 22.1	44.1 ± 22.4	0.001
Duration of anti-coagulation (days) Mean ± SD	211.0 ± 85.9	217.6 ± 73.3	0.54	230.7 ± 156.1	235.9 ± 220.2	0.80
Extended anticoagulation	9.6 %	34.5 %	0.006	20.6 %	34.8 %	0.07
Interval from diagnosis to study VQ scan (days) Mean ± SD	266.7 ± 78.0	234.5 ± 64.5	0.05	337.6 ± 113.1	305.6 ± 100.1	0.09
<u>Clinical laboratory</u>						
Factor V _{Leiden}	11.1 %	33.3 %	0.05	7.6 %	2.3 %	0.29
Prothrombin 10100a	14.8 %	6.7 %	0.67	5.9 %	4.7 %	1.00
Fibrinogen Aα T312A	53.5 %	67.9 %	0.26	36.8 %	38.5 %	0.85
AT3 (%) Mean ± SD	98.9 ± 12.5	93.9 ± 13.7	0.13	96.0 ± 10.9	97.8 ± 11.8	0.39
Protein C (IU/dL) Mean ± SD	99.1 ± 23.2	96.4 ± 29.9	0.49	105.8 ± 19.6	98.9 ± 19.2	0.10
Protein S (IU/dL) Mean ± SD	89.9 ± 21.5	86.9 ± 19.0	0.88	89.9 ± 22.0	88.5 ± 20.3	0.69
Fibrinogen (g/L) Mean ± SD	4.3 ± 1.1	4.2 ± 1.1	0.50	3.4 ± 0.8	3.8 ± 1.1	0.02

Platelets amount/nL) Mean ± SD	245.2 ± 87.2	293.8 ± 75.6	0.01	258.3 ± 70.1	260.3 ± 64.4	0.34
Prothrombin ratio (% of control) Mean ± SD	80.1 ± 17.6	76.3 ± 20.7	0.57	86.3 ± 18.5	77.0 ± 23.7	0.01
Factor II (% of control) Mean ± SD	88.5 ± 27.1	68.0 ± 34.4	0.07	94.3 ± 23.4	92.2 ± 37.1	0.72
Factor V (% of control) Mean ± SD	108.3 ± 28.0	99.9 ± 21.3	0.46	102.4 ± 26.0	107.8 ± 23.6	0.15
Factor VII (% of control) Mean ± SD	88.6 ± 39.2	81.0 ± 46.1	0.68	103.6 ± 36.1	91.1 ± 26.4	0.24
<u>Fibrin property</u>						
Aα-chains not phosphorylated (%) Mean ± SD	36.4 ± 7.0	36.2 ± 6.7	0.66	38.7 ± 10.9	38.5 ± 8.3	0.91
Aα-chains monophosphorylated (%) Mean ± SD	31.7 ± 2.4	31.7 ± 2.1	0.79	32.4 ± 3.8	32.9 ± 4.6	0.13
Aα-chains diphosphorylated (%) Mean ± SD	32.0 ± 6.2	32.1 ± 5.5	0.73	28.9 ± 9.3	28.7 ± 7.9	0.71
Phosphorylations per Aα-chain	0.96 ± 0.13	0.95 ± 0.12	0.78	0.90 ± 0.20	0.90 ± 0.16	0.95
Bβ-chains monosialylated (%) Mean ± SD	57.9 ± 7.9	59.1 ± 6.0	0.42	58.2 ± 6.8	59.7 ± 6.4	0.30
Bβ-chains hydroxylated (%) Mean ± SD	21.3 ± 5.3	20.1 ± 4.8	0.84	22.3 ± 11.5	22.6 ± 12.4	0.80
des-gln461 Bβ-chains (%) Mean ± SD	6.03 ± 1.81	5.74 ± 1.34	0.68	15.53 ± 11.49	12.11 ± 8.52	0.04
γ-chains monosialylated (%) Mean ± SD	71.9 ± 5.7	71.4 ± 6.4	0.64	69.8 ± 8.3	70.2 ± 7.8	0.80
fibrinogen γ' (%) Mean ± SD	3.6 ± 1.3	3.3 ± 1.4	0.32	2.3 ± 1.7	2.1 ± 1.5	0.61
Aα-chains crosslinked	34.5 ± 15.5	34.5 ± 13.0	0.70	27.9 ± 11.1	27.9 ± 10.1	0.68
Clot permeability (Ks Mean ± SD E-10) Mean ± SD	6.20 ± 2.40	6.10 ± 2.15	0.97	4.41 ± 2.01	4.78 ± 2.06	0.27
Anti-β15-42 N terminus bound (ug) Mean ± SD	2.05 ± 0.73	2.07 ± 1.09	0.64	2.40 ± 0.72	2.18 ± 0.57	0.13
Fibrin lot turbidity (OD _{max}) Mean ± SD	0.226 ± 0.048	0.220 ± 0.052	0.81	0.208 ± 0.061	0.201 ± 0.059	0.53
Lysis rate (OD/min) Mean ± SD	-0.002 ± 0.000	-0.002 ± 0.001	0.84	-0.001 ± 0.000	-0.001 ± 0.000	0.99
Corrected lysis rate (OD/OD _{max} /min) Mean ± SD	-0.787 ± 0.180	-0.749 ± 0.198	0.46	-0.702 ± 0.204	-0.704 ± 0.199	0.91
Lysis time (min) Mean ± SD	127.5 ± 21.1	129.4 ± 29.9	0.29	147.8 ± 39.0	143.2 ± 34.8	0.42
<u>Outcomes</u>						
CTEPH	0.0 %	6.9 %	0.08	0.7 %	10.9 %	0.004
Residual pulm vasc obstruction (%) Mean ± SD	3.3 ± 2.7	23.0 ± 16.5	< 0.001	1.1 ± 2.2	23.8 ± 15.7	< 0.001

Table S2. Comparison, within each cohort, of predictors in patients with and without residual pulmonary vascular obstruction. Wilcoxon-Mann-Whitney was used to calculate p-values for continuous variables. Fisher's exact test was used for binary variables.

Fibrin(ogen) property	Predictive models for RPVO			
	Presentation, treatment and fibrin properties		Obstruction and fibrin properties only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2 p
Initial obstruction				
p	0.000369	0.00680	0.00003	0.000423
OR per 1% increase in obstruction (95% CI)	1.041 (1.018, 1.064)	1.027 (1.007, 1.046)	1.054 (1.028, 1.080)	1.034 (1.015, 1.054)
Interval from symptoms to diagnosis				
p	0.078758	-	-	-
OR per day (95% CI)	1.026 (0.997, 1.056)	-	-	-
Age				
p	-	0.01905	-	-
OR per year (95% CI)	-	1.035 (1.006, 1.065)	-	-
Thrombolysis				
p	-	0.00986	-	-
OR if used (95% CI)	-	10.129 (1.745, 58.7)	-	-
High B β -chain mono sialylation				
p	0.100657	0.00658	0.0655	0.014425
OR per 1% increase in monosialylation (95% CI)	1.074 (0.986, 1.168)	1.178 (1.047, 1.326)	1.095 (0.994, 1.206)	1.145 (1.027, 1.276)
Slow fibrin clot lysis rate				
p	-	-	0.1737	-
OR per 1% lysis per minute (95% CI)	-	-	10.872 (0.349, 338)	-
Low fibrinogen γ'				
p	0.040079	-	0.0388	-
OR per 1% increase in γ' (95% CI)	0.641 (0.419, 0.980)	-	0.614 (0.386, 0.975)	-
Low β 15-42 N terminus accessibility				
p	-	-	-	0.132860
OR per each 1 μ g of anti- β 15-42 retained	-	-	-	0.549

within the fibrin clot (95% CI)				(0.251, 1.200)
Low des-gln461 B β -chain				
p	-	0.05757	-	0.105844
OR per 1% increase in des-gln461 B β - chains (95% CI)	-	0.945 (0.891, 1.002)	-	0.955 (0.903, 1.010)
Low γ -chain mono sialylation				
p	-	0.08098	-	0.123704
OR per 1% increase in monosialylation (95% CI)	-	0.923 (0.844, 1.010)	-	0.937 (0.863, 1.018)

Table S3. Table 3. Fibrinogen predictors between the two cohorts of patients. The p values are associated with the individual predictors within the optimal predictive model selected according to the Akaike Information Criterion for a specific cohort to be the most predictive of RPVO after acute pulmonary embolism.