

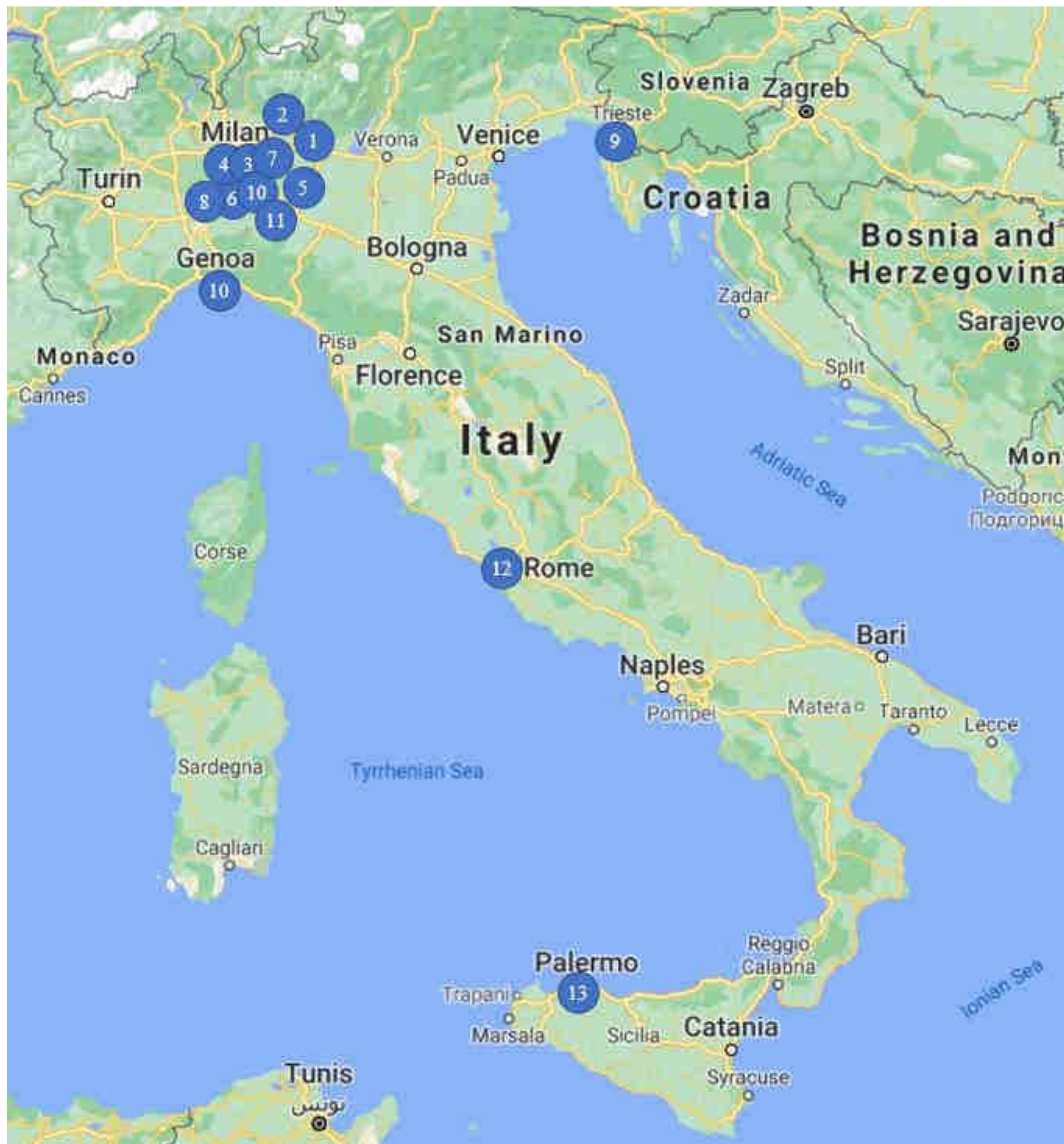
**Pulmonary embolism in patients with COVID-19: characteristics and outcomes
in the Cardio-COVID Italy multicenter study**

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Supplemental information

Supplemental Figure 1.

Map of Italy showing the location of the centres participating in the study.

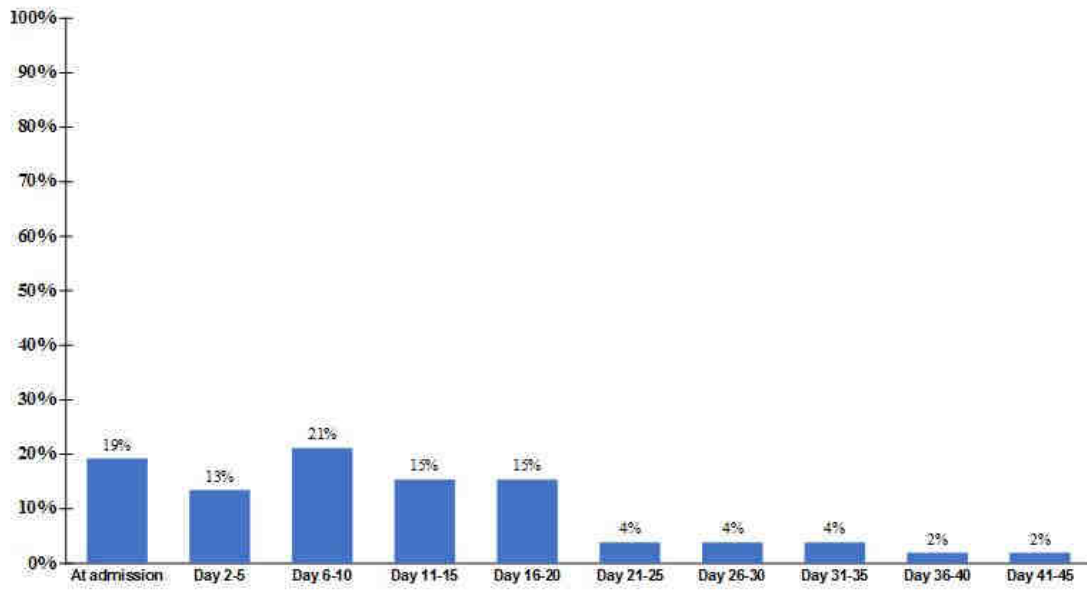


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Supplemental Figure 2.

Distribution of pulmonary embolism events, as percentage of total events, throughout the hospitalization for COVID-19.



Supplemental Table 1. Additional laboratory findings on admission in the study population, stratified by occurrence pulmonary embolism.

	All (N. 689)	No PE (N. 637)	PE (N. 52)	P value
Red blood cell count (x10⁶/μL)	4.5 (4.0-4.9)	4.5 (4.0-4.9)	4.5 (4.1-5.1)	0.63
Haematocrit (%)	39.0 (35.4-42.8)	39.0 (35.4-42.6)	38.6 (35.8-44.0)	0.53
eGFR (CKD-EPI, mL/min)	74.2 (50.3-90.4)	74.6 (49.8-90.6)	71.3 (54.3-88.7)	0.99
Serum sodium (mEq/L)	137 (135-140)	137 (134-140)	138.5 (136-141)	0.18
Serum potassium (mEq/L)	3.9 (3.6-4.3)	3.9 (3.6-4.3)	4.1 (3.6-4.4)	0.83
Procalcitonin (ng/mL)	0.2 (0.1-0.5)	0.1 (0.1-0.4)	0.4 (0.1-3.5)	0.018
Bilirubin (mg/dL)	0.6 (0.4-0.8)	0.6 (0.4-0.8)	0.6 (0.4-0.8)	0.40
Creatine phosphokinase (U/L)	112 (56.5-302)	114 (54.5-302)	92 (64-258)	0.89
Serum albumin (g/L)	32 (28-36)	32 (8-35)	33 (26-36)	0.89
Arterial pH	7.5 (7.4-7.5)	7.5 (7.4-7.5)	7.5 (7.4-7.5)	0.92

Data shown as median (interquartile range).

eGFR: estimated glomerular filtration rate.

Supplemental Table 2. Right ventricle-focused echocardiographic parameters on admission in the study population, stratified by pulmonary embolism.

	N. of patients with available data	All (N. 689)	No PE (N. 637)	PE (N. 52)	P value
RV dilation	242 (35.1)	37 (15.3)	24 (11.4)	13 (41.9)	<0.001
RV dysfunction	256 (37.1)	39 (15.2)	29 (12.9)	10 (31.3)	0.007
TAPSE (mm)	166 (24.1)	20.6 ± 4.4	20.9 ± 4.0	19.4 ± 5.9	0.12
FAC (%)	69 (10)	42.2 ± 7.1	42.9 ± 6.5	39.2 ± 9.0	0.09
S' TDI (cm/s)	80 (11.6)	12.2 ± 2.7	12.5 (12 – 13.1)	10.9 (9.1-12.8)	0.014
sPAP (mmHg)	199 (28.8)	18.3 ± 9.5	18.1 ± 9.1	19.7 ± 11.9	0.42

Data are shown as count (%), mean ± SD or median (interquartile range).

RV: right ventricle; TAPSE: tricuspid annular plane systolic excursion; FAC: fractional area change; S' TDI: S' tissue Doppler imaging-derived tricuspid lateral annular systolic velocity; sPAP: systolic pulmonary artery pressure.

RV dysfunction: TAPSE <17 mm or S' TDI <9.5 cm/s or enlarged RV (basal diameter >43 mm or dilation on qualitative assessment).

Supplemental Table 3. Baseline characteristics of the study population, stratified by region of enrolment.

	All (N. 689)	Lombardy (N. 524)	Other regions (N. 165)	P value
Age (years)	67.3 ± 13.2	67.4 ± 13.3	67.2 ± 13.0	0.91
Male gender	487 (69.4)	375 (71.6)	103 (62.4)	0.03
BMI (kg/m²)	27.2 ± 5.3	27.2 ± 5.5	27.2 ± 5.0	0.9
Ever smoker	159 (27)	127 (28.6)	32 (22.2)	0.13
Hypertension	398 (56.9)	294 (56.3)	95 (58.6)	0.60
Dyslipidaemia	188 (27.5)	145 (27.8)	43 (26.5)	0.75
Diabetes	157 (23)	126 (24.1)	31 (19.1)	0.19
Heart failure	92 (13.5)	72 (13.8)	20 (12.3)	0.64
Atrial fibrillation	105 (15.4)	85 (16.3)	20 (12.3)	0.22
Coronary artery disease	143 (20.9)	117 (22.4)	26 (16.0)	0.08
COPD	67 (9.8)	42 (8.0)	25 (15.4)	0.006
Chronic kidney disease	127 (18.6)	94 (18.0)	33 (20.4)	0.50
ACEi/ARB therapy	133 (20.6)	100 (20.3)	33 (21.4)	0.77
Oral anticoagulant therapy	90 (14.1)	74 (15.4)	16 (10.2)	0.10
<i>Direct oral anticoagulant</i>	47 (7.4)	38 (7.9)	9 (5.7)	0.37
<i>Vitamin K antagonist</i>	48 (7.5)	41 (8.5)	7 (4.5)	0.09
Statin therapy	176 (27.2)	141 (28.7)	35 (22.6)	0.14
Fever (≥37.5 °C)	440 (64.1)	332 (63.6)	108 (65.9)	0.60
Respiratory rate ≥22/minute	279 (52.0)	189 (50.8)	90 (54.5)	0.42
SBP (mmHg)	129.6 ± 21.5	131.0 ± 21.8	129.2 ± 21.4	0.34
Heart rate (bpm)	86.6 ± 18.1	86.5 ± 18.0	87.2 ± 18.4	0.66
Oxygen saturation (%)	90.5 ± 7.6	90.4 ± 7.8	90.9 ± 6.6	0.40
LV ejection fraction (%)	52.5 ± 11.3	52.3 ± 12.2	53.0 ± 9.0	0.61

Data are shown as count (%), mean ± SD or median (interquartile range).

BMI: body mass index; COPD: chronic obstructive pulmonary disease; ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; SBP systolic blood pressure; LV: left ventricular.

Supplemental Table 4. Main laboratory findings on admission in the study population, stratified by region of enrolment.

	All (N. 689)	Lombardy (N. 524)	Other regions (N. 165)	P value
Haemoglobin (g/dL)	13.4 (11.8-14.4)	13.2 (11.7-14.3)	13.7 (12.2-14.8)	0.007
White blood cell count (/μL)	6,760 (4,990-9,320)	6,945 (5,165-9,270)	6,300 (4,590-9,440)	0.09
Lymphocyte count (/μL)	921.5 (620-1,300)	920 (600-1,296)	995 (690-1,300)	0.69
Platelet count (x10³/μL)	204 (155-270)	209 (157-273)	195.5 (147.5-265)	0.15
Serum creatinine (mg/dL)	1.0 (0.8-1.3)	1.0 (0.8-1.4)	0.9 (0.8-1.1)	0.007
CRP (mg/dL)	233.5 (108.5-353.5)	237.0 (111.0-349.0)	198.0 (83.0-379.0)	0.69
Ferritin (μg/L)	698.5 (374-1,473)	722 (364-1,562)	674 (396-1,376)	0.44
Aspartate transaminase (U/L)	40 (26-64)	42 (26-68)	38 (24-56)	0.06
Lactate dehydrogenase (U/L)	362 (252-520)	384.5 (257.5-587.0)	311.0 (243.0-425.0)	<0.001
D-dimer (ng/mL)	868 (439-1,703)	818 (394-1,805)	970 (515-1,500)	0.21
INR	1.1 (1.0-1.2)	1.1 (1.0-1.2)	1.2 (1.1-1.3)	<0.001
Elevated troponin	278 (45.3)	228 (44.3)	44 (50.6)	0.27
NT-proBNP (pg/mL)	341 (96-1,323)	417 (134-2,403)	187 (71-920)	0.013

Data shown as median (interquartile range) or, for the frequency of elevated troponin, count (%).

CRP: C-reactive protein; INR: International Normalized Ratio; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Supplemental Table 5. Treatment received for COVID-19 in the study population, stratified by region of enrolment.

	All (N. 689)	Lombardy (N. 524)	Other regions (N. 165)	P value
<i>Medical therapy</i>				
Lopivanir/Ritonavir	184 (26.9)	148 (28.5)	36 (22.0)	0.10
Darunavir/Ritonavir	168 (24.6)	155 (29.8)	13 (7.9)	<0.001
Remdesivir	5 (0.7)	5 (1.0)	0 (0.0)	0.21
Corticosteroid	341 (49.9)	212 (40.8)	129 (78.7)	<0.001
Tocilizumab	79 (11.5)	38 (7.3)	41 (25.0)	<0.001
Hydroxychloroquine	574 (83.9)	431 (82.9)	143 (87.2)	0.19
<i>Ventilation support</i>				
Oxygen with FiO₂ ≥50%	375 (55.7)	257 (50.6)	118 (71.5)	<0.001
Non-invasive ventilation	298 (43.6)	198 (38.2)	100 (61)	<0.001
Intubation	108 (15.8)	78 (15)	30 (18.3)	0.31

Data are shown as count (%).

Note that oxygen was given with a FiO₂ ≥50% to both non-ventilated and ventilated patients.

sc: subcutaneous; iv: intravenous; FiO₂: fraction of inspired oxygen.

Supplemental Table 6. Correlates of pulmonary embolism in the study population, after substituting peak D-dimer for D-dimer on admission.

	Univariate		Multivariate	
	HR (95%CI)	P value	HR (95%CI)	P value
Age	0.99 (0.97-1.01)	0.19	-	-
BMI	1.06 (1.02-1.10)	0.006	-	-
Heart failure	0.32 (0.08-1.33)	0.12	-	-
Atrial fibrillation	0.43 (0.13-1.39)	0.16	-	-
Chronic kidney disease	0.45 (0.16-1.25)	0.12	-	-
Prior anticoagulant	1.83 (0.94-3.57)	0.08	-	-
Oxygen saturation	0.95 (0.93-0.98)	0.001	-	-
White blood cell count	1.00 (0.99-1.00)	0.06	-	-
Platelet count	1.00 (1.00-1.01)	0.03	-	-
Ferritin	1.00 (1.00-1.01)	<0.001	-	-
Aspartate transaminase	1.00 (0.99-1.00)	0.16	-	-
Lactate dehydrogenase	1.00 (0.99-1.00)	0.24	-	-
Elevated troponin	2.20 (1.22-3.95)	0.008	-	-
Peak D-dimer	1.78 (1.43-2.20)	<0.001	1.57 (1.01-2.45)	0.05

BMI: body mass index.

Supplemental Table 7. Correlates of pulmonary embolism in closed cases.

	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	0.99 (0.96-1.01)	0.22	-	-
BMI	1.08 (1.03-1.13)	0.001	-	-
Heart failure	0.37 (0.09-1.53)	0.17	-	-
Atrial fibrillation	0.51 (0.16-1.64)	0.26	-	-
Chronic kidney disease	0.49 (0.17-1.36)	0.17	-	-
Prior anticoagulant	1.69 (0.78-3.65)	0.18	-	-
Oxygen saturation	0.95 (0.93-0.98)	0.002	-	-
White blood cell count	1.00 (1.00-1.01)	0.06	-	-
Platelet count	1.00 (1-1.01)	0.05	-	-
Ferritin	1.00 (1.00-1.01)	<0.001	-	-
Aspartate transaminase	1.00 (0.99-1.00)	0.15	-	-
Lactate dehydrogenase	1.00 (0.99-1.00)	0.23	-	-
Elevated troponin	2.16 (1.11-4.18)	0.02	-	-
D-dimer on admission	2.18 (1.66-2.87)	< 0.001	1.60 (1.07-2.40)	0.02

BMI: body mass index.