PLOS ONE

RESEARCH ARTICLE

Incidence and characterization of acute pulmonary embolism in patients with SARS-CoV-2 pneumonia: A multicenter Italian experience

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Background

- Several studies reported a high incidence of pulmonary embolism (PE) among patients with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection.
- Moreover, abnormal coagulation parameters have been described among patients hospitalized with severe COVID-19, including elevated Ddimer and fibrin degradation products (FDP) levels, with a strong correlation with in-hospital mortality .
- However, a detailed clinical characterization of patients with PE, the D-dimer's role in predicting embolism, the nature of PE (real embolism or local inflammation process) and the prognostic value remains poorly described.

AIM of the study

- To report the rate and the distribution of PE in patients with SARS-CoV-2 infection admitted in seven hospitals located in Northern Italy during the first outbreak of the disease.
- To describe the risk factors, clinical characteristics and in-hospital outcome of this population.

Methods

- Retrospective, multicenter, observational, cohort study.
- The cohort included 333 consecutive patients with a confirmed diagnosis of pneumonia by SARS-CoV-2 admitted to seven hospitals located in Northern Italy between February 22 to May 15 2020, who underwent computed tomography pulmonary angiography (CTPA) at admission.
- Information about medical history, presence of major predisposing risk factors for venous thromboembolism, complete blood chemistry tests, and clinical outcomes were collected.

Results (I)

- Among 333 patients with laboratory confirmed SARS-CoV-2 pneumonia and undergoing CTPA, PE was detected in 109 (33%) cases.
- Clinical characteristics of the two groups were similar, although patients with PE had a higher heart rate (HR) and lower systolic blood pressure (SBP) at admission compared with those without PE.
- No main comorbidities were associated with a higher risk of PE.
- Traditional risk factors for PE were not associated with PE occurrence.
- Deep vein thrombosis (DVT) was detected in only 15 (29% of 51) patients at compression ultrasonography, which was performed in 51 (47%) patients with PE.
- Medical therapy before admission, including anticoagulant/antithrombotic treatments, were not different in the two groups.

Table 2. Major predisposing risk factors for PE.

	Total (n = 333)	PE (n = 109)	Non-PE (n = 224)	p value
Hospitalization (last 3 months)	0	0	0	//
ACS (last 3 months)	0	0	0	//
Previous DVT/PE	6 (2%)	3 (3%)	3 (1%)	0.4
Active Cancer	33 (10%)	8 (7%)	25 (11%)	0.27
Oral contraceptive therapy	1 (0.3%)	0	1 (0.5%)	1
Autoimmune diseases	11 (3%)	3 (3%)	8 (4%)	1

Data are n (%).

PE: pulmonary embolism; ACS: acute coronary syndrome; DVT: deep vein thrombosis.

Results (II)

- No PE patients presented with hemodynamic instability at the time of the diagnosis.
- No PE patient had a sPESI score higher than 4.
- All patients with PE diagnosis at CTPA received a full anticoagulant dose of enoxaparin (100 IU/Kg twice daily).
- No differences were noted between the two study groups about need for non-invasive ventilation with C-PAP (p = 0,57) and ICU admission (p = 0,39). In-hospital death occurred in 29 (27%) patients in the PE-group and in 47 (21%) patients in the non-PE group (p = 0.25).
- Both baseline and peak value of D-dimer were higher in PE-group compared to no-PE group.
- High-sensitivity cardiac troponin I levels were low and not different between the two groups.
- Patients with PE presented higher leucocyte level.

Table 4. Laboratory data.

	Normal range	Total (n = 333)	PE (n = 109)	Non-PE (n = 224)	p value
D-dimer (µg/ml) Admission value	0–0.5	2.1 (0.6–4.7)	3.6 (0.9–14.7)	1.3 (0.6–3.3)	**0.001**
D-dimer (µg/ml) Peak value	0–0.5	3.8 (2.6–9.9)	5.7 (3.3–49)	3.3 (1.9–9.6)	**0.001**
Hs-TnI (ng/L) Admission value	0–34	14.7 (8.9–107.8)	13.9 (6–238)	16.7 (8.9–93)	0.69
Hs-TnI (ng/L) Peak value	0–34	24.8 (12.8–108.9)	39 (14.6–238)	20.1 (11.2–107.7)	0.85
CRP (mg/L) Admission value	0–5	65.5 (22.8–150)	49 (23.4–220)	71 (21–140)	0.34
CRP (mg/L) Peak value	0–5	113.5 (48.3–257.7)	99 (33.3–270)	117 (55–210)	0.12
WBC (/mm^3)	3900–10600	7775 (5115–12837)	14000 (5950–21800)	7340 (4740–11700)	**0.001**
Hb (g/dL)	14–18	12.5 (10.9–14.2)	13.9 (12.1–16)	12.2 (10.8–14)	**0.015**
PTL (*10^3/mm^3)	150–400	230 (170.7–307.5)	232 (142–330)	228 (175–273)	0.84
aPTT (seconds)	25–36	30 (28.2–33.2)	30 (27.7–31.8)	30 (28.3–34)	0.054
INR	0.8–1.2	1.15 (1.08–1.30)	1.33 (1.15–1.53)	1.14 (1.06–1.23)	0.64
LDH (U/L)	<248	346 (273–448)	293 (227–476)	354 (289–447)	0.25
Creatinine (mg/dL)	0.7–1.18	1.07 (0.79–1.33)	1.09 (0.80–1.41)	1.07 (0.76–1.31)	0.94
EGFR (ml/min/1.73mq)	> 60	74.7 (50.3–94.5)	73.7 (48.1–96)	75.7 (51.1–92)	0.48
IL-6 (ng/L)	95–100	56.5 (21.7–120)	49 (16–126)	58 (24–118)	0.94

Data are median (IQR) or n (%).PE: pulmonary embolism; hs-TnI: high sensitive troponin I; CRP: C-reactive protein; WBC: white blood cell count; PTL: platelets; ALT: alanine aminotransferase; AST: aspartate transaminase; aPTT: activated partial thromboplastin time; INR: international normalized ratio; LDH: lactate dehydrogenase; EGFR: estimated glomerular filtration rate; Pa02: arterial oxygen partial pressure; S02: oxygen saturation; Fi02:fraction of inspired oxygen. Bold numbers indicate significant p-value<0.05.

Results (III)

- Subsegmental and segmental filling defects were observed in in 31 (29%) and 50 (46%) patients respectively whereas lobar thrombi and central PE were found in 20 (18%) and 8 (7%) cases .
- Thrombi were bilaterally distributed in 54 (49%) patients.
- Pneumonia severity was not different between the two groups.
- Among PE group, 77 (71%) of the patients CTPA showed PE mainly located in lung consolidation areas.

Table 5. Entity of pulmonary involvement.

	Total (n = 333)	PE (n = 109)	Non-PE (n = 224)	p
Pulmonary involvement				
0%	37 (11%)	12 (11%)	25 (11%)	0.97
< 25%	82 (25%)	29 (27%)	53 (24%)	0.6
25–50%	78 (23%)	29 (27%)	49 (22%)	0.34
50–75%	82 (25%)	23 (21%)	59 (26%)	0.3
> 75%	54 (16%)	16 (14%)	38 (17%)	0.6

Data are n (%).

PE: pulmonary embolism.

Conclusions

- These results underline the close link between COVID-19 and prothrombotic diathesis.
- PE occurres in among 1/3 of patients with SARS-CoV-2 pneumonia but it does not worsen the prognosis of the disease.
- Local inflammation might play a relevant role in the pathobiological mechanisms of PE in the setting of SARS-CoV-2 pneumonia since the predominant localization of thromboses (71% of cases) was in the correspondence of the consolidation areas of the pulmonary parenchyma.
- Patients on chronic anticoagulation therapy, and even those who took prophylactic therapy with enoxaparin during hospitalization, were not protected from the occurrence of PE.
- Based on the results of the study, a risk-adapted approach to escalating the dose of anticoagulation should be considered after assessing the individual thrombotic and bleeding risk in COVID-19 patients.
- Further prospective investigation are warranted to better clarify this aspect.