Letter to the Editor

Characteristics and predictors of pulmonary embolism in patients admitted for COVID-19 with respiratory failure

Thomas Fraccalini[1], Guido S. G. Maggiani[3], Rouslan Senkeev[2], Luciano Cardinale[2], Giovanni Volpicelli[1]

[1]Department of Emergency Medicine, San Luigi Gonzaga University Hospital, Torino, Italy; [2]Department of Oncology, Radiology Unit, San Luigi Gonzaga University Hospital, Torino, Italy; [3]Geriatric and Metabolic Bone Disease, Città della Scienza e della Salute di Torino, University Hospital, Torino, Italy

Correspondence to: Luciano Cardinale, MD. Department of Oncology, Radiology Unit, San Luigi Gonzaga University Hospital, Regione Gonzole 10, Orbassano, Torino, 10024, Italy. Email: luciano.cardinale@gmail.com.

Submitted Apr 20, 2022. Accepted for publication Jul 08, 2022.
doi: 10.21037/jtd-22-545
View this article at: https://dx.doi.org/10.21037/jtd-22-545

Many studies demonstrated that patients affected by coronavirus disease 2019 (COVID-19) may present venous thromboembolism (VTE) and respiratory complications from pulmonary embolism (PE) (1-3). However, PE in COVID-19 patients may present different clinical presentation, demographics, risk factors and laboratory values when compared to other populations (4). Clinical indicators and/or predictors of PE in COVID-19 should be carefully investigated and standardized, which might allow to rationalize the diagnostic process and the use of computed tomography pulmonary angiogram (CTPA). To this aim, we performed a retrospective analysis of medical records of consecutive adults presenting to the emergency department (ED) of the San Luigi Gonzaga University Hospital from March 2020 to December 2020 with a condition of respiratory failure in COVID-19 pneumonia. Only adult patients with suspected PE who performed CTPA scan for clinical decision of the physician in charge were considered. Criteria for respiratory failure were at least one of the following: (I) a PaO_2/FiO_2 ratio (P/F) at ED admission <300; (II) an oxygen saturation <92% on room air at arrival in the ED; (III) a decline and/or worsening respiratory state, matching the two above conditions, during the first 12 h from the arrival in the ED and clearly unrelated to the progression of pneumonia. Patients who for any pathology were already taking prophylactic or therapeutic anticoagulant medications, were excluded.

The diagnosis of COVID-19 was obtained by a reverse transcriptase-polymerase chain reaction (RT-PCR) nasal-pharyngeal swab test (BD SARS-CoV-2 Reagents for BD MAX System™).

During the study period, 299 patients with respiratory failure due to COVID-19 pneumonia were considered eligible; among them, 130 patients performed a CTPA scan for suspected PE after the clinical assessment of the physician in charge, so they were included in this study (66% of them were male, with a median age of 64 years). Patients were then divided in two groups: with and without PE confirmation (respectively, PE+ and PE–). Demographics, hematochemical data, arterial blood gas analysis, Wells score, comorbidities and the Charlson Comorbidity Index (CCI) were considered and compared between groups. The description of the overall population is reported in *Table 1*.

Statistical analysis was performed using the R language in the R Studio Integrated. Normality of the data was assessed through the Shapiro-Wilk test. Heteroschedasticity of the data was assessed through Levene's test. Data with Gaussian distribution were compared using Student's t-test for independent variables while parameters with non-Gaussian distribution were evaluated through the non-parametric Mann Withney test as appropriate. Dichotomous variables were assessed through Chi-Square Test. Data are presented as mean ± 1 standard deviation. Any result with P value <0.05 was considered statistically significant.

The PE incidence in our population was 18.5%. The differences that were found statistically significant between the two groups were: mean P/F (220±75.8 in PE+, 270±94.4 in PE–; P=0.01), serum creatinine (0.81±0.23 in PE+, 0.92±0.24 in PE–; P=0.01), prevalence of type 2 diabetes (higher in the PE- group; P=0.03). Regarding the demographic data, age and sex were not associated with PE in our population, although PE+ patients were slightly older

Table 1 Patient's characteristics in a population of 130 patients hospitalized with COVID-19 and signs of respiratory failure, divided in PE positive (n=24) and PE negative (n=106)

Variables	Total	PE	Non-PE	P value
Age, years	64±12.9	68.5±13.1	63.5±12.4	0.09
P/F	260±93	220±75.8	270±94.4	0.01
D-dimer, ng/mL	3,848±9,335	8,952±1,6300	2,661±6,381	0.83
Creatinine, mg/dL	0.90±0.24	0.81±0.23	0.92±0.24	0.01
Wells score	0.66±1.2	0.68±1.5	0.65±1.1	0.295
Charlson index	3.6±2.4	3.1±1.5	3.7±2.6	0.18
Sex				0.76
Male	86 (66.0)	17 (20.0)	69 (80.0)	
Female	44 (34.0)	7 (16.0)	37 (84.0)	
Neoplastic disease	13 (10.0)	2 (15.0)	11 (85.0)	1.00
Type II diabetes	22 (16.9)	0 (0.0)	22 (100.0)	0.01
Hypertension	59 (45.4)	11 (19.0)	48 (81.0)	1.00
Dyslipidemia	34 (26.2)	3 (9.0)	31 (91.0)	0.15
CAD	15 (11.5)	1 (7.0)	14 (93.0)	0.37
COPD	7 (33.8)	1 (14.0)	6 (86.0)	1.00
MADD	11 (8.5)	3 (27.0)	8 (73.0)	0.70

Data is presented as mean ± standard deviation or n (%). COVID-19, coronavirus disease 2019; PE, pulmonary embolism; P/F, PaO_2/FiO_2 ratio; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; MADD, mixed anxiety-depressive disorder.

(5,6). We didnt't find a statistical correlation between PE and Wells score (0.68±1.5 in PE+, 0.65±1.1 in PE–; P=0.295) nor between PE and chronic comorbidities (hypertension, cancer, COPD, CAD, MADD, chronic haepatic desease, dyslipidemia) or CCI. Moreover, we found no significant difference in D-dimer levels between PE+ and PE– patients, even if we observed a slightly higher mean D-dimer value in the PE+ group (1,603 *vs.* 1,241 ng/mL FEU).

Our study demonstrates that PE is a possible COVID-19 complication with a global incidence similar to the one observed in other high risk diseases like cancer (7). The prevalence of PE in our population is in line with previous studies that demonstrated a PE prevalence in COVID-19 patients ranging from 5% to 19% (1,2,8). The other study results were consistent with the existing literature as well: traditional risk scores for VTE have strong limitations in the COVID-19 context (8), standard risk factors and traditional comorbidities are not associated with PE occurrence in COVID-19 patients (4). Even if the current practice suggests using the conventional D-dimer cut-off values in combination with clinical pre-test probability and age adjustment (3), we found no confirmation of a significant difference between the two groups.

While the association between type 2 diabetes and creatinine levels with PE is of uncertain relevance, the statistically significant P/F value difference between the two groups may have a strong biological theoretical support. Indeed, the lower P/F values observed in the group PE+ may indicate a higher risk. However, both COVID-19 and PE can present independently with a wide range of pulmonary involvement and lung function compromission, which makes our findings difficult to translate into clinical practice.

Some limitations are the retrospective and single center nature of the analysis along with the small sample size, so the generalizability of our conclusions should be considered cautiously. Our orientation in the light of the obtained data is that a sudden respiratory function deterioration, not justified by the pulmonary damage, may indicate the presence of PE complicating the COVID-19 pneumonia. Thus, it may become of the utmost importance to have a

systematic comparison between the interstitial pneumonia extension, evaluated with bedside lung ultrasound, and the respiratory failure severity (9); in our study, we did not apply a systematic multiorgan ultrasound assessment to guide the PE diagnostic work-up (10), which can represent a further possibility in the hands of the caring physician in order to suspect the PE diagnosis and optimizing the CTPA use. In summary, in our study, it was not possible to identify any item that may be considered useful in the clinical practice to improve the prediction rule for PE. Considering that a reliable guidance is urgently needed to limit the CTPA use to the most likely cases, we believe further studies should investigate the two latter speculations.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article has undergone external peer review.

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-545/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-545/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Kunutsor SK, Laukkanen JA. Incidence of venous and arterial thromboembolic complications in COVID-19: A systematic review and meta-analysis. Thromb Res 2020;196:27-30.
2. Shi L, Xu J, Duan G, et al. The pooled prevalence of pulmonary embolism in patients with COVID-19. Intensive Care Med 2020;46:2089-91.
3. Suh YJ, Hong H, Ohana M, et al. Pulmonary Embolism and Deep Vein Thrombosis in COVID-19: A Systematic Review and Meta-Analysis. Radiology 2021;298:E70-80.
4. Cui LY, Cheng WW, Mou ZW, et al. Risk factors for pulmonary embolism in patients with COVID-19: a systemic review and meta-analysis. Int J Infect Dis 2021;111:154-63.
5. Cai H. Sex difference and smoking predisposition in patients with COVID-19. Lancet Respir Med 2020;8:e20.
6. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA 2020;323:1574-81.
7. Lee AY, Levine MN, Baker RI, et al. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. N Engl J Med 2003;349:146-53.
8. Silva BV, Jorge C, Plácido R, et al. Pulmonary embolism and COVID-19: A comparative analysis of different diagnostic models performance. Am J Emerg Med 2021;50:526-31.
9. Volpicelli G, Lamorte A, Villén T. What's new in lung ultrasound during the COVID-19 pandemic. Intensive Care Med 2020;46:1445-8.
10. Nazerian P, Vanni S, Volpicelli G, et al. Accuracy of point-of-care multiorgan ultrasonography for the diagnosis of pulmonary embolism. Chest 2014;145:950-7.

Cite this article as: Fraccalini T, Maggiani GSG, Senkeev R, Cardinale L, Volpicelli G. Characteristics and predictors of pulmonary embolism in patients admitted for COVID-19 with respiratory failure. J Thorac Dis 2022;14(8):3098-3100. doi: 10.21037/jtd-22-545