

Peer Review File

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Reviewer A

Comment 1: Table one must state the number of patients in each group, also in table one units are missing for each variable.

Reply 2: Added units for dimer and creatinine. For the dichotomous variables, there already is the numbers of the patients for each group, plus in the description of the table is stated “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**)”.

Comment 2: Did you analyze the negative predictive value of d-dimer? Usually it is useful for discarding PE when values are low.

Reply 2: We did not. If we consider a D-dimer < 400 ng/ML as the negative threshold, like in our Hospital, only 2 subjects had negative dimer values. Hence, it was not calculated.

Reviewer B

Comment 1: From lines 57- 83 the authors present results and mix these up with discussing these. This is not properly formatted and unclear. Please first present your results and then following a new line in the letter discuss these results.

Please add to the paper a statistical analysis part.

Please add a conclusion to the letter and shorten your discussion

Reply 1: we formatted the letter as suggested; we added a statistical part (line 70-76) and a conclusion (line 110-114).

Comment 2: your finding on wells and PE is a major and novel finding, please stress this more and elaborate.

Reply 2: Sadly this is not a novel finding. As we stated in the letter with appropriate reference this is already been demonstrated in the literature: “Traditional risk scores normally used to predict venous thromboembolism have demonstrated strong limitations in the context of COVID-19.”

[Reference 8. Pulmonary embolism and COVID-19: A comparative analysis of different diagnostic models performance. Am J Emerg Med 2021;50:526-31. 132 <https://doi.org/10.1016/j.ajem.2021.09.004>. As per authors: “neither Wells and Geneva scores nor the YEARS or PEGeD algorithms are reliable predictors of PE in COVID-19 patients admitted to the ED.”]. That is why we did not stress further on that subject.”]

Comment 3: Would a chi square analysis make sense.

Reply 3: in our study, the Chi-square value between positive Wells score for PE+ and PE- was not calculated because only 5 subjects out of 130 had a Wells score > 4 (suggestive of PE in the two-level score) and only 2 subjects had a Wells score of 6 (likely for PE in the three-level score). This numerosity is insufficient both for evaluation with Chi-square test and for evaluation with Fisher’s variant test due to low numerosity.

We also formatted the letter taking into account the minor issues presented.

Reviewer C

Comment 1: I do believe that the next step should be to use big data in order to develop an algorithm allowing prediction of PE in COVID-19 patients.

Reply 1: We do agree with the reviewer that an algorithm is needed. As we stated in the last paragraph further studies are needed.

Comment 2: Furthermore, I do not agree with the conclusion of the authors, due to the high incidence of PE in this population, unless an efficient algorithm is developed to predict/detect PE in this population; CTPA to eliminate PE should be systematic at the admission of COVID-19 patient with respiratory failure.

Reply 2: We respectfully disagree with the Reviewer. We strongly believe that evaluating the clinical picture along with hemato-chemical data and the application of a systematic multiorgan ultrasound is of paramount importance in trying to avoid unnecessary and harmful exposition to radiation and i.v. contrast and limit costs, if possible.

Reviewer D

Comment 1: Data should also be presented in bar graph for better understand.

Reply 1: we were allowed only one table as per the guidelines for authors of the Journal.

Comment 2: Line 79 “we found that no significant difference in D dimer levels in between PE(+) and PE (-) patients”. However, table showed there is a significant difference in the D dimer level.

Reply 2: we confirm that no statistically significant difference was observed with regard to d-Dimer. In the table presented the p value is 0.83 consistent with our previous statement.

Comment 3: As per the title it is not clear what are the predictors of PE. It should be clearly elaborated.

Reply 3: We stated in line 110-112 that “In our study it was not possible to identify any item that may be considered useful in practice to improve the prediction rule for PE”.

We elaborate our speculation in line 103-110: “our orientation in the light of the data obtained is that a sudden deterioration of the respiratory function not justified by the extension of the pulmonary damage may indicate the probability of PE complicating COVID-19 pneumonia. Thus, it may become of the utmost importance a systematic comparison between the extension of the interstitial pneumonia, evaluated by bedside lung ultrasound, and the severity of respiratory failure. [Volpicelli G, Lamorte A, Villén T. What's new in lung ultrasound during the COVID-19 pandemic. *Intensive Care Med* 2020;46:1445-8. <https://doi.org/10.1007/s00134-020-06048-9>].

Reviewer E

Comment 1: Can the authors comment on prophylactic anticoagulation and treatment protocols followed at the time? Based on clinical presentation in ER did patients receive any prophylactic anticoagulation treatments.

Reply 1: the patients in our study were free of any anticoagulant medication as stated in line 58-59 “Patients who for any pathology were already taking prophylactic or therapeutic anticoagulant medications, were excluded”.

Comment 2: line 64- Can authors add the conditions mentioned in brackets to help readers which other high-risk diseases are being referred.

Reply 2: modified as suggested.

Comment 3: One of the limitations of the study is sample size, can authors add it as a limitation of this study.

Reply 3: added as a limitation as suggested along with the single center nature of the study (line 102-103).

Comment 4: in table 1, looking a D-dimer numbers wanted the authors to check if the numbers stated are correct. In PE group, the values are 8952 +/- 16300 vs 2661 +/- 6381.

Reply 4: D-dimer values in our study start from a minimum of 312 ng/mL and reach an extreme maximum of 68291. This dispersion is responsible for the high variance of the data and the very high mean value.