

Peer Review File

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Reviewer A

Comment 1: The ROC curve should probably be shown.

Reply 1: We added the ROC curve (Figure 2).

Changes in the text: We added the ROC curve (Figure 2), shown at page 13. We also added a sentence to the results section in the main text that refers to Figure 2 (page 8, line number 5: 'The ROC curve is shown in Figure 2.'). In the list of abbreviations (page 3, line number 30) and in the main text under the subheading 'Statistical analysis' (page 7, line number 14) we added the abbreviation 'ROC'.

Comment 2: In the multivariable logistic regression analysis, the OR for D-Dimer is very close to 1, suggesting that D-Dimer may not be a very good predictor of PE in this patient population.

Reply 2: The odds ratio is close to 1, but it is an odds ratio for every increase of 100 ng/ml in D-dimer level. Given the huge range of D-dimer levels in our population (150 – 8683 ng/ml), the predicted probability of PTE can vary tremendously based on the D-dimer level alone. For example, the probability of PTE with a D-dimer level of 750 ng/ml is 5.3%, while the probability of PTE is 30% with a D-dimer level of 5000 ng/ml and 82.5% with a D-dimer level of 10000 ng/ml. The D-dimer level is the best predictor we found in our study and it is statistically significant.

Changes in the text: We added the following sentences to the discussion section. Page 9, line numbers 1-4: 'An odds ratio of 1.05 for every increase of 100 ng/ml in D-dimer level might not seem much, but given the huge range of possible D-dimer levels, it can be considered highly relevant. The D-dimer level is the best predictor for PTE in our study and it is statistically significant.'

Comment 3: Consider including clinical features such as presence of tachycardia or hypoxia as a covariate in the logistic regression if such information is available.

Reply 3: Unfortunately, information on clinical measurements such as tachycardia or hypoxia is not available for our study. We included the information as described in Table 1. Variables with a relation of $P \leq 0.10$ with the occurrence of PTE and the D-dimer level prior to CTPA were considered as potential confounders and analyzed in the logistic regression analysis. We have included this as a limitation and as a recommendation for future research.

Changes in the text: We have included this as a limitation and as a recommendation for future research. Page 8, line numbers 29-30 and page 9, line number 1: 'Clinical parameters, such as tachycardia and hypoxia, were not analyzed in this study. In future research it may be relevant to investigate the influence and diagnostic value of these parameters as these are common clinical findings in patients with acute PTE.'

Comment 4: Consider also writing a conclusion paragraph at the end.

Reply 4: We have written a conclusion paragraph as advised.

Changes in the text: We have removed the last sentence from the discussion section ('Nevertheless, based on this study, the most optimal D-dimer cut-off value in COVID-19 patients and suspected PTE is 750 ng/ml'). We have written a separate conclusion paragraph. We used the first two sentences of the discussion section. See page 9, line numbers 7-10: 'Conclusion. In our population of patients hospitalized with COVID-19, a D-dimer level <750 ng/ml safely excluded PTE. Compared to the YEARS 500 ng/ml cut-off value, 13% fewer patients are in need of a CTPA, with similar sensitivity.'. Because we used the first two sentences of the discussion section, we have written a slightly different beginning of the discussion section. See page 8, line numbers 9-12: 'This study aimed to determine the optimal D-dimer cut-off value to predict PTE in COVID-19 patients. Based on our population of patients hospitalized with COVID-19, the optimal D-dimer cut-off level was 750 ng/ml. This cut-off value is higher than the widely used YEARS 500 ng/ml cut-off value, resulting in 13% fewer patients in need of a CTPA, with similar sensitivity.'.

Comment 5: COVID-19 it-self has evolved as a disease partly due to a level of population immunity so results from early pandemic may not apply to patients now and that should probably be mentioned as a limitation.

Reply 5: We agree with this comment. We added the above-mentioned limitation to the discussion section.

Changes in the text: We added the above mentioned limitation to the discussion section. See page 8, line numbers 27-29: 'Besides, results from this early pandemic study may not apply to patients nowadays as COVID-19 it-self has evolved as a disease, partly due to a certain degree of population immunity. Future research is required for external validation.'.

Reviewer B

Comment 1: Please add the following reference: Conte G, Cei M, Evangelista I, Colombo A, Vitale J, Mazzone A, Mumoli N. The Meaning of D-Dimer value in Covid-19. Clin Appl Thromb Hemost. 2021 Jan-Dec;27:10760296211017668.

Reply 1: We added the above mentioned reference.

Changes in the text: We added the above mentioned reference to the introduction section to the following sentence: 'Nevertheless, whether conventional cut-off values do apply to COVID-19 patients is unknown.'. See page 6, line numbers 9-10. We added the reference to the reference list (page 10, line numbers 14-15).