

Peer Review File

Article information: <http://dx.doi.org/10.21037/atm-20-5320>

Reviewer comments:

Comment 1: It's a very interesting study with its novelty and promising value regarding clinical practice. The O-A interval can be really helpful for physicians at emergency room regarding triaging people and is easy to calculate. However, the disadvantages of the study include limited sample size, questionable generalizability to other healthcare system in different regions or countries. But I feel it's still worth publishing and further revisions are needed.

Reply 1: Thanks for your critical comments and suggestions. We have revised our manuscript according to your suggestions. However, the page number and line number may change a lot in the revised manuscript with markers.

Comment 2: Page 3, line 50-52, would briefly specify O-A interval subgroups and mention using log-rank test.

Reply 2: We revised in page 3, line 49-53.

Comment 3: Page 3, line 51: would change “mortality during hospital” to “in-hospital mortality”.

Reply 3: We revised in page 3, line 51.

Comment 4: Page 3, line 54: would correct the typo to “severe-to-critical”.

Reply 4: We revised in page 3, line 55.

Comment 5: Page 3, line 56-58: instead of saying “no prognostic role”, would be better

to mention that no association identified.

Reply 5: We revised in page 3, line 57-60.

Comment 6: Page 3, line 60: would change “health-seeking” to “healthcare-seeking”.

Reply 6: We revised in page 4, line 63.

Comment 7: Page 3, line 59-53: the conclusion part in abstract feels a little redundant, can stress that the OA interval might have prognostic value regarding disease progression in mild to moderate form of COVID-19.

Reply 7: We revised in page 4, line 61-67.

Comment 8: Page 5, line 75: would better use severity instead of “prognosis”

Reply 8: We revised in page 5, line 79.

Comment 9: Page 5, line 76: would specify comorbidities associated with disease severity here, including hypertension (Lippi G, Wong J and Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. Pol Arch Intern Med. 2020;130:304-309.), diabetes (Palaiodimos L, Chamorro-Pareja N, Karamanis D, Li W, Zavras PD, Mathias P, Kokkinidis DG. Diabetes is associated with increased risk for in-hospital mortality in patients with COVID-19: a systematic review and meta-analysis comprising 18,506 patients. medRxiv. 2020 Jan 1.)

Reply 9: We revised in page 5, line 80. Also, we added the related references.

Comment 10: Page 5, line 79: “suspected patients” can be changed to “suspected COVID-19 patients”

Reply 10: We revised in page 5, line 88.

Comment 11: Page 5, line 80: “ask medical help” can be changed to either “seek

medical attention” or “present to healthcare facility”

Reply 11: We revised in page 6, line 89.

Comment 12: Page 5-6, line 65-91: can put the explanation of how China coped with COVID-19 crisis in the introduction part with comparison of the healthcare system in UK

Reply 12: We revised in page 5, line 83-88.

Comment 13: Page 6, line 94-102: no exclusion criteria are mentioned

Reply 13: We revised in page 6, line 107-108.

Comment 14: Page 7, line 109-110: would paraphrase from “the worst disease severity” to “the most severe form of the disease”

Reply 14: We revised in page 7, line 118-119.

Comment 15: Page 7, line 113-114: would change from “light” to “mild”, and specify imaging

Reply 15: We revised in page 7, line 122-125.

Comment 16: Page 7, line 117: would specify the oxygen saturation on pulse oximetry or arterial blood gas

Reply 16: We revised in page 7, line 127.

Comment 17: Page 9, line 160: would correct the typo to “severe-to-critical”

Reply 17: We revised in page 10, line 170.

Comment 18: Page 9, line 165: would be better to specify comorbidities and separate them into analysis

Reply 18: Considering the limited sample size of our study, including the comorbidities separately in the regression model will lead to over-fitting. So, we combine these comorbidities and incorporate them into the regression model as one variable, as previous study did (Liang et al. *Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19*. JAMA Intern Med). We revised in page 10, line 176-178.

Comment 19: Page 10, line 169-172: although Thrombin Time (TT) most closely correlated with D-dimer in analysis, it's rarely tested in clinical practice which weakens the external validity of this study and its correlation coefficient is only 0.417

Reply 19: Previous studies have already confirmed the prognostic values of D-dimer; however, we did not include D-dimer in the multivariate regression because of the high missing data rate. Instead, we decided to choose another coagulation parameter to reflect the coagulation status of patients which is of prognostic value. Among these coagulation parameters, TT is selected because of its closest correlation with D-dimer. However, TT is not included in the final multivariate regression model seeing that TT has no prognostic role in the univariate analysis. Besides, in supplementary sensitive analysis, we include D-dimer as a covariate, and further confirm the prognostic role of O-A interval.

Comment 20: Page 11, line 195: would change “health-seeking” to “healthcare-seeking”

Reply 20: We revised in page 11, line 207.

Comment 21: Page 12, line 223-225: would elaborate more on this, in countries or regions with different health system like UK/US where people with mild diseases are encouraged to self-isolate at home, the interval between disease onset and presentation to urgent care or emergency room can be prognostic for progression to severe form of

disease as well for patients with mild to moderate disease, which can help healthcare providers at those situations decide the disposition of the patients.

Reply 21: We revised in page 13, line 237-245.

Comment 22: Page 13, line 242: would correct the typo to “severe-to-critical”

Reply 22: We revised in page 14, line 260.

Comment 23: It would be nice to see a table comparing characteristics of mild-to-moderate patients with short O-A interval with long O-A interval.

Reply 23: We add a table as supplementary file. We revised in page 10, line 170-172.