



PEER-REVIEW REPORT

Name of journal: *World Journal of Critical Care Medicine*

Manuscript NO: 72354

Title: Retrospective analysis of aspirin's role in the severity of COVID-19 pneumonia

Provenance and peer review: Unsolicited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02885211

Position: Peer Reviewer

Academic degree: DO

Professional title: Associate Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: United States

Manuscript submission date: 2021-11-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-19 06:13

Reviewer performed review: 2021-12-01 01:07

Review time: 11 Days and 18 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

See attached General Comments This retrospective study to determine if use of ASA impacts clinical outcome in patients admitted to Covid-19 disease. Outcomes measured were icu admission, mechanical ventilation and mortality. Overall despite small number the paper would provide important evidence to current Covid -19 literature. The paper needs revisions. I applaud the investigators performing this difficult analysis with patients receiving multiple agents which may impact the results The investigators employed univariate analysis and multinomial logistic regression analysis. Their results suggest that ASA does not improve clinical outcomes. However this study suffers due to its small size and the environmental fallacy inherent in all retrospective studies. Furthermore many patients were on more than 1 anticoagulant or antiplatelet agents. In order to make a stronger case for their results the authors should consider: I major revisions: When was ASA started were patients admitted on ASA? Or was it initiated on admission. If so this should be stated. If so consideration for a cox proportional hazards analysis with asa use as a time dependent covariate. Why were not routine labs analyzed or at least markers of inflammation pao2/FIO2 ratio neutrophils/ lymphocyte ratio DDIMER Fibrinogen CRP Ferritin measured can investigators provide? Was heparin either for dvt prophylaxis or systemic anticoagulation used used this should be documented and analyzed? Please consider propensity adjusted or consider propensity matched analysis. How many patients received corticosteroids this clearly should be analyzed Minor many issues with tables The tables need work for univariate categorical variables odds ratio and 95% CI Also in the logistic regression beta should be expressed as odds ratio and lower upper as 95% CI Table 2 needs p values and odds ratios. In all the tables it would make the results



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understood better if Only the group with the risk factor present should be displayed as an N and percentage and the percentage should be expressed as a percentage of the exposure group in way of example (N present/N exposure $\text{asa} \times 100$) ASA (n=38) No ASA (n=87) HTN 32 (86%) 50 (57%) This should be the same for figures for age distribution percentages as it makes data more meaningful and understandable



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Reviewer's code: 06006212

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2021-11-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-02 04:34

Reviewer performed review: 2021-12-02 06:58

Review time: 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you very much for letting me contribute to this scientific study. Many studies showed the association between worse outcomes of COVID-19 and comorbidities, such as hypertension, diabetes, chronic kidney diseases. Patients with those background factors often take daily aspirin. Therefore, evaluating the benefit of aspirin in COVID-19 patients is meaningful. However, this study has several concerns, mainly in the design. My comments are below. 1) In the results section of the abstract, the authors showed the reduced ICU admission of the aspirin intake group without statistically significant difference. However, the sentence states otherwise. 2) HTN, DM, and HLD should be spelled out. 3) Introduction and Methods are not consistent. If the purpose of the study was to elucidate the relationship between the daily aspirin intake and COVID-19 outcomes, the study should be designed more specifically, rather than putting lots of possible variables into SPSS. 4) Over-explanation of meanings of basic statistical values is not necessary. 5) Table 1 and Figure 1, and Table 2 and Figure 2 are redundant. Overall, I understand that the study aims to evaluate the effect of daily aspirin use on COVID-19 outcomes. In that sense, a direct comparison between the aspirin and non-aspirin groups will be more applicable to clinical practice than multivariate logistic regression. Propensity score matching or inverse propensity weighting will be helpful to add some more value to what the authors are doing.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2021-11-18

Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2022-01-12 06:38

Reviewer performed review: 2022-01-12 07:23

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Thank you very much for letting me contribute to this study. The authors investigated the preventive effect of daily aspirin intake against COVID-19 progression to ICU. The revised manuscript is clearly more sophisticated and impactful. I still have some questions for the authors. 1) In the manuscript, 38 patients were taking daily aspirin before hospitalization. However, according to the propensity analysis they performed following several suggestions from reviewers and editors, there were 47 patients on the aspirin-taking arm. Did the authors allow duplication when they performed propensity analysis? 2) Propensity matching is not quite suitable in a study with small sample size, as the authors replied. However, did they try the inverse weighting technique as well? That could be the solution to assimilate the baseline characteristics in the two groups and enhance the generalizability of this study. I still do not understand why the variables the authors included in the logistic regression are supposed to improve the prediction performance of the statistical model.



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Author's Country/Territory: United States

Manuscript submission date: 2021-11-18

Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2022-01-13 03:14

Reviewer performed review: 2022-01-13 03:22

Review time: 1 Hour

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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SPECIFIC COMMENTS TO AUTHORS

It is acceptable for publication in my opinion propensty score matching or adjustment can be added as a supplementary file however i will leave to discretion of science editor
Cheers!