

Response to Reviewer Comments for manuscript

Dear Dr. Lian-Sheng Ma:

Thank you for your letter and for the reviewers' comments on our manuscript entitled "Epidemiological and Clinical Characteristics of 65 Hospitalized Patients With COVID-19 in Liaoning, China" (ID: 59586). These comments were very helpful. We have revised the manuscript to address these points, which we believe have significantly improved the quality of this work. The changes to the manuscript are highlighted by using the track changes mode in MS Word. The main corrections in the paper and the point-by-point responses are listed below each comment.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors reported their experience on the epidemiological and clinical characteristics of 65 COVID-19 patients hospitalized in Liaoning (China). Two groups of patients were retrospectively evaluated. The topic is of great interest to many researchers and clinicians. The paper is well written and easy to follow. However, some concerns should be addressed by the authors.

Response: Thank you for your encouraging and constructive comments on our paper. We have revised our paper according to your suggestions.

Comment 1: - ABSTRACT, METHODS: the authors should clearly stated that patients were divided into two groups.

Response: Thanks for your good suggestion. We have added the description of groups in the METHODS section.

Comment 2: - The follow-up is quite short. I was wondering whether all patients, included the severe ones, were discharged at the end of the follow-up- Could the authors comment on that?

Response: We appreciate your valuable comment. We regret for the short-term follow up, and the main reason for the short-term follow up was that many patients outside Liaoning Province were lost to follow-up after being discharged. All patients have been discharged when deemed clinically recovered, including afebrile for at least 3 days, resolution of symptoms, radiologic improvement, and two negative results of consecutive nucleic acid tests taken at least 24 h apart.

Comment 3: - How many of these patients were admitted in the ICU? - Did any of these patients die during the follow-up period?

Response: Thank you for your comment. Among these patients, 8 patients were admitted in the ICU. These patients are still alive during the follow-up period.

Comment 4: - The distinction between severe and non-severe patients were based on the presence of one of the followings: shortness of breath, respiratory rate >30 breaths/minute, oxygen saturation $\leq 93\%$ at rest, and oxygenation index ≤ 300 mm Hg. Is that correct? If so, a patient having only shortness of breath with all other parameters within the normal range was considered as a severe COVID-19 case. I think it's quite questionable. Could the authors comment on that? In my opinion a severity score based on the lung involvement on the chest CT-scan should be included and considered for defining a COVID-19 patient as a severe patient.

Response: Thank you for your careful reading. We are very sorry for the confusion caused by our punctuation mistakes in this passage. We have modified the punctuation in this passage as follows: “(1) shortness of breath, respiratory rate >30 breaths/minute; (2) oxygen saturation level using a pulse oximeter $\leq 93\%$ at rest; and (3) oxygenation index (partial pressure of artery oxygen/fraction of inspired oxygen, $\text{PaO}_2/\text{FiO}_2$) ≤ 300 mm Hg;”

We appreciate your constructive comment and agree with your suggestion. When this manuscript was initially submitted, the diagnostic criteria for severe Covid-19 in adults refer to the New Coronavirus Pneumonia Diagnosis and Treatment Protocol (Trial Version 7) (Protocol TV7) released by China’s National Health Commission. As you pointed out, Protocol TV7 mentioned that patients with pulmonary imaging showing obvious progression of the lesion within 24-48 hours $> 50\%$ should be managed as severe pneumonia. We have also considered the changes in chest CT during the diagnosis and treatment of severe COVID-19. Indeed, in the next Trial Version 8 of the protocol (Protocol TV8), lung imaging changes have been officially included in the diagnostic criteria for severe Covid-19 in adults as “Article (4)”. Based on your suggestion and Protocol TV8, we thus added “Article (4)” as the diagnostic criteria for severe Covid-19 in adults in the manuscript as follows: “(4) Progressively worsening clinical symptoms, pulmonary imaging showing significant progression of the lesion within 24-48 hours $> 50\%$.”

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: 1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes 3 Key words. Do the key words reflect the focus of the manuscript? Yes

Response: We appreciate the careful reading of our manuscript and valuable suggestions. We have carefully considered your comments and have revised the manuscript accordingly.

Comment 1: 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Background is limited and very general, and does not highlight the aim of the manuscript

Response: Thanks for your valuable suggestion. We have revised the background to highlight the aim of the manuscript.

Comment 2: 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? There is no real method involved, only basic descriptive statistics

Response: Thanks for your comment. This is a descriptive study, and we have described the data design, data collection, data analysis, definitions, and statistical analysis in the Methods section.

Comment 3: 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? This is the major issue: there is no clear goal associated to the study, only a descriptive statistical analysis of the involved variables. Coupling this observation with the extremely small sample size, and the fact that such samples are hardly representative of the overall distribution, the novel contribution to the field provided by the manuscript is extremely limited, being just one of the several similar studies appearing recently in the literature. I would recommend strengthening the aim of the study, adding more comparison with similar efforts and, if possible, widening the sample dataset.

Response: Special thanks to you for your good comments. We regret the small sample size in this paper. It is inconvenient for us to collect more cases to increase the sample size because the principle investigator of this study has recently been transferred to another post in another hospital. We have highlighted the aim of the study and adding more comparison in the revised manuscript.

Comment 4: 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? See Q6 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? The tables and the only figure are reasonable. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? No real biostatistics involved, only descriptive statistics. 10 Units. Does the manuscript meet the requirements of use of SI units? Yes 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Reference list is heavily biased towards Chinese contributions to the field: I would strongly recommend to include a number of recent contributions appeared in top journal (Nature, Science, etc) providing a more complete landscape and SOTA of the current knowledge.

Response: Thank you for your good comment. According to your suggesting, we

have added more references regarding COVID-19 studies from Europe and North America including some recent contributions in the top journal (such as Nature, N Engl J Med, Science, Lancet, JAMA, Science) to providing a more complete understanding of the current knowledge.

Comment 5: 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Yes 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? N/A 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes.

Response: Thank you for your reminder. We have prepared this manuscript according to manuscript type and the appropriate categories “(4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study”.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Comment 1: Specific Comments to Authors: I read the manuscript with great interest and appreciate the authors' work. The paper is important, but it lacks a proper presentation throughout. The study design is unclear to me. Observational studies are crucial in COVID-19; however, they have to be categorized correctly according to its type. I could not agree with the following statement in the manuscript 'A total of 65 adult patients with confirmed COVID-19 who were diagnosed and treated by the principle investigator were enrolled.....'. It is a good practice to credit everyone involved in the treatment of COVID-19 patients like laboratory technicians, nurses, and paramedics. As a clinician, we seldom take entire credit of treating patients ourselves.

Response: Thank you for your good comments. We have strengthened the aim of this study. We hope that the analysis of the epidemiological, clinical, and the main therapeutic strategy of hospitalized COVID-19 patients in Liaoning Province can help clinicians to identify critically ill patients and prevent poor outcomes. We have redefined the level of COVID-19 severity in the manuscript.

We sincerely apologize for not completely addressing the statement mentioned

above and have made some corresponding revisions in METHODS section. In the process of clinical diagnosis and treatment of COVID-19 patients, many medical staff including laboratory technicians, nurses, paramedics, residents, and attending doctors have participated and worked hard. And we very much agree with you. As a clinician, we trust and thank them for their hard work because we work together as a group of medical staff but not only doctors to serve patients. While as a member of the Liaoning Province COVID-19 medical treatment expert team, the principle investigator of our study participated in the clinical guidance on diagnosis and treatment of COVID-19 patients in current study.

Comment 2: The abstract needs shortening.

Response: Thank you for your suggestion. According to Guidelines for Manuscript Preparation and Submission, in abstract section, METHODS is required to be no less than 80 words, RESULTS is no less than 120 words, and ABSTRACT is no less than 350 words. And thus, we appropriately modified the Abstract section.

Comment 3: Also, the introduction needs rewriting. In this section, please include an exhaustive literature review about COVID-19 from the Chinese perspective.

Response: We are grateful for your advice. We have modified the introduction section accordingly.

Comment 4: The methods, results and discussion, and conclusion section need exhaustive revision.

Response: We appreciate your comment, and have exhaustively revised the manuscript.

Comment 5: I shared additional comments in the attached file. Overall, there is potential in your data to generate novel evidence, but it needs to be properly formatted, presented, and scientifically communicated. I will be happy to review it again if the authors revise the manuscript exhaustively. Thanks.

Response: We appreciate the careful reading of our manuscript and valuable suggestions. We have carefully considered your comments and have revised the manuscript accordingly.

Comments in attached file:

Comment 6 (P2): Abstract needs to be shortened.

Response: Please see Response 2 to Comment 2, which is same as this Comment.

Comment 7 (P3): “are essential” are deleted.

Response: Thanks for your comment. We have removed the duplicate content.

Comment 8 (P3): In Abstract-Aim section: improve the preceding para to rationalize the aim better.

Response: Thanks for your good suggestion. We have modified the

Abstract-Background section to rationalize the aim better.

Comment 9 (P3): In Abstract-Methods section: not clear. rewriting advised.

Response: Thanks for your comment. We have revised the Abstract-Methods section.

Comment 10 (P3): In Abstract-Methods section: interesting to know that all 65 individuals diagnosed and treated by one individual. I think you can clarify this statement regarding any role of other professionals. Also, this much of details are generally not appreciated in the abstract.

Response: We are very sorry for not completely addressing the statement mentioned above. We have removed this unclear description, and made a corresponding revision in METHODS-Study design and subjects section. Many medical staff including laboratory technicians, nurses, paramedics, residents, and attending doctors have been involved the clinical diagnosis and treatment of COVID-19 patients. While the principle investigator of our study, as a member of the Liaoning Province COVID-19 medical treatment expert team, participated in the clinical guidance on diagnosis and treatment of COVID-19 patients in current study.

Comment 11 (P3): In Abstract-Methods section: sequence of events not clear. which one was done first?

Response: We appreciate your comment, and have rearranged these sentences following chronological order.

Comment 12 (P4): In Introduction: Too brief and not with a extensive literature review to rationalize your aims. Since this is a China-based study it needs a COVID-19 literature review from China as background information.

Response: Thank you for your valuable suggestion. We have revised the Introduction section accordingly.

Comment 13 (P5): In Introduction: why are you sharing old data? the pandemic is ongoing. I would like to see more recent data.

Response: Thank you for your reminder. We have updated these data in the manuscript.

Comment 14 (P5): In Introduction: your aims are exhaustive; however, it is not backed by a good rational. For each of your aims, in the preceding paragraphs introduce them with respect to the contemporary COVID-19 literature.

Response: We appreciate your advice. We have strengthened the aim of the study, and modified the background to back this aim of the study according to your suggestion.

Comment 15 (P6): In Methods-Study design and subjects: did you have an exclusion criteria?

Response: Thanks for your comment. We have excluded eight patients due to missing medical records.

Comment 16 (P6): In Methods-Study design and subjects: what is your study design actually?

Response: Thank you for your good comment. We regret the omission of the description of groups, and have added the corresponding description in the METHODS section.

Comment 17 (P6): In Methods-Study design and subjects: was the study done in this hospital? please clarify.

Response: Thank you for your comment. Initially, 3 patients with COVID-19 were diagnosed and treated in Shengjing hospital, and later they are transferred to the Sixth People's Hospital of Shenyang. Shengjing hospital has dispatched doctors and experts to the Sixth People's Hospital of Shenyang to diagnose and treat patients with COVID-19. The principle investigator of our study participated in the clinical guidance on these patients with COVID-19, as a member of the Liaoning Province COVID-19 medical treatment expert team. Collection of some raw data, all successive raw data processing and data analysis were all carried out in Shengjing hospital.

Comment 18 (P6): In Statistical analysis: how was this imputation done?

Response: Thanks for your comment. We replace the missing value with a mean if the variable follows a normally distribution, and with a median for a non-normal distributed variable.

Comment 19 (P6): In Statistical analysis: are you accepting statistical significance at 0.05?

Response: We are sorry for this mistake, and have modified it to “<0.05”.

Comment 20 (P6): In Results-Epidemiology and clinical characteristics: I understand why you mention the Wuhan origin, but that should be properly stated in the introduction.

Response: We appreciate your comment. We have modified the introduction accordingly.

Comment 21 (P9): In Discussion: how? not clear.

Response: We apologize for not explaining this issue clearly and have revised this text to be clearer.

Comment 22 (P21): In Table 1: include proper footnotes.

Response: Thank you for your comment. We have added proper footnotes in Table 1.

Comment 23 (P22): In Table 1: bpm?

Response: We are sorry for causing your confusion about this word. We have added footnotes to “bpm”.

4 LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

Response: Thank you for your comment. After the manuscript was revised, we have asked the English language editor to correct English errors and polish the language in the manuscript once again.

5 EDITORIAL OFFICE COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor: 1 Scientific quality: The manuscript describes a retrospective study of the clinical features of COVID-19 cases in Liaoning. The topic is within the scope of the WJCC. (1) Classification: Grade D, Grade B and Grade C; (2) Summary of the Peer-Review Report: The topic is of great interest to many researchers and clinicians. The paper is well written and easy to follow. However, some concerns should be addressed by the authors. Overall, there is potential in your data to generate novel evidence, but it needs to be properly formatted, presented, and scientifically communicated. The questions raised by the reviewers should be answered; and (3) Format: There are 4 tables and 1 figure. A total of 30 references are cited, including 29 references published in the 2020. There are no self-citations. 2 Language evaluation: Classification: Grade A, Grade A and Grade C. A language editing certificate issued by Editage was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, and the Institutional Review Board Approval Form. Written informed consent was waived. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by 345 Talent Project of Shengjing Hospital; and Scientific Research Projects Related to Prevention and Control of Coronavirus Disease 2019 (COVID-19) of China Medical University. The topic has not previously been published in the WJCC. The corresponding author has published 2 articles in the BPG. 5 Issues raised: (1) I found the language classification was grade C. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>; (2) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (3) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or

arrows or text portions can be reprocessed by the editor; and (4) I found the authors did not write the article highlight section. Please write the article highlights section at the end of the main text. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.

Response: Thank you for your careful reading. We have revised the manuscript according to the Editorial Office's comments and suggestions, and provided the required Forms and materials in the attachment.

(2) Editorial office director: I have checked the comments written by the science editor.

(3) Company editor-in-chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

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Best regards,

Lian-Sheng Ma, Science Editor, Company Editor-in-Chief, Editorial Office

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