

A review of the presentation and outcome of left ventricular thrombus in COVID-19 infection

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Review timeline:

Received: 20 June, 2021
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Editorial reponse: 31 August, 2021
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1st Editorial decision
23-Jul-2021

Ref.: Ms. No. JCTRes-D-21-00107

A Review of the Presentation and Outcome of Left Ventricular Thrombus in COVID-19 Infection

Journal of Clinical and Translational Research

Dear Dr Philip,

Reviewers have now commented on your paper. The reviewer recommended a reject on the basis of the low number of case studies sampled and the lacking causality between SARS-CoV-2 and LVT. However, the editorial board would like to provide you with the opportunity to address the reviewer's comments to the maximum extent, focusing on the following points:

- please include any new studies that may have appeared in the interim to increase sample size;

- please evaluate the quality of each included study using a Downs & Black analysis scheme. The Downs & Black score can be inserted into Table 1. Also, please prepare a supplementary document in which the evaluation criteria are listed;

- please make sure the manuscript conforms to the PRISMA guidelines as much as possible (http://prisma-statement.org/documents/PRISMA_2020_checklist.pdf)

If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Aug 22, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The authors aimed to review all the available reports concentrating on LV thrombosis in COVID-19 patients. It is well-known that thrombotic complications are common manifestations of COVID-19. The authors gave a very nice review about LV thrombosis but its relation to COVID-19 is only an assumption based on a limited number of case reports which could not prove a causal relation. We can certainly say that the thrombotic milieu created by the infection increase the probability of thrombus formation in LV, but it is possible and even more plausible that LVT is created by the LV dysfunction. The validity of each of these hypotheses need observation with much more sample size.

Here are my other concerns:

1. The introduction is somehow irrelevant to main research question. I think they should discuss on the thrombogenic properties of COVID-19 and the potential explanation for that (as the discussion).
 2. Keywords and databases used for the systemic search are limited. Medline is a subset of PubMed. Why not Embase or other databases which are very routine in a systemic search. At least different keywords for COVID-19 (e.g. SARS- CoV-2) should be selected for the review.
 3. No explanation regarding the quality assessment of the chosen studies.
 4. Why reports in which COVID-19 were not definitely proven (RT-PCR) were selected?
 5. "four had preexisting dilated cardiomyopathy or heart failure". Vague
 6. "eight had new-onset heart failure(four secondary to myocarditis, two due to myocardial infarction) and two had probable takotsubo cardiomyopathy". It is essential to explain how these diagnoses were made? It can be presented in a supplement table.
 7. Lots of information in results. Might better to be presented in different tables or figures.
 8. How pulmonary embolism were related to LV thrombosis? Any sign of PFO and paradoxical emboli?
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Authors' response

Reviewer #1: The authors aimed to review all the available reports concentrating on LV thrombosis in COVID-19 patients. It is well-known that thrombotic complications are common manifestations of COVID-19. The authors gave a very nice review about LV thrombosis but its relation to COVID-19 is only an assumption based on a limited number of case reports which could not prove a causal relation. We can certainly say that the thrombotic milieu created by the infection increase the probability of thrombus formation in LV, but it is possible and even more plausible that LVT is created by the LV dysfunction. The validity of each of these hypotheses need observation with much more sample size.

Here are my other concerns:

1. The introduction is somehow irrelevant to main research question. I think they should discuss on the thrombogenic properties of COVID-19 and the potential explanation for that (as the discussion).

Response

Thank you for your comments, the necessary corrections have been made.

2. Keywords and databases used for the systemic search are limited. Medline is a subset of PubMed. Why not Embase or other databases which are very routine in a systemic search. At least different keywords for COVID-19 (e.g. SARS- CoV-2) should be selected for the review.

Response

Thank you for your comments, the necessary corrections have been made. Articles have been added and updated till august 16th 2021.

3. No explanation regarding the quality assessment of the chosen studies.

Response

The chosen studies were case series, mini reviews and case reports.

4. Why reports in which COVID-19 were not definitely proven (RT-PCR) were selected?

Response

There were 20 patients for whom the modality of diagnosis of COVID has not been specified as PCR vs Rapid antigen tests. We have excluded 5 case reports where diagnosis of COVID could not be made by both microbiology or serological means. Patients with diagnosis of COVID on CT, and no other alternative diagnosis have been included since the sensitivity of CT has been reported to be greater than RT-PCR(98 % vs 71%)-Yicheng Fang et al

5. "four had pre-existing dilated cardiomyopathy or heart failure". Vague

Response

Thank you for the comment. The sentence has been modified. Elevated levels of BNP can be seen in both dilated cardiomyopathy and heart failure due to other causes. Since all patients in the review with DCM, had reduced EF, the broader term heart failure has been used.

6. "eight had new-onset heart failure(four secondary to myocarditis, two due to myocardial infarction) and two had probable takotsubo cardiomyopathy". It is essential to explain how these diagnoses were made? It can be presented in a supplement table.

7. Lots of information in results. Might better to be presented in different tables or figures.

Response

Thank you for the comment. Corrections have been made and a supplementary table added

8. How pulmonary embolism were related to LV thrombosis? Any sign of PFO and paradoxical emboli?

Response

Thank you for these comments. No intracardiac defect has been recorded in 2 patients and no mention regarding patent foramen ovale has been made in the others. Since 8 of the 11 patients had presence of either right ventricular thrombus or peripheral venous and arterial embolisms, it can be assumed that the pulmonary embolisms were related to the state of hypercoagulability rather than intracardiac defects.

Editor comments

Please include any new studies that may have appeared in the interim to increase sample size;

- please evaluate the quality of each included study using a Downs & Black analysis scheme. The Downs & Black score can be inserted into Table 1.
Also, please prepare a supplementary document in which the evaluation criteria are listed.

- please make sure the manuscript conforms to the PRISMA guidelines as much as possible (http://prisma-statement.org/documents/PRISMA_2020_checklist.pdf)

Response

Thank you for these comments. The article has included all relevant articles till 16th august 2021 and has been modified to conform to the PRISMA guidelines. The downs and black score could not be used in our review as the data pooled has been case series and case reports.

2nd Editorial decision
31-Aug-2021

Ref.: Ms. No. JCTRes-D-21-00107R1
A Review of the Presentation and Outcome of Left Ventricular Thrombus in COVID-19 Infection
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Sep 30, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Thank you for submitting a revised draft to JCTR.

The editorial board has perused over your manuscript and we can now proceed to publication because the peer review process has been completed.

However, I need you to insert into the manuscript text related to the essence of what the reviewer postulated previously, namely that the association between LV thrombosis and COVID-19 is not grounds for considering the latter as a cause of the former (until this has been unequivocally proven in a larger, focused study). As the reviewer postulated, LV dysfunction could be the primary cause in a hypercoagulative context. This can be fitted into the limitations section.

Moreover, as is stipulated in the author guidelines (<https://www.jctres.com/en/author-guidelines/>), the language must be up to par with academic standards. The manuscript is still replete with grammar/spelling/syntax errors that we kindly ask you to properly address.

Examples:

- Abstract: "Though the severe acute respiratory syndrome virus (SARS-CoV-2) is primarily a respiratory pathogen, the association between coronavirus disease (COVID-19) and cardiovascular complications is well documented" - the word "though" implies something to the contrary to the predicate should follow, which is not the case. This is a typical syntax error made by non-native speakers. Moreover, in the following sentence, "this" refers to something in the preceding sentence that allegedly constitutes a concern, but it is hard to distill what "this" is from that sentence.

- Abstract: ...incidence of left ventricular (LV) thrombus... should read left ventricular (LV) thrombosis. Not sure why you did not abbreviate it to LVT (left ventricular thrombosis).

- Abstract: ...during the acute phase of illness... should read "during the acute phase of the illness".

- Abstract: "Also, it was identified in 6 patients with mild symptoms during the acute phase and had tested positive only for COVID-19 antibodies during the time of LV thrombus formation" should read "LVT was identified...acute phase who had tested..."

- Abstract: do not begin a sentence with a number written in numerals.

- "medical comorbidities" seems a pleonasm to me. Are there any non-medical comorbidities? (answer is NO - definition: the simultaneous presence of two or more diseases or medical conditions in a patient).

Our advice is to do one of the following three things:

- 1) engage a native speaker to meticulously go through the text and eliminate all errors and preferably streamline the language;
- 2) contract a third-party proofreading service, although in our experience this has resulted in suboptimal quality with several authors already;
- 3) make use of the paid editing service offered by JCTR, which comes at a cost to cover the

editor's expenses but the deep dives performed to date has in all cases resulted in acceptance of the quality and subsequently the paper.

In case of the third option please contact the editor (m.heger@jctres.com).

I kindly ask you not to underestimate this final task. Proper language use is not only a good selling point for your work but also represents a quality tag for the journal and hence the whole organization and people involved in that organization (authors, reviewers, editors, publisher). We therefore take this part very seriously.

We are looking forward to your revision.

Kindest regards,

Michal Heger
Editor

3rd Editorial decision
30-Sep-2021

Ref.: Ms. No. JCTRes-D-21-00107R2
A Review of the Presentation and Outcome of Left Ventricular Thrombus in COVID-19 Infection
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: