Journal of Clinical and Translational Research
Peer review process file 06.202005.003

Predicting thromboembolic complications in COVID-19 ICU patients using machine learning

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Handling editor:
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Review timeline:

Received: 30 September, 2020
Editorial decision: 01 October, 2020
Revision received: 01 October, 2020
Editorial decision: 01 October, 2020
Published online: 14 October, 2020

1st Editorial decision
01-oct-2020

Ref.: Ms. No. JCTRes-D-20-00107
Predicting thromboembolic complications in COVID-19 ICU patients using Machine Learning
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 Oct 31, 2020.

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 manuscript is well written and sound. Although the number of individuals included in the study is limited, the study is of sufficient interest to support publication. The application of machine learning is a nice feature, and a promising method for future analyses of data from Covid-19 patients.

Reviewer #2: I have attached my comments to this email.

Please follow these strictly so that publication of the paper can be expedited.

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

Authors response

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Re: revision JCTRes-D-20-00107 Rotterdam, 01 October 2020

Dear Dr. Heger,

Thank you for giving us an opportunity to resubmit a revised version of our manuscript entitled "Predicting thromboembolic complications in COVID-19 ICU patients using machine learning."

We have addressed all comments of the reviewers using the track changes function in Word (attached as supplementary material not for publication). Moreover, every modification or rebuttal of the reviewer's comments is detailed per comment below in red italics.

We are grateful for the useful comments of the reviewers, as a result of which the paper has been considerably improved.

On behalf of the authors, kindest regards,

Davy van de Sande

REVIEWER COMMENTS

We are grateful for your commentary and suggestions, which we have addressed to the fullest extent as indicated below for every one of your comments. The language and terminology as well as the graphical presentation of the figures have been further polished in accordance with your suggestions.

Reviewer #1: The manuscript is well written and sound. Although the number of individuals included in the study is limited, the study is of sufficient interest to support publication. The application of machine learning is a nice feature, and a promising method for future analyses of data from Covid-19 patients.

Reviewer #2: I have attached my comments to this email.

List of abbreviations:

Include all used abbreviations, including the clinical chemistry in the tables.

We have applied the appropriate adjustments and extended the list of abbreviations with:

- *Polymerase chain reaction (PCR)*
- *Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD)*
- *Body mass index (BMI)*
- *C-reactive protein (CRP)*
- *Interleukin-2 receptor (IL-2R)*
- *Interleukin-6 (IL-6)*
- *High-sensitive troponin t (hsTnT)*
- *N-terminal prohormone of brain natriuretic peptide (NT-proBNP)*
- *Alanine aminotransferase (ALAT)*
- *Krebs von den Lungen-6 (KL-6)*
- *Neutrophil gelatinase-associated lipocalin (NGAL)*
- *Procalcitonin (PCT)*
- *Prothrombin time international normalized ratio (PR INR)*
- *Soluble urokinase-type plasminogen activator receptor (suPAR)*
- *Activated partial thromboplastin time (APTT)*
- *Interquartile range (IQR)*

2.5 Statistical analysis

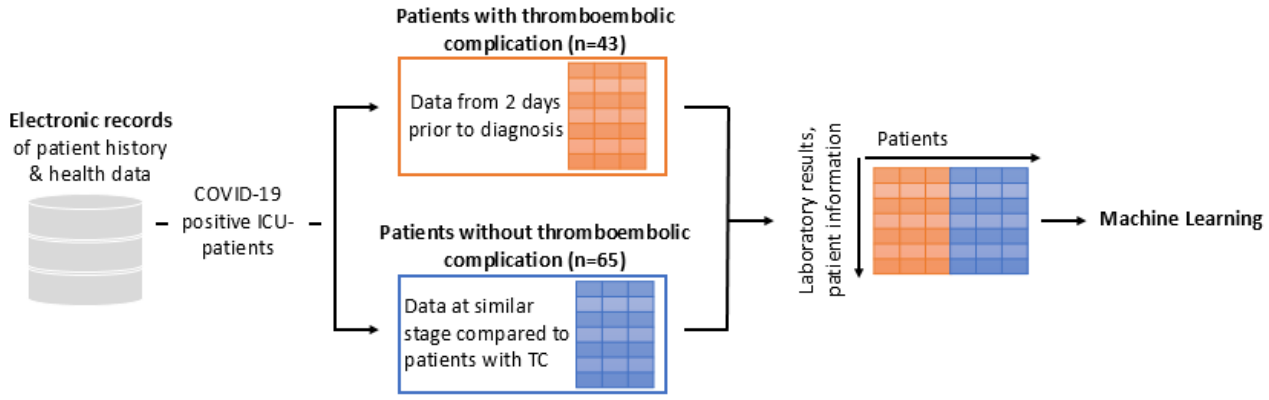
Inconsistent with results section, where $p < 0.01$ was used.

*The p-values were modified accordingly since they were inconsistent with the results section. We adjusted the p-values in 3. Results, at the bottom of table 2 and 3 to 'A p-value of < **0.05** was considered significant'.*

3. Results:

Please enlarge the figure's text font.

The figure's text font was enlarged accordingly from 12 to 14



Explain what the brackets mean

The brackets represent the interquartile range. We applied the appropriate adjustments and noted the interquartile range at the bottom of both table 2 and table 3 as follows: 'interquartile range [25th and 75th percentile per group]'

Inconsistent with the methods section

*The p-values were modified accordingly since they were inconsistent with the methods section. We adjusted the p-values under table 2 and 3 to 'A p-value of < **0.05** was considered significant'.*

Not mentioned in section 2.5.

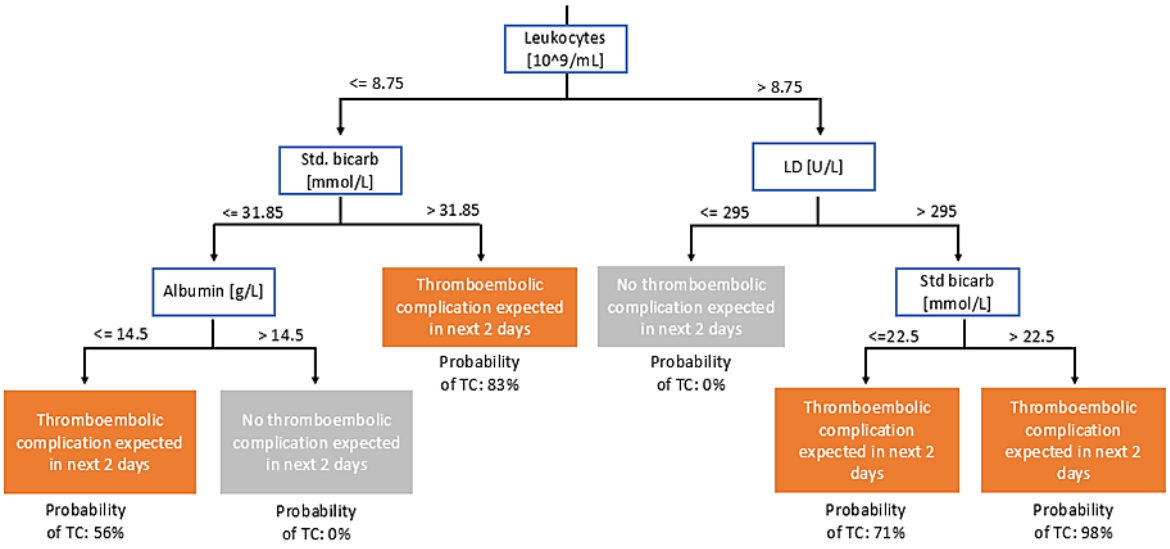
We modified the text in section 2.5 Statistical analysis accordingly and introduced the Spearman's correlation coefficient: 'Furthermore, the correlation between continuous variables was evaluated using Spearman's rank correlation coefficient.'

Describe in the methods how the inclusion was performed for training and testing data sets. It is important that readers understand that no cherry picking was performed to increase model specificity and selectivity.

The text was modified accordingly in the methods section, 2.6 Model development as follows: The predictive model was obtained by training a decision tree classifier on 'a randomly selected subset' of 66% out of the available data.

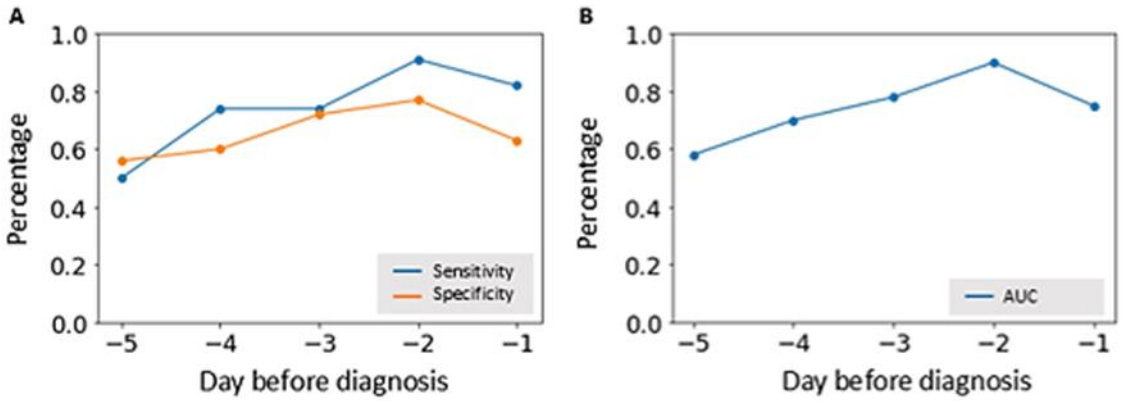
It would help to increase the font of the text.
Also, please change 'ML' in the leukocytes rectangle to read 'mL'. ML means megaliter, and that seems a bit too leukopenic.

The figure was modified accordingly. The font of the text was enlarged from 12 to 14 and ML was noted as 'mL'.



Render the panels into 1 figure side-by-side, 600 dpi, 6" length. The B panel requires a y-axis label.

The two sepparate figures were modified accordingly and rendered into 1 figure. Panel B was assigned a y-axis label accordingly.



2nd Editorial decision
01-oct-2020

Ref.: Ms. No. JCTRes-D-20-00107R1
Predicting thromboembolic complications in COVID-19 ICU patients using Machine Learning
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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: