Reviewer’s report

Title: Hospital mortality in acute coronary syndrome: adjustment of GRACE score by D-dimer enables a more accurate prediction in a prospective cohort study

Version: 0 Date: 11 Jul 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are minor issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions
PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The present paper deals with the value of D-dimer as prognostic marker in patients with acute coronary syndrome. The study design is prospectical with a large sample size. The authors showed that patients with higher D-dimer levels have worse outcome. However, the GRACE score performed better than D-Dimer (as shown in the figure), and D-dimer associated with GRACE score was only slightly better than GRACE score alone. The authors did not explain how to merge the value of D-dimer with the GRACE score to improve the mortality risk estimation.

REQUESTED REVISIONS:

The associations between clinical characteristics of the study population and mortality were tested with univariable analysis followed by multivariable analysis. When testing the association between D-dimer and mortality, I suggest a parsimony model including predictors associated with a p-value < 0.1 as reported in table 1 to improve precision and avoid over-fitting.

Heparin treatment can lower D-dimer levels, this variable (patients with LMWH or heparin vs those without) should be included in the model.

What are the "normal" value of D-dimer according to the local lab? I would suggest to test the association of $D$-dimer $\geq$ the upper limit of normal value and mortality, and, if statistically significant, derive a novel score by adding some points to the GRACE score for patients with D-dimer $\geq$ the upper limit of normal value.

ADDITIONAL REQUESTS/SUGGESTIONS:

Linguistic revision from a native English-speaking medical translator should been done.

In the discussion section, too many data are reported: par 2 at page 11 seem a par of the results section. The authors should discuss the clinical implication of their finding. Do they suggest to use a new score for mortality risk estimation? Only two study limitations are reported, where is several limitations: single centre, heparin use, quite all the patients included in the study seem to have D-dimer below the normal value.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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