

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Association between low-density lipoprotein cholesterol level and mortality in patients with cardiogenic shock: a retrospective cohort study
<b>AUTHORS</b>	Jin, Jiali; Shi, Zhewei; Pang, Xiaomin

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Hayiroğlu, Mert Haydapasa Sultan Abdulhamid Han Training and Research Hospital
<b>REVIEW RETURNED</b>	29-Oct-2020

<b>GENERAL COMMENTS</b>	<p>The authors have tried to evaluate the effect of LDL level on in-hospital and short term outcomes among patients complicated with CS.</p> <p>First of all, the language and typo errors make it difficult to evaluate the manuscript, please check.</p> <p>Tables cannot be evaluated since there are no tables in the pdf?</p> <p>The references are very old should be exchanged with newer ones such as 'Predictors of In-Hospital Mortality in Patients With ST-Segment Elevation Myocardial Infarction Complicated With Cardiogenic Shock' and 'Effect of acute kidney injury on long-term mortality in patients with ST-segment elevation myocardial infarction complicated by cardiogenic shock who underwent primary percutaneous coronary intervention in a high-volume tertiary center'.</p>
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<b>REVIEWER</b>	Khan, Muhammad West Virginia University, medicine
<b>REVIEW RETURNED</b>	05-Nov-2020

<b>GENERAL COMMENTS</b>	<ol style="list-style-type: none"><li>1. It is important that author emphasize further on the observational nature of this study rather than trying to infer a causal relationship between lower LDL-C levels and mortality. I would expand upon the limitation part of this manuscript. Possible alternative explanation for this paradox should be explored in discussion.</li><li>2. Please clarify which model was used, cox regression model or KM model for survival? were both used?</li><li>3. when &amp; why were means and medians used/selected? what stat test was used for medians?</li><li>4. please add the rationale for using 1.8 mmol as LDL-C level.</li><li>5. why were patients with &gt;100 days stay excluded?</li><li>6. what variables were used as adjustment in cox model?</li></ol>
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	7. was effect of >10% and p<0.1 uniformly used for all variables for cox model or was selection also made based upon strong clinical judgement?
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Mert Hayiroğlu, Haydapaşa Sultan Abdulhamid Han Training and Research Hospital

Comments to the Author:

The authors have tried to evaluate the effect of LDL level on in-hospital and short term outcomes among patients complicated with CS.

First of all, the language and typo errors make it difficult to evaluate the manuscript, please check.

Response: Thanks, and we have addressed there errors carefully.

Tables cannot be evaluated since there are no tables in the pdf?

Response: Tables were listed at the end of submitted article according to journal submission guidelines.

The references are very old should be exchanged with newer ones such as 'Predictors of In-Hospital Mortality in Patients With ST-Segment Elevation Myocardial Infarction Complicated With Cardiogenic Shock' and 'Effect of acute kidney injury on long-term mortality in patients with ST-segment elevation myocardial infarction complicated by cardiogenic shock who underwent primary percutaneous coronary intervention in a high-volume tertiary center'.

Response: These two references were not cited in our study. However, we have revised some errors in our references.

Reviewer: 2

Dr. Muhammad Khan, West Virginia University

Comments to the Author:

1. It is important that author emphasize further on the observational nature of this study rather than trying to infer a causal relationship between lower LDL-C levels and mortality. I would expand upon the limitation part of this manuscript. Possible alternative explanation for this paradox should be explored in discussion.

Response: Thanks for the suggestion, we have added this emphasis in our limitation in and highlighted it.

2. Please clarify which model was used, cox regression model or KM model for survival? were both used?

Response: Both cox regression model and KM model were used for survival analysis and were clarified and highlighted in our METHOD.

3. when & why were means and medians used/selected? what stat test was used for medians?

Response: If data is normal distribution, we select means; if not, medians are used. In the present study, data included were of normal distribution, so no medians were used. We did comparisons between groups of medians by Wilcoxon test and was revised and highlighted in our METHOD.

4. please add the rationale for using 1.8 mmol as LDL-C level.

Response: Both in clinical practice and current guidelines (ESC and AHA)<sup>1,2</sup>, the target of lipid management is LDL-C level <1.8mmol/L, so it is rationale to use 1.8mmol/L as LDL-C level. We have added this reason in the METHOD and highlighted it.

5. why were patients with >100 days stay excluded?

Response: Thanks. Because the baseline data values in patients with >100 days stay were exceeded the mean  $\pm$  3 times the standard deviation (SD), which were considered as outliers. We revised in manuscript with an exclusion criteria "Patients were also excluded as follows: 1. with more than 10% individual data were missing; 2. Individual data values exceeded the mean  $\pm$ 3 times the SD." and highlighted in METHOD.

6. what variables were used as adjustment in cox model?

Response: In cox model, the adjusted variables included age, gender, APSIII, ASPSI, using MCS, mechanical ventilation, RRT, milrinone, dobutamine, dopamine, epinephrine, norepinephrine, phenylephrine, and vasopressin.

7. was effect of >10% and p<0.1 uniformly used for all variables for cox model or was selection also made based upon strong clinical judgement?

Response: Thanks, we selected these potential confounders on the basis of their associations with the outcomes of interest or a change in effect estimate of >10% or P-values <0.1 in univariable analyses, as well as upon strong clinical judgement. We have revised it and highlighted in the Statistical analysis section.

Reviewer: 1

Competing interests of Reviewer: None declared

Reviewer: 2

Competing interests of Reviewer: none

#### Reference:

1. Authors/Task Force M, Guidelines ESCcFP, Societies ESCNC. 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk.

*Atherosclerosis* 2019;290:140-205. doi: 10.1016/j.atherosclerosis.2019.08.014 [published Online First: 2019/10/09]

2. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019;73(24):e285-e350. doi: 10.1016/j.jacc.2018.11.003 [published Online First: 2018/11/14]

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Khan, Muhammad West Virginia University, medicine
<b>REVIEW RETURNED</b>	08-Feb-2021
<b>GENERAL COMMENTS</b>	none