

Risk factors for cardiogenic shock incidence and mortality after acute myocardial infarction: A systematic review and meta-analysis

Corresponding Author: Professor Yinzi Jin

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

In this manuscript, the authors seek to systematically review the impact of certain baseline characteristics on the development of cardiogenic shock and as well, the impact of 30-day mortality.

As the authors point out correctly, cardiogenic shock remains a significant health issue, with high in-hospital mortality.

A few comments however.

1. Unfortunately, the diagnosis of CS is based on coding systems, instead of clinical characteristics. Therefore, we do not have any information on baseline lactate levels, culprit vessel, time of symptom onset to PCI, which are also established predictors at least of 30-day and 1 year mortality of cardiogenic shock. Another important predictor is, whether or not these patients had been resuscitated before hospital admission. Were these data not available at all in the included studies? Or did the authors choose to focus solely on characteristics such as age etc?

2. When considering predictors for mortality, also treatment characteristics and additional laboratory results, echocardiography etc are of importance. The same question; were these data available, and if so, in my opinion, it would be valuable to add such important characteristics to the analysis.

3. As the authors point out, there is some heterogeneity when considering the impact. However, factors such as age, DM, female sex and STEMI are still rather established risk factors, and not particularly new

4. The risk factors as mentioned may be of importance, as already established, but what kind of intervention do the authors have in mind, when not taking into account treatable and potentially modifiable risk factors, to prevent CS or to mitigate its mortality?

To summarize, the authors should add other strong and established CS risk factors if available, more specifically describe the additional value of their findings, and be more specific as to what practical implications their article could have.

Reviewer #2

(Remarks to the Author)

This article conducts a systematic review and meta-analysis to discover risk factors related to AMI-CS. The study is well-conducted following the PRISMA guidelines, with rigorous design, sufficient subgroup analysis and sensitive analysis, which makes the results more robust. The topic is highly relevant and valuable for cardiologists seeking to improve patient outcomes by understanding the AMI population at high risk based on current analysis. While the evidence and methods are clearly described, there are still some problems in the full text. The details are as follows:

1. Page 7, line 8-9, Regarding the "risk factors analyzed in this review included: female sex, advanced age, smoking, hypertension, diabetes, and STEMI", the authors included STEMI as a risk factor, but STEMI is one type of AMI. Why was STEMI, not other types like NSTEMI and UA, considered as risk factor and?

2. Page 7, line 15-16, the authors defined 30-day death and 1-year death as "the all-cause death that occurred during the first month and first year after hospital discharge". Obviously, when considering the all-cause death, it is likely to amplify the effect of CS on AMI, because patients might not die from CS. Since the article is examine the risk factors of AMI-CS mortality,

it should be better to eliminate the influence of other factors. So, I suggest to only focus on the AMI-CS patients that died from CS if there were enough studies to support meta-analysis or subgroup analysis.

3. The authors mentioned that “Some studies estimated the effect of agewe extracted the OR of the last age group” (Page 9, line 3-6), and when performing sensitive analysis, they excluded studies reporting the OR of age considering it as a categorical variable (page 9, line 20). Please clarify in the result section that in which sensitive analysis the studies considering age as a categorical variable were excluded.

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5. Page 17, line 19-21, “Further research is warranted to confirm.....to develop specific strategies for risk stratification and management of this severe cardiovascular condition.” As quite a few studies already discover the risk factors of AMI-CS, the focus of next step is how to tackle the risk factors so that prevent avoidable poor outcomes (not to confirm the underlying role of the factors). Please be more cautious when making the conclusion.

6. Supplementary Table 2 is quite important. If it is allowed by the publication requirement of the journal, please consider to put it in the main text, not only present several significant effects as figures.

Version 1:

Reviewer comments:

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(Remarks to the Author)

Thanks to the authors for their response to the questions raised; no further questions or comments

Reviewer #2

(Remarks to the Author)

The authors addressed all the comments I had. I suggest accepting this manuscript.

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Point-by-point response to the reviewers

Dear editors,

We appreciate the opportunity to respond the comments from the reviewers for our manuscript. We have revised the manuscript accordingly. The following are the point-to-point responses to these comments.

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Authors' response: Thanks for your suggestion. Although there are a number of studies that examined the risk factors of AMI-CS, such as sociodemographic factors, behavior factors, and clinical characteristics, they were merely conducted in a single setting with small sample sizes, and their results were not consistent, still leaving a lack of convincing evidence for clinical practice and decision making. Thus, we conducted this systematic review to synthesize the current evidence and increase the statistical power. Given the lack of enough data, it was not allowed to add clinical characteristics and laboratory results to the meta-analysis, they are very important though. It is not only the limitation of our review, but also might be the potential direction of future research. We have revised the sentences in the limitation to remind the readers about this concern as following (line 6-10, page 17):

“Last, the lack of adequate studies keeps us from conducting data synthesis to identify the possible predictors of AMI-CS, such as clinical characteristics, laboratory results, and treatment characteristics. Failure to detection cannot eliminate a negative effect or vice versa. Thus, it is warranted to conduct well-designed prospective studies, such as RCT and cohort studies that are particularly from low- and middle-income countries, to verify the influence of these risk factors on AMI-CS from a comprehensive perspective.”

2. When considering predictors for mortality, also treatment characteristics and additional laboratory results, echocardiography etc. are of importance. The same question; were these data available, and if so, in my opinion, it would be valuable to add such important characteristics to the analysis.

Authors' response: Thanks for your suggestion. Treatment characteristics and additional laboratory results are indeed important factors for AMI-CS, but we did not find enough studies to synthesize data on these factors, as we responded the above.

3. As the authors point out, there is some heterogeneity when considering the impact. However, factors such as age, DM, female sex and STEMI are still rather established risk factors, and not particularly new.

Authors' response: As we stated in the limitations (line 2-6, page 17), heterogeneity across studies might be resulted from many reasons. Given the limited information of the included studies, we failed to address the heterogeneity for several outcomes. Of course, the heterogeneity found in our study did not deny the influences of these factors on the AMI-CS development and outcomes.

4. The risk factors as mentioned may be of importance, as already established, but what kind of intervention do the authors have in mind, when not taking into account treatable and potentially modifiable risk factors, to prevent CS or to mitigate its mortality?

Authors' response: Thanks for the suggestion. We provided several possible interventions to prevent CS and hereby reduce its serious consequences in the discussion section (line 9-19, page 16). They include initial examinations of risk factors, early recognition of people at risk, patient education, and predictive therapy for AMI-CS, such as immediate revascularization.

To summarize, the authors should add other strong and established CS risk factors if available, more specifically describe the additional value of their findings, and be more specific as to what practical implications their article could have.

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Authors' response: STEMI is the most acute manifestation of coronary artery disease and is

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