Author’s response to reviews

Title: Effects of Intravenous Hydration on Risk of Contrast Induced Nephropathy and In-hospital Mortality in STEMI Patients Undergoing Primary Percutaneous Coronary Intervention: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Author’s response to reviews:

January 30, 2019,

Iddo Z. Ben-Dov, MD, PhD
BMC Cardiovascular Disorders
Dear Dr. Iddo Z. Ben-Dov

BCAR-D-18-00728

Many thanks for reviewing our manuscript titled “Effects of Intravenous Hydration on Risk of Contrast Induced Nephropathy and Mortality in STEMI Patients Undergoing Primary Percutaneous Coronary Intervention: A Systematic Review and Meta-analysis of Randomized Controlled Trials”.

The reviewer’s comments were highly insightful and enabled us to greatly improve the quality of our manuscript.

In the following pages are our point-by-point responses to each of the comments.

Revisions in the manuscript are shown as red text. In accordance with the first comment, the title has been revised to “Effects of Intravenous Hydration on Risk of Contrast Induced Nephropathy and In-hospital Mortality in STEMI Patients Undergoing Primary Percutaneous Coronary Intervention: A Systematic Review and Meta-analysis of Randomized Controlled Trials” and the entire manuscript has undergone substantial English editing.

We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in the BMC Cardiovascular Disorders.

Reviewer reports:

Amartya Kundu (Reviewer 1): The authors describe a systematic review and meta analysis evaluating the role of IV hydration during PCI for STEMI. Although only 3 RCTs were included in this meta-analysis, the authors showed a statistically significant reduction in the incidence of CIN with IV hydration. Overall, the manuscript flow is well organized and the topic is of relevance to contemporary clinical practice. Following are a few suggestions:

Response: Thank you for your sincere comments and positive summary for our study.

1. Further elaboration on the clinical importance of CIN (risk factors, mechanisms, financial implications, etc) is warranted in the discussion section.

Response: Thank you for your good comments. We have added “Besides the preventative effect of intravenous hydration on the risk of CIN, the baseline patients characteristics, including renal insufficiency, age, heart failure were contribute to the development of CIN and even mortality [1,14]. In addition, the association between CIN and mortality is strongly confounded by baseline clinical characteristics, large meta-analysis also showed CIN, as common complication of coronary angiography and/or coronary intervention (CAG/PCI), associated with increased lengthen of hospitalization, cardiovascular events, renal failure and mortality, so did that in
Recent large STEMI Registry (e-PARIs) study among patients with STEMI undergoing primary PCI[15,16].” (Paragraph 1, Page 9) in Discussion section in the revised manuscript.


2. No mention has been made about the Mehran Risk Score- which is extremely relevant to the present topic. Recommend citing the following article for reference- Catheter Cardiovasc Interv. 2017 Aug 1;90(2):205-212.

Response: Thank you for your good comments. We have added “Therefor the risk stratification of CIN was the key step for prevention for patients with STEMI, while the infarct-related artery (IRA) only PCI were not associated with lower risk of CIN, adequate hydration maybe the optimal prophylaxis for primary PCI [17].” (Paragraph 1, Page 9) in Discussion section in the revised manuscript.


Marwan Saad (Reviewer 2): Title: Effects of Intravenous Hydration on Risk of Contrast Induced Nephropathy and Mortality in STEMI Patients Undergoing Primary Percutaneous Coronary Intervention:

A Systematic Review and Meta-analysis of Randomized Controlled Trials
Liu et al conducted a systematic review and meta-analysis of RCTs comparing prophylactic IV hydration versus no hydration at the time of primary PCI in STEMI patients. The authors concluded that compared with no hydration, IV hydration was associated with reduction in the incidence of CIN.

I would like to congratulate the authors for their work. I have few comments to consider:

Response: Thank you for your sincere comments and positive summary for our study.

1. **It may be more accurate to report the weighted incidences of the outcomes rather than unweighted incidences, with the sample size of each trial being its weight.**

Response: Thank you for your good comments, sorry to miss the weighted incidences of the outcomes and the sample size of each trial being its weight. We have added the fixed effect weighted incidences of the outcomes in Supplementary Figures 2 and added “, so did that with fixed effect model (Supplementary Figure 3)” (Paragraph 3, Page 7) in the revised manuscript as follow:

2. **I assume that these outcomes are all in-hospital outcomes as mentioned in the figures. This has to be more clear in the title and throughout the manuscript.**

Response: Thank you for your sincere suggestions! Yes, we have changed the “Mortality” to “In-hospital Mortality” in the Title and throughout the manuscript (Abstract, Background, Methods, Results, Discussion, Conclusions) in the revised manuscript.

3. **What was the weighted mean duration of following the creatinine level after primary PCI?**

Response: Thank you for your good suggestions! We have added the “duration of following the creatinine level after primary PCI” in Supplementary Table 1 in the revised manuscript.

4. **Did the included trials report the mean duration of IV hydration used?**

Response: Thank you for your good suggestions! We have added the “duration of IV hydration” or other detail of IV hydration in Supplementary Table 1 in the revised manuscript.

5. In table 1, the authors reported some of the baseline characteristics of the cohort of each study. However, it is also important to report and statistically compare the baseline risk factors of the 2 arms (if reported by the studies), as this may impact the outcomes (ex. baseline creatinine and GFR, DM, female sex, etc.)
Response: Thank you for your good suggestions! We have added the “baseline creatinine and GFR, DM, female sex” or other detail of IV hydration in Supplementary Table 1 in the revised manuscript.

6. The authors reported that they used GRADE tool for assessment of risk of bias, however I do not see it reported. The authors may want to include the table for GRADE tool for assessment of quality of evidence at each outcome.

Response: Thank you for your sincere suggestions! We have added “GRADE tool also suggested high quality for quality of evidence at CIN and in-hospital mortality (Supplementary Figure 2)”(Paragraph 2, Page 7) in the revised manuscript.

7. In absence of details regarding the characteristics of the included STEMI patients (such as baseline EF, outcomes of primary PCI, TIMI flow after primary PCI, coronary anatomy, etc.) it would be hard to comment on the outcome of in-hospital mortality in relation to IV hydration alone. In-hospital mortality after primary PCI is largely related to the area of jeopardized myocardium, clinical and electrical instability, success of primary PCI etc.. The authors should elaborate on that in the discussion.

Response: Thank you for your good suggestions! Yes, the patients’ characteristics was associated with CIN and In-hospital mortality after primary PCI. We have added the “the characteristics of patients and coronary procedure” in Supplementary Table 1 in the revised manuscript. In addition, we also added “In the present three included studies, there were no significant dereference in characteristics of patients and coronary procedure, including treated coronary, age, diabetes , female, renal and heart function, which were predictors for CIN and in-hospital [4,5,9].” (Paragraph 1, Page 9) in the revised manuscript.

Supplementary Table 1. Additional characteristic of studies.

| PCI=Percutaneous Coronary Intervention; GFR=Glomerular filtration rate; LVEF= left ventricular ejection fraction; TIMI= Thrombolysis in Myocardial Infarction; LAD= Left anterior descending artery. |
| ※late hydration group: 3 mL/kg of sodium bicarbonate solution in 1 hour, starting in the emergency room, followed by infusion of 1 mL/kg per hour for 12 hours after PCI; #early hydration group: received isotonic saline (1 mL/kg per hour 0.9% sodium chloride) for 12 hours immediately after PCI. |