

Response to Reviewers' reports and Editors' comments:

We are grateful to the reviewers for the insightful comments, which have helped markedly improve our work. We have addressed all questions, remarks, and suggestions in a point by point response found below. In addition, we have sought help from an experienced native English speaking scientist, who has proofread the whole manuscript. We hope the current version will fulfill the editorial requirements for publication.

Reviewer #1: The topic of early vasopressor initiation in septic shock is clinically relevant and understudied.

A systematic review would be valuable for researchers and clinicians.

COMMENT 1-1. However, it is essential that systematic reviewers follow a standardized approach describing of why the review was done, how studies were identified and selected and what they found (such as characteristics of contributing studies and results of meta-analyses). Such a standardized approach is absent in the present study.

**Response 1-1: Thanks for the reviewer's suggestion. We have gained a comprehensive understanding of the guidelines established by PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) and conducted a meticulous revision of our review article. We have not only emphasized the guideline in abstracts and search methods, but also incorporated some key points regarding methodology, such as primary outcomes required by PRISMA guidelines, into both the abstracts and Part 3. Additionally, we have presented specific data regarding the primary outcomes.**

COMMENT 1-2. I would encourage the authors to follow the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and checklist for their study.

**Response 1-2: We appreciate the invaluable suggestions provided by the reviewer. We have meticulously restructured our review article to conform to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and checklist. We will upload the checklist as an appended file.**

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Reviewer #2: Greetings I read your manuscript with interest. The topic has clinical relevance. Systematic search strategy to formulate the evidence is a strength. Overall the manuscript is also well written.

COMMENT 2-1. However, I would suggest a major revision to present the manuscript as per PRISMA guideline. Otherwise the study and content has no major limitations. Best of luck

**Response 2-1: Thank you to the reviewers for their valuable feedback. We have revised the manuscript by PRISMA guidelines, ensuring a more structured and comprehensive presentation of our research findings. We have not only emphasized the guideline in abstracts and search methods, but also incorporated some key points regarding methodology, such as primary outcomes required by PRISMA guidelines, into both the abstracts and Part 3. Additionally, we have presented specific data regarding the primary outcomes. We will upload the checklist as an appended file.**

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Reviewer #3: Dear Authors I apologise to accept the review. I realised that this is more of a critical care kind of paper and not much surgical critical care. This is largely outside my scope and i am unable to "undo" the review selection. So i shall only make brief comment and recommend as "good" so that i am not unfair to you.

I shall also separately mention the same to editor too and he can activate another reviewer.

COMMENT 3-1. 1. I find >10 grammar errors and sentence formation errors.

**Response 3-1. Thanks for their your valuable suggestions. We have thoroughly reviewed the manuscript for any language-related issues, including grammar and sentence formation errors. In addition, we have sought help from an experienced native English speaking scientist, who has proofread the whole manuscript.**

COMMENT 3-2. 2. I do not see any mention on source control within your protocol of early vasopressor.

**Response 3-2. Thanks to the reviewers for their valuable comments. As source control is a crucial measure in the management of septic shock, we emphasize in Part 6, paragraph 3, that "source control should be required as an emergent intervention as soon as a specific anatomical diagnosis of infection is identified". However, we will not pursue this issue further in this manuscript, as our review discussion focuses primarily on the timing of vasopressors.**

COMMENT 3-3. 3. I also do not see interplay with early steroid or choice of fluid like 5% albumin etc.

**Response 3-3. As pointed out by the reviewer, early administration of steroids and appropriate fluid type are crucial interventions in the management of septic shock. We conducted a literature review using these two keywords through a standardized process, screened relevant studies, and added the content to Part 6, paragraph 2 and 3 in the manuscript.**

COMMENT 3-4. 4. The problems of early vasopressors in underfilled patient with myocardial ischaemia?

**Response 3-4. As noted by the reviewers, early administration of vasopressors raises concerns regarding myocardial infarction. To address this issue comprehensively, we conducted a review of the relevant literature and dedicated a section to this topic, incorporating clinical practice insights. We amalgamated the preceding Part 5 with this section and designated it as a novel Part 5, entitled "5. Possible adverse effects of early initiation of vasopressors."**