

Peer-review report

Reviewer #1: Anwar Khedr et al. evaluated the incidence of fibrinolytic therapy before and during the COVID-19 pandemic, and its effect on all-cause mortality via a systematic review and meta-analysis. They found that the incidence of fibrinolytic therapy during the COVID-19 pandemic was higher than that before the COVID-19 pandemic, but it cannot rise the risk of all-cause mortality of STEMI patients. The idea of the study is well, but there are still many major issues to be addressed. Major Abstract In the Conclusions section, it is not suitable to use “be associated with” to describe your conclusion. Introduction 1. “Gold standard” is commonly used to describe the diagnosis methods, rather than treatment methods. Please revise it. 2. The sentence “A recent systematic review and meta-analysis by Kamarullah et al. showed that there was a decline in STEMI care performance and a deterioration in clinical outcomes in STEMI patients” seems not complete. Do you want to say “there was a decline in STEMI care performance and a deterioration in clinical outcomes in STEMI patients during COVID-19 pandemic”? Methods Please give the abbreviation of “odds ratio” when it first appeared. Double-check the similar problems throughout the manuscript. Results 1. In the section of All-cause mortality, the phrase “patients receiving treatment” is confusing. What treatments were received by patients? Please describe it clearly. 2. The sentence “Patients receiving treatment in LMIC [OR 1.16 (1.03 to 1.30); I²=0%; P=0.01; GRADE: Very Low] were at a higher risk of all-cause mortality than patients receiving treatment in HICs [OR 1.13 (0.76 to 1.66); I²=72%; P=0.55; GRADE: Very Low]” seems not right, because there is not statistically significance in HICs. You cannot compare LMIC with HICs as you described. 3. In section of Meta-regression for exploring specific covariates, you cannot provide so much cited evidence to discuss, because this is the section of results. Just describe your results. 4. Whether the incidence of fibrinolysis is increased with the rising incidence of STEMI? Please give the incidence of STEMI before and during the COVID-19 pandemic. 5. Please compare the incidence of fibrinolysis and the incidence of PCI before and during the COVID-19 pandemic. 6. Whether COVID-19 affects the duration from symptoms (for example, chest pain) to intervention (for example, PCI, fibrinolysis) in patients with STEMI? Please provide more data. Figures The resolution of the figure is too low. Please satisfy the requirement of the journal. Tables Please revise your tables to three-line tables. Similarity The similarity is too high. Please rephrase and revise.

Reviewer #2: In the article titled " Fibrinolytic-based reperfusion as the preferred strategy in STEMI patients during the COVID-19 pandemic: A systematic review and meta-analysis" by Anwar Khedr et al, investigation of the incidence of fibrinolytic therapy during the COVID-19 pandemic and its effects on STEMI clinical outcomes were described. The authors found that there is an increased incidence of fibrinolysis during the pandemic period, but it is not associated with the risk of all-cause mortality. However, there are some points that need to be revised: 1. The title is inaccurate. The manuscript does not reflect that fibrinolytic-based reperfusion is preferred strategy for all STEMI patients during the COVID-19 pandemic. 2. The manuscript doesn't adequately describe the background and present status of the study. 3. The manuscript does not provide a full discussion of the results, and relevance to clinical practice sufficiently 4. The quality of figures is not good. Figure 2 is blurred. 5. Although the authors acknowledge several limitations inherent, there is probably scope for the authors to discuss answers to a number of clinically relevant questions that the results present.

Reviewer #3: In the paper “Fibrinolytic-based reperfusion as the preferred strategy in STEMI patients during the COVID-19 pandemic: A systematic review and meta-analysis “ the authors well focused on the

problem of STEMI treatment during COVID outbreak. Data are well exposed and supported. Even if fibrinolysis-based reperfusion was found to be a major reperfusion strategy during the pandemic period all over the world in the discussion they should insert the concept that in countries with a high income status a well re-organized emergency system allowed to maintain primary PCI as the treatment of choice for patients and operators (Impact of COVID-19 on STEMI: Second youth for fibrinolysis or time to centralized approach? G.Tumminello et al; Int J Cardiol Heart Vasc. 2020 Oct; 30: 100600)

Response:

Suggested additions and changes have been represented by yellow highlight with red font color.

Rephrasing due to high similarity has been represented by green highlights.

Reviewer # 1

Major abstract: The phrase “be associated with” has been removed, and the sentence has been rephrased as “There is an increased incidence of fibrinolysis during the pandemic period, but it has no effect on the risk of all-cause mortality.”

Introduction: 1. The sentence has been rephrased and the term “gold-standard” has been removed. The new sentence is: “The preferred treatment for STEMI is primary percutaneous coronary intervention (PPCI) [3].” 2. Yes, we meant to say that there was a decline in STEMI care performance and a deterioration in clinical outcomes in STEMI patients during COVID-19 pandemic. The phrase “during the COVID-19 pandemic” has been added at the end of the respective sentence.

Methods: Odds ratio has been abbreviated when it appeared for the first time in the methods and similar mistakes have been addressed.

Results: 1. Patients receiving treatment has been changed to “who received fibrinolytic therapy.” 2. The comparison in the sentence has been removed. 3. The cited evidence of meta-regression has been removed from the results and moved to the second paragraph of discussion. 4. No, the incidence of fibrinolysis did not increase with the increasing incidence of STEMI. In fact, the incidence of STEMI decreased during the pandemic. New evidence has been cited in the second paragraph of discussion and details have been added as “Moreover, the incidence of STEMI has been reported to decrease during the COVID-19 pandemic. A study by Furnica et al. found that the incidence of STEMI decreased by 48.8% during the COVID-19 pandemic compared to the same time in the previous year. Another study by Oettinger et al. reported a similar increase in STEMI incidence of 22.9% during the COVID-19 pandemic. These findings suggest that there may be an association between the declining incidence of STEMI and the COVID-19 pandemic”. 5. The comparison of incidence of PCI and fibrinolysis has been made in the second paragraph of discussion and details have been added as, “The use of fibrinolysis and PCI in the management of STEMI has been reported to differ before and during the COVID-19 pandemic. A study found that the use of fibrinolysis increased by 20.2% during the COVID-19 pandemic, while the use of PCI decreased by 74.6% [16]”. 6. The data has been added in the second paragraph of discussion as, “A study reported that the mean time from symptoms to intervention was longer during the COVID-19 pandemic compared to the previous year”.

Figures: All the blurred figures have been changed.

Tables: The GRADE table has been moved to supplement and has been named as Supplement table 1. The baseline characteristics tables have been named as Table 1A and Table 1B. In Table 1A, previously

three separate columns have been merged and the table now consists of three columns. Table 1B could not be changed.

Similarity: Several parts of the manuscript have been rephrased and rephrasing has been represented by green highlights.

Reviewer # 2

1. The title has been changed to “Effect of Fibrinolytic Therapy on STEMI Clinical Outcomes during the COVID-19 Pandemic”. 2. The last paragraph of the introduction has been elaborated further as “Therefore, the aim of this systematic review is to examine the significance of the increase in fibrinolytic therapy in adult STEMI patients during the COVID-19 pandemic compared to the pre-COVID-19 era, and to assess the impact of this treatment strategy on clinical outcomes, particularly the risk of all-cause mortality, in comparison to patients who received standard of care before or during the pandemic.” 3. Some more details regarding the relevance to results and clinical practice has been added in the last paragraph of discussion as, “Overall, the results of our study highlight the impact of the COVID-19 pandemic on the incidence, treatment, and outcomes of STEMI. These findings have important implications for clinical practice, as they underscore the need for continued efforts to promote timely recognition and treatment of STEMI, even in the midst of a pandemic. Strategies such as public education campaigns, telemedicine, and streamlined healthcare delivery systems may help to mitigate the impact of the pandemic on the management of STEMI and improve patient outcomes”. 4. Figure 2 has been changed. 5. The discussion of the results has been extended in the last paragraph of discussion as “Regarding the clinical relevance of our findings, our results suggest that there may have been a decrease in the use of PCI during the COVID-19 pandemic, which could have important implications for patient outcomes. PCI is generally considered the preferred treatment for STEMI, as it has been shown to reduce mortality and the risk of complications compared to fibrinolysis. Therefore, any reduction in the use of PCI should be carefully evaluated to ensure that patient care is not compromised”.

Reviewer # 3

Response: The concept has been inserted as the last line of fourth paragraph and the suggested paper has been cited.