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The association between myocardial infarction and COVID-19 related mortality: A meta-analysis based on adjusted effect estimates

To the Editor,

Several published articles have reported the association between myocardial infarction and the risk of fatal outcomes in patients with coronavirus disease 2019 (COVID-19), but individual studies yielded conflicting conclusions [1-4]. For example, some studies reported myocardial infarction was associated with a significantly increased risk for mortality among COVID-19 patients [1,2], while other studies did not observe the significant association [3,4]. Therefore, it is urgently required to address the association between myocardial infarction and COVID-19 mortality through a quantitative meta-analysis. Studies have proved that risk factors such age, gender and comorbidities have a significant impact on the prognosis of patients with COVID-19 [5-8], which suggests that these factors might affect the association between myocardial infarction and COVID-19 mortality. Therefore, this metaanalysis was conducted on the basis of adjusted effect estimates to investigate the relationship between myocardial infarction and the risk of mortality in COVID-19 patients.

All the related articles were searched from Spinger Link, Wiley, Elsevier ScienceDirect, Scopus, PubMed and Web of Science on December 30th, 2021 by using the following keywords: ("COVID-19" OR "coronavirus disease 2019" OR "SARS-CoV-2") AND ("myocardial infarction" OR "myocardial infarct") AND ("mortality" OR "death" OR "fatality" OR "non-survivor" OR "deceased"). Articles that reported the adjusted effect estimates on the association between myocardial infarction and the risk of mortality among COVID-19 patients were included. Case reports, repeated articles, protocols, reviews, errata and articles without sufficient information were excluded.

Meta-analysis was performed using R statistical software. The inconsistency index (I^2) was used to assess heterogeneity. A fixed-effect model would be applied if $I^2 < 50\%$, otherwise a random-effect model would be implemented. Sensitivity analysis by eliminating single study at a time was implemented to check the robustness of the results. Publication bias was assessed by Egger's linear regression test and Begg's rank correlation test. Statistical significance of testing standard was set as $P \le 0.05$.

A total of twenty-six studies of 1,175,537 patients were included in this meta-analysis. Basic characteristics of the included studies are presented in supplementary Table 1. Totally, meta-analysis based on adjusted effect estimates showed that myocardial infarction was positively associated with higher risk for COVID-19 mortality (pooled effect = 1.20, 95% confidence interval (CI): 1.09–1.32; heterogeneity test: $I^2 = 74\%$, P < 0.01, Fig. 1A). Moreover, in the subgroup analysis by cases, the results supported the overall results (14 studies reported cases <5000: pooled effect = 1.35, 95% CI: 1.10–1.66 and 12 studies reported cases >5000: pooled effect = 1.14, 95% CI: 1.03–1.26). Following subgroup analyses by effect estimates, cohort type, area, age, setting and

proportion of males demonstrated that this significant association between myocardial infarction and the increased risk for COVID-19 mortality did exist among OR-reported studies (14 studies, pooled OR = 1.29, 95% CI: 1.12–1.50), retrospective studies (24 studies, pooled effect = 1.19, 95% CI: 1.07–1.32), Europe (9 studies, pooled effect = 1.09, 95% CI: 1.04–1.15), Americas (8 studies, pooled effect = 1.30, 95% CI: 1.13–1.50), age \geq 60 (15 studies, pooled effect = 1.21, 95% CI: 1.10–1.32), hospitalized patients (14 studies, pooled effect = 1.29, 95% CI: 1.12–1.49) and proportion of males \geq 50% (13 studies, pooled effect = 1.26, 95% CI: 1.11–1.42). Sensitivity analysis demonstrated the robustness of this meta-analysis (Fig. 1B). Publication bias was not found in the Begg's test (P = 0.2801, Fig. 1C) and Egger's test (P =0.1629, Fig. 1D).

In conclusion, this meta-analysis observed the positive association between myocardial infarction and increased risk for COVID-19 mortality on the basis of risk factors-adjusted effects. Further researches on the potential pathophysiology were also in demand.

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Author contributions

Haiyan Yang and Yadong Wang designed the study. Shuwen Li, Mengke Hu and Ruiying Zhang searched articles and extracted the data. Shuwen Li, Hongjie Hou and Jie Xu analyzed the data. Shuwen Li wrote and reviewed the manuscript. All the authors approved the final manuscript.

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Data availability statement

All data relevant to this study are included in this article or uploaded as supplementary information.

Ethics approval

Not applicable.

Credit authorship contribution statement

Shuwen Li: Writing – review & editing, Writing – original draft, Supervision, Software, Project administration, Methodology, Data curation. **Mengke Hu:** Writing – review & editing, Data curation. **Ruiying Zhang:** Writing – review & editing, Data curation. **Jie Xu:** Writing – review & editing, Software. **Hongjie Hou:** Writing – review & editing, Software. **Yadong Wang:** Writing – review & editing,



Fig. 1. The forest plot indicated the relation between myocardial infarction and the risk of fatal outcomes in patients with coronavirus disease 2019 (COVID-19) based on 26 studies with 1,175,537 patients (A); Sensitivity analysis demonstrated the robustness of this meta-analysis (B); Publication bias was assessed by both Begg's test (C) and Egger's test (D). * indicated combined effects based on subgroups; ** published by CAPACITY-COVID Collaborative Consortium and LEOSS Study Group.

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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