



PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 84145

Title: Prognostic role of metformin in diabetes mellitus type 2 patients with hepatocellular carcinoma: A systematic review and meta-analysis

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03302550

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Croatia

Manuscript submission date: 2023-02-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-02-27 23:58

Reviewer performed review: 2023-02-28 06:37

Review time: 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this paper, The prognostic role of metformin in diabetes mellitus type 2 patients with hepatocellular carcinoma was studied, which was innovative. This is a good paper about the relationship between metformin and diabetes mellitus type 2 patients with hepatocellular carcinoma. The methods described in sufficient detail for materials, statistical analysis and others. The results of research that support the conclusions. The conclusions is a reasonable extension of the Metformin and relevant impact in preventing adverse effects after HCC treatment. The study's design, data presentation, and citations comply with standard COPE ethical guidelines. Although this manuscript has strong practicability, there are still several points to be explained. For example: 1. Metformin is one of the main drugs for the treatment of diabetes. One item in the user manual is not recommended for patients with severe liver injury. Therefore, the patients with hepatocellular carcinoma in this study may have different degrees of liver injury, which is inconsistent with the drug instructions. 2. The quality of the 13 studies included should be scored to illustrate its quality.



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Peer-review model: Single blind

Reviewer's code: 05843587

Position: Peer Reviewer

Academic degree: N/A

Professional title: N/A

Reviewer's Country/Territory: China

Author's Country/Territory: Croatia

Manuscript submission date: 2023-02-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-13 14:09

Reviewer performed review: 2023-03-18 15:12

Review time: 5 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
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Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Comments: Metformin, a low-cost oral hypoglycemic drug, has been proposed to have antitumor effect. Several meta-analyses have shown that metformin can reduce the risk of hepatocellular carcinoma in patients with diabetes. This meta-analysis tried to evaluate the effect of metformin in preventing HCC adverse events (i.e., death, tumor progression, and recurrence) after HCC treatment. The results showed that the combined ORs were not statistically significant. This research can guide clinical practice and provide direction for future research. However, major revision should be considered before publication as following suggestions. Major point: Introduction 1. Two related meta-analyses have been published recently, and both have positive results (doi: 10.3389/fendo. 2021.1060768; doi: 10.1016/j.clinre.2021.101781). The authors can quote and explain the similarities and differences with these studies in introduction or discussion section. In addition, the authors can search the literatures included of previous meta to check whether there is any missing study in his own research. Methods 2. If the study has been registered, please provide the registration website name and registration number in the methods section. If not, I suggest that the authors



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register this meta-analysis. 3. After searching two databases, the authors initially produced 107 documents to be screened. This number is relatively small. The authors can try to search other databases to increase the number of included documents. 4. I suggest that the authors conduct sensitivity analysis to further explore the stability of the results. In addition, publication bias should also be tested, especially for more than 10 studies. Results 5. The authors only used one sentence to describe the quality evaluation of included studies, and I recommend giving a figure or table to show the results more intuitive and convincing. 6. In “Death in HCC patients with T2DM receiving vs. not receiving metformin” part, the authors only selectively displayed the subgroup received curative therapies, and I suggest that the subgroups that did not receive should also be displayed. In addition, subgroup analysis can also be carried out by country or race to explore whether there are differences in the role of metformin among different races. Minor point: Some abbreviations are included in Table 1, 2 and 3. Please give the full name below the table.



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Peer-review model: Single blind

Reviewer's code: 03809896

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Iran

Author's Country/Territory: Croatia

Manuscript submission date: 2023-02-27

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-04-03 11:38

Reviewer performed review: 2023-04-07 03:25

Review time: 3 Days and 15 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I think the topic of study is interesting. In the table number 1(study 2) USA should be written in capital letters.