

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: 1. The authors put forward new point about the potential correlation between atrial flutter and DPP-4 inhibitors administration, it is an interesting finding, which can provide a new direction for the study about the DPP-4 inhibitors function on the cardiovascular system.

Authors: We are grateful to the Reviewer for his/her encouraging comments.

2. But as we all know, Atrial flutter is an unstable state, therefore, we suggest authors add some discussions about other types of atrial arrhythmia (atrial premature beats, atrial fibrillation and so on).

Authors: This is indeed a very important point. Based on the Reviewer's comment we discuss other types of atrial arrhythmia:

“Several studies have demonstrated that antidiabetic drugs may have differing effects on the risk of new-onset AF (Lee TW, et al. *Cell Mol Life Sci.* 2021;78(3):923-934) Metformin has been associated with anti-atrial arrhythmic benefits (Nantsupawat T, et al. *Cardiovasc Diabetol.* 2020;19(1):198). A case control study revealed no association between sulfonylurea and incident AF, whereas the use of insulin was associated with increased risk of new-onset AF (Liou YS, et al. 2018; *PLoS ONE* 13(8):e0197245). A recent meta-analysis showed that DPP-4 inhibitor treatment resulted in a non-significant decrease in the risk for AF, whereas both GLP-1RA and SGLT2-inhibitors were associated with a significant decrease in the risk for AF, equal to 14% and 19%, respectively (Patoulias D, et al. *Am J Cardiol.* 2021 Jan 15;139:139-141). Liraglutide (a GLP-1RA) demonstrated favorable effects on electrophysiological changes regarding atrial fibrillation inducibility and conduction velocity decrease (Nakamura H, et al. *Heart Vessels* 2019, 34(8):1389-1393)”

3. In the second paragraph of the main text, authors quoted reference[4], but we doesn't found the matched results described here (DPP-4 inhibitors was associated with an increased risk of atrial flutter equal to 52% (RR = 1.52, 95%CI: 1.03-2.24, I2 = 0%).) in original study.

Authors: We thank the Reviewer for the comment. Reference 4 has been updated “*Patoulias DI, Boulmpou A, Teperikidis E, Katsimardou A, Siskos F, Doumas M, Papadopoulos CE, Vassilikos V. World J Cardiol. 2021 Oct 26;13(10):585-592. doi: 10.4330/wjc.v13.i10.585.*”

“Of note, DPP-4 inhibitors were associated with a significant increase in the risk for atrial flutter, equal to 52% (RR = 1.52, 95%CI: 1.03-2.24, I2 = 0%), as shown in Supplementary Figure 1B”

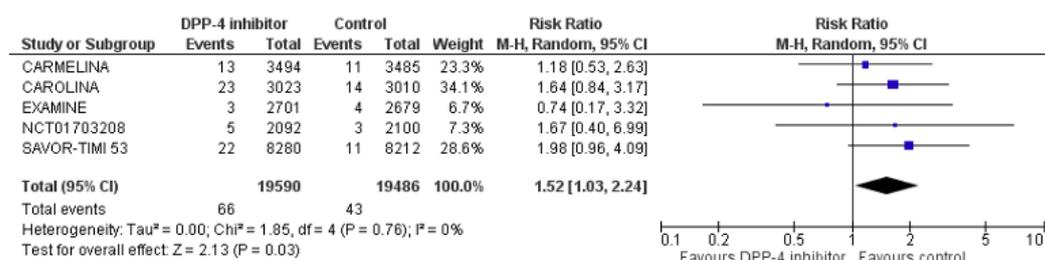


Figure 1B

Patoulas DI, Boulmpou A, Teperikidis E, Katsimardou A, Siskos F, Doumas M, Papadopoulos CE, Vassilikos V. Cardiovascular efficacy and safety of dipeptidyl peptidase-4 inhibitors: A meta-analysis of cardiovascular outcome trials. *World J Cardiol* 2021; 13(10): 585-592 [PMID: 34754403 DOI: 10.4330/wjc.v13.i10.585]

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This paper is very interesting on illustrating the relationships between DM medicine and cardiovascular events, and raising some questions. that is meaningful.

Authors: We are grateful to the Reviewer for his/her supportive comments.

Nevertheless, there seems to be a mistake in this sentence in page 7 "Glucagon-like peptide-1 receptor agonists (GLP1-RA) are oral hypoglycemic drugs which mimic the endogenous hormone and bind to its receptor. "

Authors: We thank the Reviewer for the comment. Accordingly, the sentence has been revised to "GLP1-RA are oral hypoglycemic drugs which mimic the effects of the incretin hormone GLP-1. GLP-RA stimulate insulin release, inhibit glucagon secretion and slow gastric emptying."

(1) Science editor:

In the manuscript, the author states that hypoglycemic action does not necessarily reduce cardiovascular risk in type 2 diabetic patients. The manuscript is well written and can be helpful for the readers to ameliorate the diagnostic and therapeutic approach for this scenario. The author's manuscript is complete, but it can be reduced appropriately.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Authors: We are grateful to the Science Editor for the valuable comments. Based on the Science Editor's comment, the manuscript has been shortened.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Cardiology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Authors: We are grateful to the Company Editor-in-Chief for the valuable comments. The figures have been prepared using the PowerPoint and the original figure documents have been uploaded via the submission system.