

December 11, 2023

Prof. Lu Cai

The Editor-in-Chief

World Journal of Diabetes

Dear Editor,

I would like to thank you and the reviewers for your concise and helpful comments and suggestions.

I will re-submit my revised manuscript entitled "The Effects of Tai Chi in Diabetes Patients: Insights from Recent Research" to *World Journal of Diabetes*.

According to the reviewers' comments, I completely corrected our manuscript. I will show you the list of modifications on the following pages. All the changes made to the manuscript appear as highlighted text in yellow. I appreciate your re-consideration for the publication of my revised manuscript in your journal.

I look forward to hearing from you at your earliest convenience.

Sincerely,

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The List of Modification

Reviewer #1.

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors wrote a quite interesting review on Tai Chi and diabetes. This is generally of interest. Following things should be addressed and the authors should improve the paper. The authors should discuss the importance of foods and lifestyle in combination with Tai Chi. That can improve impact. Indeed there are many environmental, dietary, and lifestyle factors that influence the metabolic mechanisms. The authors should discuss factors other than exercise and diet, such as smoking, alcohol, obesity, bowel habits, etc. There are also influences of gene-by-environment interactions, which should be discussed. In these lines, research on dietary / lifestyle factors, and personalized disease biomarkers is needed for prevention and treatment research. The authors should discuss molecular pathological epidemiology research that can investigate those factors combined with Tai Chi in relation to molecular pathologies and clinical outcomes. Molecular pathological epidemiology research can be a promising direction as discussed in Ann Rev Pathol 2019, Curr Colorectal Cancer Rep 2017, Gut 2022, etc.

Thank you very much for your suggestions.

As per your suggestions, the author has added the following text to the discussion:

“The molecular mechanisms underlying the effects of Tai Chi on noncommunicable diseases (NCDs) remain unclear. However, recent research provides valuable insights that helped elucidate the benefits of Tai Chi in patients with diabetes. Tai Chi exercise has reduced epicardial adipose tissue volume and heart rate by inactivating the mitogen-activated protein kinase/extracellular signal-regulated kinase pathway, along with an increase in serum miR-126 levels in patients with coronary heart disease [21]. Additionally, Tai Chi influences specific gene expression involved in neutrophil activation, T-cell activation, and the Nod-like receptor signaling pathway in patients with

Parkinson's disease. The key candidate genes play a role in modulating peripheral immunity and inflammation [22]. A recent study revealed that Tai Chi intervention reduced the expressions of inflammatory factors, including Never in Mitosis A-related Kinase 7, nucleotide-binding domain, leucine-rich-containing family, pyrin domain-containing-3, reactive oxygen species, nuclear factor-kappa B, and IL-1 β in individuals with prediabetes [23]. Further, Tai Chi exercises may induce beneficial epigenetic changes [24]. Furthermore, Tai Chi may modulate the autonomic nervous system and the hypothalamus-pituitary-adrenal axis, providing potential therapeutic effects on depression, mood disorders, stress, and gut dysbiosis [25-29] (Figure 1).

However, the effect of gene-environment interactions is likely substantial, considering the etiology of complex diseases, such as diabetes, making the combined effects of environmental and lifestyle factor assessment essential along with Tai Chi on metabolic mechanisms [30]. The combination of a healthy diet, nonsmoking habits, and appropriate alcohol intake with Tai Chi practice demonstrated potential for improving health outcomes in patients with diabetes in terms of the exercise aspect of Tai Chi. No studies directly compare the effectiveness of Tai Chi with these lifestyle factors on a one-to-one basis, while holistic lifestyle interventions are crucial for addressing metabolic disturbances and improving the prognosis of patients with diabetes [31-33]. Moreover, abnormal bowel health, such as chronic diarrhea or constipation, is associated with an increased risk of cancer, CV diseases, and diabetes. Chronic constipation contributes to a higher risk of CV mortality (hazard ratio = 1.698; 95% CI, 1.144 to 2.520) [34]. Indeed, high-fiber diets have improved glycemic control and insulin sensitivity, thereby decreasing all-cause mortality (risk ratio = 0.55; 95% CI, 0.35 to 0.86) when comparing the highest with the lowest fiber intakes [35]. In summary, Tai Chi exercise should be integrated with various lifestyle modifications to improve the management of patients with diabetes.

Molecular pathological epidemiology (MPE) research, which investigates the combined effects of Tai Chi in association with molecular pathologies and clinical outcomes, demonstrates the potential for elucidating the biological mechanisms of Tai Chi in the

human body. Traditional epidemiological studies may underestimate true associations between diet, physical activity, smoking, drinking habits, and other lifestyle-related factors concerning molecular markers of genetic pathways and NCD risk. In contrast, MPE studies can help determine the association of such factors with the risk of colorectal cancer [36] and the relationship of host and microbial tryptophan metabolites with T2D risk [37]. The MPE research paradigm not only provides future perspectives on the dynamics among the environment, NCDs, and hosts but also introduces new areas for investigation. Emerging advancements, including computational digital pathology, systems biology, big data analytics, and artificial intelligence, will continue to revolutionize the fields of pathology and MPE [38]. This approach offers a promising direction for fully investigating the effects of Tai Chi on patients with diabetes.”

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The form of tables need to be improved.

I appreciate the time and effort that was invested in reading the manuscript.

In accordance with your comment, the author increased the width of the table and added line breaks where necessary to improve the readability.

Reviewer No. 2446525

Language correction required.

Thank you for your time and effort for reading the manuscript.

The manuscript has been carefully reviewed by an experienced editor whose first language is English and who specializes in editing papers written by scientists whose native language is not English.