

Dear Dr. Ma and the reviewers of *World Journal of Clinical Cases*,

Thank you very much for your decision letter and additional advice on our manuscript (Manuscript NO: 59340) entitled “Metabolic syndrome, ApoE genotype, and cognitive dysfunction in an elderly population: a single-center, case-control study”. We also thank the reviewers for their review of our revised manuscript and further comments. We are pleased to have the opportunity to address their additional concerns, and as before, all amendments are indicated by red font in the revised manuscript. In addition, our point-by-point responses to the latest comments are listed below this letter.

This revised manuscript has again been edited and proofread by *Medjaden Bioscience Limited*.

We hope that this further revised draft of the manuscript is now acceptable for publication in your journal and look forward to hearing from you soon.

With best wishes,

Yours sincerely,

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First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1

Reviewer #1:

Specific Comments to Authors:

1) Polymorphism research was done by PCR-RFLP. Was there confirmation by sequencing (random selection of some samples)?

Response: Thanks for your comments. In this study, the restriction endonuclease was used to cut PCR products. Electrophoresis was used to evaluate the combined bands and to determine the genotype. Therefore, sequencing was not performed.

2) It is not clear to me whether the Hardy-Weinberg balance was assessed. If not, I think it is necessary.

Response: Thanks for your comments. All the samples in this study were from the Chinese Han population, which is relatively stable in northern China. Therefore, the Hardy Weinberg balance analysis was not performed to evaluate genetic stability and/or balance.

Reviewer #2:

Specific Comments to Authors: The authors performed repeated data collection after one year. I think this-like repeated ANOVA measurement was for increasing validity, not for cohort evaluation. Because one year follow-up for cognitive deterioration is too short to evaluate. So, your study was not enough to designate cohort study. I suggest you should discard the expression of cohort in the Conclusion (page 20). See "In conclusion, the results of our study showed ~~~ in our cohort of ~~Chinese individuals."

Response: Thanks for your comments. We have reworded the sentence to remove the term "cohort" from the Conclusion accordingly.

Reviewer #3:

Specific Comments to Authors: Dear author thank you for submitting your manuscript in the journal. The important points regarding your manuscript are as follow- 1. The title of the article "Metabolic syndrome, ApoE genotype, and cognitive dysfunction in an elderly population: a single-center, case-control study" very aptly reflected the main subject. 2. Abstract was giving the good insights about the main manuscript. 3. As the author found diagnosis with MetS and ApoE ϵ 4 carrier status were potential risk factors related to cognitive dysfunction in an elderly population in China. Though the association was already studied, why the author think about this in old age. How this study helpful in treating cognitive disorders in old age if early preventive measures had not be taken?

Response: Thanks for your comments. We believe that the impairment of cognitive function caused by various aspects of metabolic syndrome (MetS) is a continuous process.

Aging-related cognitive impairment in the elderly is also affected by the coexistence of MetS. Therefore, it is still of practical significance to evaluate the relationship between MetS and cognitive impairment in the elderly. At the same time, in real-world medical practice, interventions targeting various components of MetS could be beneficial for improving patient health, including cognitive function.

Reviewer #4:

Specific Comments to Authors: I want to ask the authors what are the original findings in this manuscript? What are the new methods proposed in this study? What are the important issues that this study has solved? What is the clinical contribution of this study to geriatrics?

Response: Thanks for your comments. Although effects of the MetS and ApoE ϵ 4 allele on cognitive function have been suggested in previous studies, these results were mainly derived from general populations, rather than the elderly. We focused on the influence of these two factors on cognitive decline in the elderly, where cognitive dysfunction is common. Elderly populations were rarely evaluated in previous studies. We also followed the elderly patients included in this study for up to one year, which enabled us to dynamically evaluate cognitive function, and to further clarify the continuous effects of MetS and ApoE ϵ 4 alleles on cognitive function, which were also rarely reported. For these reasons, we believe that our study could add some new evidence regarding the effects of MetS and ApoE ϵ 4 allele on

cognitive function in the elderly.

Reviewer #5:

Specific Comments to Authors:

1- why you didnot divide geriatric patients in to groups according to their age .ie older old, old,

Response: Thanks for your comments. We did not further divide geriatric patients into groups according to age because the total number of patients was limited. Moreover, further stratification of the included elderly patients according to age may have led to an imbalance of baseline characteristics within each subgroup, which could have confounded the results of subgroup analysis.

2- it is applicable to include another non geriatric group to your research.

Response: Thanks for your comments. This study was designed for the elderly in China, and the non-elderly population was excluded. However, we agree with the reviewer that studies evaluating the effect of age on the association among MetS, ApoE ε4, and cognitive function deserves further investigation.

3- the small sample size and single center study is another issue

Response: Thanks for your comments. We have acknowledged these limitations in the revised manuscript. Our results should be validated in large-scale multicenter studies.

4- language and grammar need polishing

Response: Thanks for your comments. The revised manuscript has been proofread by Medjaden Bioscience Limited to improve the English.