Author’s response to reviews

Title: Association of insulin, C-peptide and blood lipid patterns in patients with impaired glucose regulation

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Author’s response to reviews:

A point-by-point response letter must accompany your revised manuscript. This letter must provide a detailed response to each reviewer/editorial point raised, describing exactly what amendments have been made to the manuscript text and where these can be viewed (e.g. Methods section, line 12, page 5). Please also ensure that all changes to the manuscript are indicated in the text by highlighting or using track changes. If you disagree with any comments raised, please provide a detailed rebuttal to help explain and justify your decision.

Editor Comments:
We found it necessary to approach an additional reviewer regarding your revised manuscript, and unfortunately, they have raised several additional points that we would ask you to address. Please be
Response: We have now had the manuscript edited and grammar checked by a professor at Oxford University who is an expert in this field of study.

We thank the reviewers for their very helpful comments, which have all been incorporated in the revised manuscript.

Reviewer reports:

Fernando Bril (Reviewer 3): In a large cohort (n=354) of patients with T2DM, prediabetes, or normal glucose tolerance (NGT), Wang et al assessed the changes that occurred in plasma glucose, insulin and c-peptide during an OGTT, as well as changes in the lipid panel. Their main findings were that patients with prediabetes and T2DM had similar abnormalities in the lipid panel, and that patients with T2DM had blunted insulin secretion during the OGTT compared to patients with prediabetes.

The main issues to consider are the following:

1- Lack of Novelty: what does this study add to the vast amount of literature on the metabolic response of patients with NGT vs. IFG vs. IGT vs. T2DM? This issue has been extensively addressed in the past and it is not clear why the authors believe their study is different from the prior literature. Response: Since considerable racial differences regarding insulin sensitivity even within Asians have been reported, the present study represents a ‘snap shot’ of the current state in China. We added this information to the Background with a new reference in the revised manuscript. (Background section, line 13-15, page 4)

2- Grammar: it should be revised to clarify many sentences along the manuscript. Response: The manuscript has now been edited by a native English speaker at Oxford University who is an expert in this field (vide supra).

3- Lack of information on medications: no information is provided regarding use of diabetes medications, insulin, statins, fibrates, etc. This is important as it can affect the results reported. Were any of these medications excluded? Response: Diabetes medication included insulin aspart injections, insulin detemir Injections (Novo Nordisk Pharmaceutical Co. Ltd.), insulin glargine injections, glimepiride and alogliptin benzoate tablets (Sanofi Pharmaceutical Co. Ltd.), metformin hydrochloride extended release tablets (Merck Pharmaceutical Co. Ltd.) and acarbose tablets (Bayer HealthCare Co. Ltd.). No statins and fibrates were used. We have added this new information to the Methods section in the revised manuscript. (Method section, line 6-11, page 6)

4- More information regarding patient recruitment should be provided. Specifically, how were these patients recruited? Are they a good representation of the overall population? Response: In our study, all participants came to our hospital for physical examination and the diabetes group met the WHO diabetes diagnostic criteria. T2DM patients aged between 55-65 years are a good representation of the overall population, since according to the Centers for Disease Control and Prevention (CDC) most diabetes cases are diagnosed in individuals aged 45 and 64 years old. However, patients with type 1 diabetes, secondary diabetes, primary disease of the heart, brain or kidney, various acute chronic infectious diseases, endocrine disorders or with serious systemic diseases such as malignant tumors were excluded from the study. In addition, written, informed consent was obtained from all participants prior to being enrolled in the study. (Method section, line 1-6, page 6)
5- Use of a glucose-lowering agent does not appear described in the manuscript as a criterium for diabetes.
Response: Glucose-lowering agents were only prescribed for patients who met the WHO diabetes diagnostic criteria already. In the case of hyperglycemia, OGTT and islet release tests were performed when blood glucose control was close to normal. No medication was taken before the OGTT and no prolactin was used 1 week before the examination. We have added the last sentence to the Methods section in the revised manuscript. (Method section, line 11-12, page 6)

6- No information is provided regarding the methodologies used to measure insulin and c-peptide.
Response: Electroluminescence was used to measure insulin and C-peptide (Roche Cobas 6000 Automatic Electrochemical Luminescence Analyzer).
We have added this information to the biochemical index detection section of the revised manuscript. (Method section, line 20-22, page 7)

7- Measures of insulin resistance were calculated based on fasting information (HOMA-IR or QUICKI) despite the fact that an OGTT was performed. Better IR measurements, such as Matsuda Index could be used.
Response: We calculated the Matsuda indices and added the new data to Table 1 in the revised manuscript.