Author’s response to reviews

Title: Association of kidney function-related dietary pattern, weight status, and cardiovascular risk factors with severity of impaired kidney function in middle-aged and older adults with chronic kidney disease: a cross-sectional population study

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Author’s response to reviews:

Dear Dr. Clare Collins,

We have revised throughout the manuscript (NUTJ-D-18-00363) entitled “Association of kidney function-related dietary pattern, weight status, and cardiovascular risk factors with severity of impaired kidney function in middle-aged and older adults with chronic kidney disease: a cross-sectional population study” according to the editor’s comments and suggestions. If you have any questions, please feel free to call me at +886-2-2736-1661 ext. 6548. I am looking forward to your response.

Sincerely,

Jane C.-J. Chao, Ph.D., Professor (corresponding author)
RESPOND TO THE EDITOR on January 9th, 2019

1. Please include a Conclusions section (with subtitle) as the last section of the text. This should state clearly the main conclusions of the research and give a clear explanation of their importance and relevance. Summary illustrations may be included.
   Reply: We have revised accordingly.

RESPOND TO THE EDITOR on December 1st, 2018

1. The objectives are not clearly stated.
   Reply: We have revised and mentioned our aims more clearly in the text (lines 93-101) as follows:

   Additionally, compared with other methods for deriving dietary patterns such as principal component analysis (PCA), the RRR-derived dietary pattern is more likely to be associated with health-related outcomes. To our knowledge, there is no study using the RRR method to derive dietary patterns which are associated with kidney function. Therefore, the aims of the present study are to (1) investigate the association of abnormal weight status and cardiovascular risk factors with the severity of impaired kidney function and (2) identify whether RRR-derived kidney function-related dietary pattern is associated with abnormal weight status, cardiovascular risk factors, and severity of impaired kidney function among middle-aged and older participants with CKD.

2. The timeline is rather unclear: the title states that it is a cross-sectional study, yet the authors use the words "progression of kidney disease" / "progression from mildly to moderately/severely impaired kidney function" which implies a follow-up.
   Reply: Our study was a cross-sectional study. We used the words “progression from mildly to moderately/severely impaired kidney function” originally because we investigated whether the dietary pattern could predict the progression to advanced impaired kidney function. However, we understand that using the word “progression” can lead to misunderstanding, which implies further follow-up. Therefore, we revised and used the words “moderately/severely impaired kidney function” or “predict moderately/severely impaired kidney function” throughout the text.

3. In the methods, authors talk about "a series of health check-up" but no more information is given.
   Reply: We have added the information about the health check-up in more details in the manuscript (lines 108-111) as follows:

All the participants had a series of health check-up including anthropometric assessment, blood tests, stool and urine tests, physical examination, and completed a self-reported questionnaire to collect information about sociodemographic, lifestyle, medical history as well as dietary habits.

4. The method of the RRR should be explained in more details. How can the food group explain >100% of the cumulative variation (l.240)? Also how is the % explained variance presented in Table 3 calculated?
   Reply: We have added the information about RRR method in more details in the manuscript as follows: (lines 84-95) The RRR method is a multivariate linear regression method where it combines a priori...
and a posteriori approaches to derive dietary patterns. Recently, the RRR method has been widely used to assess dietary patterns in several studies. By using the RRR method, the researcher is able to identify a linear combination of the predictor variables, select response variables, and find dietary patterns related to the disease of interest. The predictor variables refer to the food groups, which are derived from food frequency questionnaire (FFQ). The response variables refer to the nutrients or blood biomarkers associated with the disease based on prior knowledge about the relationship of specific biomarkers or nutrients in predicting the disease. Additionally, compared with other methods for deriving dietary patterns such as principal component analysis (PCA), the RRR-derived dietary pattern is more likely to be associated with health-related outcomes.

The RRR method focuses on identifying linear functions of food groups, which explained as much variation as possible in a set of intermediate response variables.

The RRR method allows researchers to identify the explained variation for each food group and it shows the percentage of variation already explained by each food group corresponding to the response variables. The explained variation of each food group would contribute to the factor loading in each pattern. The higher the explained variation in the food group, the higher factor loading was produced by that food group.

The cumulative percentage of variation explained by the RRR-derived kidney function-related dietary pattern was 6.67%. The eight response variables was explained 2.7% for the total variation and largely driven by the explained variation in WHR (6.7%), TC/HDL-C ratio (2.6%), and TG (2.2%).

The food groups containing preserved or processed foods, meat, organ meats, and sauces contributed to a total 64% explained variation in the RRR-derived kidney function-related dietary pattern.

In comparison, PCA focuses only on explaining the total variation in food group consumption and does not provide explanation on the variation in important biomarkers. In addition, RRR method using PROC PLS procedure allows researchers to identify the percentage variation from predictor variables and response variables, which both contributing to the dietary factor. Factor scores extracted by RRR can be evaluated by their corresponding response scores and by the explained variation in predictor variables as well as response variables that should be related to disease of interest. The association between food groups and response variables can also be used to interpret beneficial effects of individual food group as components of predictor variables in the dietary pattern. However, it is not necessary to report explained variation for each food group as a total percentage. The explained variation in each food group shows how many percentage of variation already explained by each food group corresponding to the response variables which both contributing to the explained variation in dietary factor score or factor loading. The higher explained variation in the particular food group, the higher factor loading produced or contributed by that food group to the dietary factor.

5. The value of assessing the association between the dietary pattern derived by RRR and kidney function should only be with validation purpose, but not a result in itself, as the RRR is designed to identify a dietary pattern associated with kidney function. Reply: We considered to put the value of assessing the association between dietary pattern derived by RRR and kidney function because we would like to know whether the type of dietary pattern can
predict the severity of impaired kidney function or not. Several previous studies also addressed the same way in reporting their findings. Several studies have investigated the association between RRR-derived dietary pattern with type 2 diabetes mellitus (T2DM) using response variables that correlated with T2DM, such as adiponectin, HDL-C, triglyceride, HbA1c, fasting glucose, HOMA-IR, and C-reactive protein [1-3]. Additionally, study in Northern German have used RRR method to identify the dietary pattern related to metabolic syndrome (MetS) using response variables that associated with MetS, such as waist circumference, HDL-C, HbA1c, and blood pressure [4]. A recent published study by Hu et al. also used RRR to identify the association between testosterone-associated dietary pattern and low testosterone levels and hypogonadism [5]. In the present study, we found that RRR-derived kidney function-related dietary pattern not only had a positive association for predicting the severity of impaired kidney function but also had a positive association with abnormal weight status and cardiovascular risk factors.

6. The discussion lacks focus, and the limitation section should be developed.
Reply: We have added some information in the discussion section. Our main findings were (1) abnormal weight status and all cardiovascular risk factors were positively correlated with the severity of impaired kidney function and (2) RRR-derived kidney function-related dietary pattern was correlated with increased risk of abnormality of weight status and cardiovascular risk factors as well as the severity of impaired kidney function. Therefore, we discussed each main finding in the discussion section.

(lines 256-281) We discussed about the association between RRR-derived kidney function-related dietary pattern and weight status. (lines 282-306) We discussed about the association between RRR-derived kidney function-related dietary pattern and cardiovascular risk factors. (lines 307-317) We discussed about the association between RRR-derived kidney function-related dietary pattern and the severity of impaired kidney function. Lastly, (lines 318-337) we discussed that abnormal weight status and cardiovascular risk factors could lead to a high risk for developing the severity of impaired kidney function.

We have added some of limitations in our study (lines 361-370) as follows:
Fourth, clinical definition of CKD is either decreased kidney function (eGFR < 60 mL/min/1.73 m2) in the absence of persistent albuminuria or having kidney damage (albumin-creatinine ratio > 30 mg/g), which presents for 3 months or more. Although, MJ Health Institute provided periodic health check-up (mostly one examination per year per person) for its members, not all the participants had annual examination and the clinically diagnosis of CKD cannot be made based on single measurement only. Therefore, the results found in this study may not reflect with the clinically diagnosed CKD participants. Finally, we have adjusted our results with some potential confounders. However, there are still some confounders that should be considered in the future study such as energy and protein intake and the use of renal medications, which can influence the findings of the present study.

7. Overall, the language needs extensive revision (grammar, tenses, inadequate use of causal language).
Reply: We have asked someone who is fluent in English to review our manuscript and revised it throughout the manuscript.

References

