Title: Dietary inflammatory index: a potent association with cardiovascular risk factors among patients candidate for coronary artery bypass grafting (CABG) surgery

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Author’s response to reviews:

Dear Professor Leah Cahill

I hope you are well and thanks a lot for your close attention to our submitted article. Following is our response to the reviewer’s comments. The comments by reviewers are presented in black color and the responses from the authors are presented in blue color. The comments which were given alongside the papers of the manuscript have been corrected and marked with yellow color. Moreover, we revised all of the manuscript for grammatical and typological errors and they are highlighted with yellow color too. I hope that these corrections will be acceptable for you and I did not miss this great opportunity to publish my manuscript in the valuable journal of “Nutrition Journal”.

Yours sincerely,

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Best wishes,
Reviewer reports

Reviewer #1

1) The power of DII to predict CVD risk factors cannot be inferred from a cross-sectional study, especially in a patient population with pre-existing CVD and multiple other comorbidities. A cross-sectional study can only demonstrate presence of an association. The power of DII to predict CVD would have to be demonstrated with a prospective cohort study. Hence, the manuscript title and conclusion have to be revised.

Action or explanation: Thank you for your comment. The correction has been made and the word “prediction” for DII has been omitted throughout the manuscript.

2) Abstract

a. Missing information about statistical methods.

Action or explanation: The correction has been made as requested.

b. No mention of the heart failure risk scores (NYHA, Euro SCORE, etc.) in methods

Action or explanation: The correction has been made as requested. The detailed explanations of the clinical assessments were also added into the Methods in the body of the manuscript.

c. Multiple acronyms without definitions (e.g.: MI, HCT)

Action or explanation: The corrections have been made as requested. All of the abbreviations have been corrected and defined in their first appearance in the text.

3) Introduction

a. The first sentence is outright wrong. Iran has only 1% of the world’s population. How can 50% of all CVD deaths occur in Iran?

Action or explanation: The sentence has been corrected to resolve this misunderstanding. In fact, the CAD, is accounted for more than 50% of deaths per year in Iran.

b. The sentence on l. 13 starts with a reference to a "mechanism", but no description of any mechanism follows. Instead, the authors list a number of loosely related associations between C-reactive protein, cytokines, adipose tissue, and insulin.

Action or explanation: This section has been fully replaced with a paragraph to better identify the underlying mechanisms.

c. Missing a clearly stated hypothesis
Action or explanation: The hypothesis has been clearly mentioned in the final part of the introduction.

d. Could be strengthened by a discussion of the practical application of DII in CABG patients (e.g.: counseling, post-operative risk assessment)

Action or explanation: The possible practical applications of DII has been explained in the introduction and is highlighted.

4) Methods:

a. Missing explanation of the heart failure risk scores (EuroSCORE, NYHA, etc.)

Action or explanation: The detailed explanations of the clinical assessments were also added into the Methods in the body of the manuscript.

b. The description of statistical analysis is unclear. The authors mention conducting three tests (t-test, Mann-Whitney, logistical regression), but do not specify which test was applied to which variables. Also, were the statistical tests corrected for multiple comparisons?

Action or explanation: The statistical analysis in the methods section and also in the abstract has been modified and was explained in detail. However, about the multiple comparisons, our hypothesis in the current work was to assess the association between DII and cardiovascular risk factors among patients candidate for CABG. Therefore we applied all of our analytical procedures according to these hypotheses. For multiple comparisons, the Bonferroni correction is a conservative test and increases the probability of type II error. We also applied MANOVA test (multivariate analysis of variance) adjusting for confounders and no meaningful change has been occurred. We will respect to the reviewers’ request and if they insist to present the results of multiple comparisons, we apply it.

5) Discussion:

a. Fails to follow a clear logic. The authors support their findings with similar studies pointing to an association between inflammation and CVD comorbidities (impaired kidney function, diabetes), but fail to address the question of causality: is inflammation a cause or an effect of these conditions?

Action or explanation: The correction has been made. A complete paragraph for detailed explanation of the causality between inflammation and chronic disease has been added into the discussion.

b. The entire section on the impact of BMI on post-operative survival is irrelevant.

Action or explanation: The entire paragraph had been replaced to better identify and explain the observed association between DII and BMI relying to consistent studies.
c. Missing description of study strengths and limitations

Action or explanation: The correction had been made as requested. The limitation and strengths of the study has been explained in a paragraph in the final part of the discussion before conclusion.

6) Throughout the manuscript:

a. Wrong use of punctuation, poor word choice, numerous grammatical and syntactic errors

Action or explanation: The correction has been made as requested. The manuscript has been revised deeply for any grammatical and syntactic errors.

b. Line numbers are not aligned with the lines. It is very difficult to make line-specific comments.

Action or explanation: The correction has been made as requested. Line and page numbers were inserted.

c. Missing references (e.g.: l. 25, 29)

Action or explanation: The references were corrected and revised completely.

7) Figures:

a. Missing indices of statistical significance

Action or explanation: The correction has been made as requested.

b. Perfunctory figure legends

Action or explanation: The correction has been made as requested. The abbreviations, level of significance and other details were added into the figure legends.

Reviewer #2

Reviewer comments

1) MI should be expanded as myocardial infarction in the abstract.

Action or explanation: The correction has been made as requested.

2) Page 7, line 45: The dietary inflammatory index was calculated based on literature review of six inflammatory biomarkers: IL-1β, IL-4, IL-6, IL-10, TNF-α and CRP. What was the method used to determine these inflammatory markers. Authors should specify in the manuscript.
Action or explanation: The cause of choosing the above-mentioned inflammatory molecules and also the detailed explanation of the scoring algorithm has been added in the discussion.