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Identifying novel metabolite biomarkers of adherence to a cluster analysis-derived healthy dietary pattern

Shirin Macias[1], Dr. Brian D. Green[1] and Prof. Jayne V. Woodside[1,2]

[1]*Institute for Global Food Security, Queen's University Belfast, Belfast, UK, Belfast, United Kingdom and* [2]*Centre for Public Health, Queen's University Belfast, Belfast, United Kingdom*

Abstract

The MEDDINI intervention study investigated how advice improved the adoption of a Mediterranean diet (MD) in cardiovascular disease patients. Earlier research profiled the levels of blood metabolites in MEDDINI participants, in the process discovering a number dietary biomarkers indicative of a MD. However, a potential limitation of this approach is that MD scores are semi-quantitative, and don't reflect the absolute amounts of food consumed. Therefore, the present study identified distinct dietary patterns based on quantified food diary data from 58 MEDDINI participants by applying k-means clustering analysis. Previously measured blood metabolites (90) using targeted and untargeted methods were then assessed for their performance as dietary biomarkers. After careful standardisation (z-scores), optimisation and cross-validation dietary data were reduced to 6 specific food groups and this led to the formation of two clusters. Cluster 1 included participants who had the lowest intakes of fruit and vegetables, legumes, fish and whole grain cereals and the highest intake of meat and sweet foods (including carbonated drinks). Cluster 2 comprised the participants with highest intake of fruit and vegetables, legumes, fish and whole grain cereals and the lowest intake of meat and sweet foods (including carbonated drinks). Discriminatory metabolites (p derived from untargeted analysis included Citric acid, Tyrosine, Malonate, Pyroglutamic acid, Succinate, Betaine, L-asparagine and Fumaric acid which were significantly increased in cluster 2, and 2-Hydroxybutyric acid and Pyruvic acid which were significantly decreased in cluster 2. Targeted biomarker analysis showed 8 discriminatory metabolites which were significantly (p increased in cluster 2. These were Docosahexaenoic acid (DHA), alpha-Carotene, beta-Carotene, beta-Cryptoxanthin, Vitamin C, Lutein, alpha-Linolenic acid and Lycopene. Conversely Osbond acid, Cholesterol *and* Dihomo-γ-linolenic acid (DGLA) were significantly lower in cluster 2. Metabolites significantly correlated with some of the 6 groups in the clusters. For example, Citric acid, Betaine and Vitamin C positively correlated with combined fruit, fruit juice and vegetable intake: ($r = 0.20$, $p = 0.018$; $r = 0.20$, $p = 0.02$ and $r = 0.34$, $p = 5.7E\text{-}5$ respectively). DHA, alpha-Carotenoid and beta-Carotenoid significantly correlated with fish intake ($r = 0.58$, $p = 1.94E\text{-}13$; $r = 0.40$, $p = 2E\text{-}6$ and $r = 0.30$, $p = 3.5E\text{-}4$ respectively). The present study demonstrates the utility of clustering analysis for effectively assessing adherence to healthy dietary patterns and the discovery of novel dietary biomarkers.

Conflict of Interest

There is no conflict of interest