

DEFINITIONS OF MEDITERRANEAN DIET INCONSISTENTLY ASSOCIATE WITH MARKERS OF GUT BARRIER FUNCTION OR SUBCLINICAL INFLAMMATION IN A POPULATION-BASED COHORT

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Background: The Mediterranean Diet (MD) is proposed to reduce the risk of Crohn's disease (CD) onset in cohort studies, with inconsistent results. This inconsistency may be due to heterogeneity in defining MD scores. Additionally, relationships between MD compliance and intestinal permeability or sub-clinical inflammation are not defined.

Aims: We examined correlations between different MD scores, and determined associations between MD compliance and intestinal permeability or subclinical inflammation in a cohort of first degree relatives of CD patients.

Methods: We used food frequency questionnaire data from 2,112 subjects of the Crohn's Colitis Canada- Genes, Environment, Microbial (CCC-GEM) project. We obtained 12 MD definitions from the literature and calculated daily percent compliance, we further compared MD scores via pairwise correlations (Kendall's Tau). We measured intestinal permeability via urinary fractional excretion ratio of lactulose to mannitol (LMR) (LMR \geq 0.03 defined abnormal), and subclinical inflammation via fecal calprotectin (FCP) measured with BÜHLMANN fCAL® ELISA (FCP \geq 250 defined abnormal). We fit multivariable regression models between MD compliance and abnormal LMR and FCP, respectively. Two-sided p $<$ 0.05 defined significance.

Results: There was large variation in cross-correlations among MD scores, from nil (t=0.0, p=0.54) to highly significant (t=0.97, p $<$ 2.2e-16). Associations of MD compliance and abnormal LMR or FCP were in both directions of effect, largely non-significant. Of the 12 MD scores, none associated with abnormal LMR, while 4 associated with abnormal FCP-Odds Ratios =1.22, 1.23, 1.24, and 1.30; p=0.02, 0.02, 0.01, and 0.009, and 95% Confidence Intervals = [1.03,1.45], [1.04,1.45], [1.05,1.47], and [1.07,1.59] respectively. No diet remained significant after correcting for multiple testing.

Conclusions: Currently MD definitions vary widely. Despite discrepancies, we expected consistent directions of effect for MD compliance on LMR or FCP. The largely non-significant

associations between MDs suggest limitations in definition, interpretation, and relation to biological outcomes.

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