Diet-Mediated Heart Disease Risk via the Gut Microbiome

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Overview
A surge in global metabolic and heart disease has paralleled the expansion of the Western diet and lifestyle, giving rise to an epidemic. Though both noncommunicable and largely preventable, atherosclerotic heart disease—especially coronary artery disease (CAD)—continues to rise, necessitating a change in education or public narrative.

In this systematic review, we examined twenty-two randomized controlled trials using human diet intervention to elucidate the effects of specific foods and food groups on biomarkers of atherosclerosis and associated gut microbiome shifts. To identify current gaps and potential targets of diet education in the microbiome context, we used the heart-healthy guidelines from the American Heart Association (AHA) for reference.

Heart Disease Death Rates, 2018 - 2020
Adults, Ages 35+, by County

Methods
- Search conducted until June 20, 2023, via PubMed, CINAHL, and Embase
- Eligibility criteria:
  - Randomized controlled or clinical trials
  - Human subjects aged 18-85 years old, healthy or exhibiting subclinical disease manifestations
  - Diet intervention consisting of one food or food group
  - Fecal samples were collected and analyzed
  - Cardiometabolic markers were measured (short chain fatty acids, inflammatory / immune markers, and cholesterol)
- Twenty-two articles included from 605 initial results on the basis of inclusion and exclusion criteria
  - Exclusion criteria: n>15, whole-diet alterations (e.g. Mediterranean diet), lack of washout period, frequent populations, history of disease that could cause dysbiosis

Results
- Probiotics:
  - Fermented dairy decreased low-density lipoprotein (LDL) and total cholesterol while increasing short chain fatty acid (SCFA) production, especially butyrate
- Prebiotics:
  - Dietary fiber and whole grains tended to reduce inflammatory markers, C-reactive protein (CRP) and interleukin-6 (IL-6), especially when compared to refined grain
  - SCFA and blood lipid changes were variable
- Processed foods:
  - NOVA grades 3 and 4 tended to exhibit pro-inflammatory, pro-cholesterol, and anti-SCFA effects, especially when fiber was artificially removed (commercial fruit juices)
  - Interindividual variability of microbiota shifts prevalent
- NO trial was powered to detect significance at the metagenomic level, but trends were seen throughout
  - Cardiac health correlated with Bifidobacterium genus
  - Positive effects: Parabacteroides, Lachnospira, Roseburia, Ruminococcaceae and Faecalibacterium
  - Negative effects: Victivallaeaceae, Butyricococcus, Erysipelatoclostridium ramosum, Flavonifractor and Ruminococcus

Discussion
NOVA group 3 processed foods in the form of refined grain products had greater negative effect on cardiometabolic health than whole grains did positive. In crossover studies with refined grains used as control, improvements in whole grain treatments were attributed to worsening markers in the control group from baseline. Yet refined grains have shown no significant effects on cardiovascular risk in prospective cohort studies. This may suggest that the gut microbiome is an important mediator in our studies since those that altered SCFAs had the greatest results. Previous research has established a protective effect of these molecules against systemic inflammation and cancer in humans, while others revealed protective cardiovascular effects in hypertensive mice.

Interindividual variability in microbiome shifts appear to be partially dependent on subject comorbidities. This is in keeping with previous studies that indicate a large potential for use of diet modification in patients with cardiac-related dysbiosis to improve vascular health. Increasing gut permeability decreases endotoxemia which predisposes arterial plaque, and some studies have found that pathogenic bacteria are a common denominator in cultures of atherosclerotic plaque.

Though our findings are mostly in keeping with the AHA heart-healthy guidelines, it is evident that a shift is needed to account for the burgeoning microbiome research. The rapid expansion in gut microbiome research serves as a reminder of the intricate connectedness of organ systems which requires a holistic approach to improve health-span.

References

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