TREATMENT GUIDE FOR PHYSICIANS

Cardiovascular Conditions

OVERVIEW

Cardiovascular disease is the leading cause of death worldwide. Risk factors include obesity, diabetes, hypertension, high cholesterol, and genetic predisposition. Current treatment includes prevention through dietary and lifestyle changes, as well as medications and surgical intervention as needed.

Growing evidence suggests that the gut microbiome is associated with cardiovascular disease (CVD). In particular, certain bacterial populations appear to produce TMA (trimethylamine) which is then converted to trimethylamine oxide (TMAO) in the liver; TMAO may impact cholesterol metabolism and atherosclerosis, leading to increased risk of myocardial infarction, stroke, and premature death.

Cardiovascular disease treatment and prevention may benefit from interventions targeted at the human microbiome [1-5]. Please refer to the Metabolic Disorders Treatment Guides (hyperlink) for more information on related conditions.

INDICATIONS FOR SMARTGUT TESTING

• Elevated cardiovascular disease risk >10% based on Framingham Risk Score or Atherosclerotic Cardiovascular Disease (ASCVD) Risk Assessment Score
• Risk factors for CVD including: family history of CVD, personal history of smoking, hypertension, dyslipidemia, diabetes, obesity, or peripheral vascular disease
• Personal history of CVD including prior myocardial infarction or stroke
• Associated symptoms: shortness of breath, angina, heart palpitations, dizziness or lightheadedness, abdominal pain, cold and/or painful legs and feet
SMARTGUT RESULTS ASSOCIATED WITH CVD

- **Low Microbial Diversity:** This parameter is associated with decreased cardiorespiratory fitness [6] as well as increased lifetime CVD risk [8].

- **High levels of the following:** Collinsella [1], and Tyzzerella [8]

- **Low levels of the following:** Roseburia [1], Alloprevotella [8], and Catenibacterium [8]

CLINICAL TREATMENT SUGGESTIONS

**Interventions to Consider:**

- **Prescribe dietary change:** If clinically appropriate, consider avoiding dietary choline and carnitine (found in meat, eggs, and dairy products). These are degraded to TMA which then forms TMAO and is associated with atherosclerosis. Vegans and vegetarians have been found to have lower TMAO levels [3,4,9]; additionally, TMAO levels also decrease significantly in people with higher adherence to a Mediterranean diet [10].

- **Suggest DMB containing foods and drinks:** Studies suggest 3,3-dimethyl-1-butanol (DMB), a structural analog of choline, may inhibit microbial TMA formation. DMB is found naturally in some foods and alcoholic beverages such as red wine, balsamic vinegar, and some cold-pressed extra virgin olive oils and grapeseed oils [11].

- **Increase exercise:** Studies show that exercise improves microbiome diversity. If clinically appropriate, consider incorporating 30 minutes of moderate intensity 5-7 days/week [12].

- **Consider probiotics:** A meta-analysis using 15 different randomized control trials showed that the use of different probiotic sources (e.g. yogurt, fermented milk, capsules) have a positive effect in the reduction of total cholesterol, LDL, and other coexisting risk factors of CVD [15]. While there have been limited clinical studies on dosing and type of probiotic for cardiovascular disease, studies have shown the following to have benefit in weight reduction and/or improved metabolic profile:
  - *Lactobacillus gasseri* SBT 2055 in fermented yogurt: 2 doses of 100g/day of 5 x 10^{10} CFU [16,17].
  - Combination probiotic with *Lactobacillus spp.*, *Bifidobacterium spp.*, and *Streptococcus thermophilus* (VSL#3) [18].
Consider prebiotics: Animal studies have demonstrated that prebiotic fibers improve microbial diversity and beneficial bacteria. The optimal dose of prebiotics is still unknown though studies in humans suggest 10 g inulin/day or 21 g oligofructose/day may be beneficial. Some sources of prebiotic fiber include soybeans; unrefined grains; fruits such as bananas and tomatoes; and vegetables such as asparagus, onion, garlic, beet, artichokes, and leeks [21-24].

Consider synbiotics: If clinically appropriate, a combination of probiotics and prebiotics may reduce CVD risk, including the following interventions:

- Daily consumption of a synbiotic containing $1 \times 10^9$ CFU *L. acidophilus* CHO 220 and 0.20 g of inulin, two capsules twice daily for 6-12 weeks [25].
- Daily consumption of 300 g yogurt containing $10^6-10^8$ CFU *L. acidophilus* 145, $10^3-10^5$ CFU *B. longum* 913, and 1% oligofructose for 7 weeks [26].
- Daily consumption of 125 mL fermented milk containing $10^7-10^8$ CFU *L. acidophilus* and 2.5% fructo-oligosaccharides at breakfast, lunch, and dinner for 3 weeks [27].
- Metabolic profiles in diabetic patients may improve with a combination synbiotic containing $2 \times 10^9$ CFU *L. acidophilus*, $7 \times 10^9$ CFU, *L. casei*, $1.5 \times 10^9$ CFU *L. rhamnosus*, $2 \times 10^8$ CFU *L. bulgaricus*, $2 \times 10^{10}$ CFU *B. breve*, $7 \times 10^9$ CFU *B. longum*, $1.5 \times 10^9$ CFU *S. thermophilus*, and 100 mg fructo-oligosaccharide [19,20].

Recommend eliminating artificial sweeteners: Studies in mice suggest that artificial sweeteners alter the gut microbiota and increase risk of obesity and metabolic disease, increasing potential for cardiovascular disease [28].

Avoid non-steroidal anti-inflammatory drugs (NSAIDs): Studies have shown that the continuous use of a variety of different non-steroidal anti-inflammatory drugs (NSAIDs) are associated with higher risk of CVD [29]. Additionally, NSAIDs can change microbiome composition [30] and can induce damage to gut mucosa [31].

Avoid proton pump inhibitors (PPIs): Studies show these medications may alter the healthy gut microbiome [30,32], and may be associated with increased risk of cardiovascular diseases [33].
POTENTIAL OUTCOMES

• Lowered CVD risk
• Reduced need for medication or surgical intervention
• Decreased related morbidity and mortality
REFERENCES


