



# Vasculogenic Erectile Dysfunction: The Impact of Diet and Lifestyle

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## ABSTRACT

Vasculogenic erectile dysfunction has been aptly called the “canary in the coal mine” for cardiovascular disease because it almost always precedes other manifestations of atherosclerotic cardiovascular disease, including myocardial infarction and stroke. It is common, associated with the presence of modifiable cardiovascular risk factors, and impacted by diet and lifestyle choices. This concise review provides an update on the use of dietary and other lifestyle interventions to improve vasculogenic erectile dysfunction and atherosclerotic cardiovascular disease.

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**KEYWORDS:** Cardiovascular disease; Diet; Erectile dysfunction; Lifestyle

**Funding:** This publication was made possible, in part, by CTSA Grant Number [TL1 TR001864](#) from the National Center for Advancing Translational Science (NCATS), a component of the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NIH.

**Conflicts of Interest:** RJO reports research grants from the Purjes and Greenbaum Foundations, serving as consultant to Better Therapeutics, 2018; a speaker, Main Street Vegan Academy and International Plant-Based Nutrition Healthcare Conference; serving on the board of directors (uncompensated) for the T. Colin Campbell Center for Nutrition Studies; serving on the scientific advisory board (uncompensated) for the Physician Committee for Responsible Medicine; and serving as director, Cardiac Wellness Program, Montefiore Health System. AS reports being the author of the *Penis Book* and serving on the speakers bureaus of AbbVie pharmaceuticals and Metuchen Pharmaceuticals. JO'K reports major ownership interest in CardioTabs. MA reports receiving honoraria for speaking on nutrition, prevention, and cardiovascular disease; receiving royalties from

the book, *Body on Fire*; and her position is partially funded by the Gatorade Foundation. SK reports serving as a consultant for Prime Therapeutics and Amgen; receiving research support for True Health, DSMB Member at Applied Clinical Intelligence; and serving as chair of board of directors at Mayo Clinic Support Services, Texas. DO reports receiving book royalties, lecture honoraria, and licensing fees from Sharecare. AMF reports serving as a consultant for Boehringer-Ingelheim and Actelion; nonpromotional speaking for Boehringer-Ingelheim; serving on advisory boards for Regeneron and The Medicines Company. KEA, KA, EJB, JL, DB, MM, CB, BW, NS, HH, TB, RB, and KR report none

**Authorship:** All authors had access to the data and a role in writing this manuscript.

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## INTRODUCTION

Erectile dysfunction is clinically defined as the inability to attain or maintain a penile erection “sufficient for satisfactory sexual performance.”<sup>1</sup> Estimates of erectile dysfunction prevalence vary widely because of heterogeneity in definitions and survey methods, but as with many other chronic diseases, erectile dysfunction is highly age-dependent.<sup>2</sup>

In the United States, erectile dysfunction has been self-reported in about 15% of men ages 40-59, 45% of those in their 60s, and 70% of those 70 or older.<sup>3</sup> Among 1290 men ages 40-70 years in the Massachusetts Male Ageing Study (MMAS), 52% reported erectile dysfunction.<sup>4</sup> Furthermore, from 40 to 70 years of age, the prevalence of moderate and complete erectile dysfunction doubled (17%-34%) and tripled (5%-15%), respectively.<sup>4</sup>

The causes of erectile dysfunction are broadly categorized as organic, psychogenic, or mixed.<sup>5</sup> Organic etiologies account for 80% of cases, and include vascular, neurogenic, hormonal, or drug-induced.<sup>5,6</sup> Vasculogenic erectile dysfunction now accounts for most organic erectile dysfunction and may be due to abnormalities in penile arterial inflow or venous outflow.<sup>6</sup> Not surprisingly, vasculogenic erectile dysfunction has been associated with both the presence of traditional modifiable cardiovascular risk factors and future atherosclerotic cardiovascular disease events, including myocardial infarction, ischemic stroke, and cardiovascular death.<sup>5,7,8</sup> Furthermore, in a prospective cohort (n = 1913) of men living in Europe and aged 40-79, erectile dysfunction was associated with a 1.40 times higher risk of mortality ( $P = 0.001$ ).<sup>9</sup>

Symptomatic erectile dysfunction frequently precedes other manifestations of atherosclerotic cardiovascular disease, typically developing 2-3 years before the onset of angina and 3-5 years before the development of other cardiovascular events, in part, because penile arteries are smaller in diameter than coronary arteries, approximately 1-2 and 3-4 mm in diameter, respectively.<sup>10</sup> Thus, erectile dysfunction has been aptly called the “canary in the coal mine” for coronary heart disease.<sup>11</sup> Based on these data, “The Princeton III Consensus Recommendations for the Management of Erectile Dysfunction and Cardiovascular Disease” has identified erectile dysfunction as an independent risk factor for cardiovascular disease and recommended screening men with vasculogenic erectile dysfunction for cardiovascular risk.<sup>12</sup>

This review for primary care physicians provides an update on the use of dietary and other lifestyle interventions

to improve vasculogenic erectile dysfunction and, in turn, atherosclerotic cardiovascular disease outcomes.

## MEASURES OF ERECTILE DYSFUNCTION

Several measures have been used to quantify erectile dysfunction. Most clinical studies reviewed here make use of

the abridged, validated 5-item International Index of Erectile Function score. This numerical score is derived from 5 questions on the ability to achieve and maintain an erection and classifies erectile dysfunction into 5 categories: severe (5-7), moderate (8-11), mild to moderate (12-16), mild (17-21), and no erectile dysfunction (22-25) (Table). Other scores, as well as penile Doppler flow, have been developed and validated to measure erectile dysfunction but have been used less in clinical trials.<sup>13,14</sup>

## EFFECTS OF WEIGHT LOSS AND DIETARY INTERVENTIONS ON ERECTILE DYSFUNCTION OUTCOMES

Erectile function appears to improve after: 1) weight loss,<sup>15,16</sup> 2) consuming a Mediterranean dietary pattern rich in plant-based foods, olive oil, nuts, and fish,<sup>17</sup> and 3) consuming more fruits and vegetables.<sup>18</sup>

## Weight Loss Trials

A series of randomized controlled trials has shown positive effects of weight loss on measures of erectile dysfunction. Esposito et al<sup>15</sup> randomized 110 men with erectile dysfunction based on an International Index of Erectile Function-5 score of 21 or less, plus obesity but *no* type 2 diabetes mellitus to active treatment with detailed instruction on weight loss through diet and exercise or to general instruction on diet and exercise. At 2 years, the active treatment arm had significantly greater decreases in mean body mass index (5.7 kg/m<sup>2</sup> vs 0.7 kg/m<sup>2</sup>,  $P < 0.001$ ), serum levels of inflammation, and significantly higher International Index of Erectile Function-5 scores (17 vs 13.6,  $P < 0.008$ ) compared with the control group. Moreover, 17 men in the active arm versus 3 in the control group reported International Index of Erectile Function-5 scores of 22 or higher. In a subsequent study, Esposito et al randomized 209 subjects with or at risk for erectile dysfunction to lifestyle change versus control.<sup>19</sup> The lifestyle changes were weight reduction by >5%, increased monounsaturated fat consumption to ≥10% of calories, increased fiber consumption to >15 g/1000 calories, decreased saturated fat

## CLINICAL SIGNIFICANCE

- Erectile dysfunction is a “canary in the coal mine” warning for increased risk of future atherosclerotic cardiovascular disease events.
- Erectile function can be improved by a healthful dietary pattern, weight loss, physical activity, and smoking cessation.
- A healthier lifestyle may increase nitric oxide synthesis and reduce reactive oxygen species formation, thereby improving erectile function.
- Improving erectile function with lifestyle changes may reduce the risk of future atherosclerotic cardiovascular disease events.

**Table** Definition of International Index of Erectile Function-5 Questionnaire\*

Over the past six months:	Very Low	Low	Moderate	High	Very High
1 How do you rate your <b>confidence</b> that you could get and keep an erection?	1 Almost never/never	2 A few times (much less than half the time)	3 Sometimes (about half the time)	4 Most times (much more than half the time)	5 Almost always/always
2 When you had erections with sexual stimulation, <b>how often</b> were your erections hard enough for penetration?	1 Almost never/never	2 A few times (much less than half the time)	3 Sometimes (about half the time)	4 Most times (much more than half the time)	5 Almost always/always
3 During sexual intercourse, <b>how often</b> were you able to maintain your erection after you had penetrated (entered) your partner?	1 Almost never/never	2 A few times (much less than half the time)	3 Sometimes (about half the time)	4 Most time (much more than half the time)	5 Almost always/always
4 During sexual intercourse, <b>how difficult</b> was it to maintain your erection to completion of intercourse?	1 Extremely difficult	2 Very difficult	3 Difficult	4 Slightly difficult	5 Not difficult
5 When you attempted sexual intercourse, <b>how often</b> was it satisfactory for you?	1 Almost never/never	2 A few times (much less than half the time)	3 Sometimes (about half the time)	4 Most times (much more than half the time)	5 Almost always/always

\*The International Index of Erectile Function-5 (IIEF-5) score is the sum of the ordinal responses to the five items; thus, the score can range from 5 to 25. Reproduced with permission from: JSM. 2000; 11: 319-326.

consumption to <10% of calories, and increased exercise to at least 2.5 h/wk. Control subjects received general guidance on both consuming a healthful diet and increasing physical activity. After 2 years, significantly more subjects in the lifestyle change arm compared to the control arm achieved normal erectile function (increasing from 34% to 56% in the intervention arm compared with 36% to 38% in the control arm,  $P = 0.015$ ). Furthermore, a positive dose-response relationship between lifestyle change and restoration of normal erectile function was also observed.

In an ancillary study of the Look Ahead Trial, Wing et al randomized 306 overweight or obese men with erectile dysfunction and type 2 diabetes mellitus to intensive dietary and exercise counseling aimed at both reducing total calorie and fat consumption and increasing exercise up to 175 minutes per week or to a control group provided only diabetes education and support, which included diet and exercise information.<sup>16</sup> After 1 year, those in the intervention group lost significantly more weight and had a small but significant increase in mean International Index of Erectile Function-5 score (18.6 vs 17.3,  $P < 0.05$ ) compared with the control group, which showed no significant improvement in mean International Index of Erectile Function-5 score.

Collins et al performed a 6-month randomized trial on the impact of weight loss on erectile function in 145 overweight or obese men both with and without erectile dysfunction. The intervention arm participated in a self-help exercise and diet program using information technology, and the control arm received no specific intervention. Overall, the intervention group lost significantly more weight and had a significantly increased mean International Index of Erectile Function-5 score compared with control subjects. In subjects with erectile dysfunction at baseline, the intervention group experienced a greater and significant increase in International Index of Erectile Function-5 score, of 4.2 points, versus control.<sup>20</sup>

In summary, although these studies were relatively small and of short duration and did not control for all potential confounders (eg, changes in psychological measures), each suggests that achieving weight loss through caloric reduction and increased energy expenditure can be recommended to men with obesity as a means of improving erectile function.

### Mediterranean Diet Trials

The Mediterranean diet varies across countries but is generally high in fruits, vegetables, olive oil, whole grains, tree nuts, and lean proteins including beans, legumes, fish, and moderate in poultry and red wine.<sup>21</sup>

A randomized controlled trial of the effects of the Mediterranean dietary pattern on erectile dysfunction was first reported by Esposito et al<sup>22</sup> who randomized 65 men with erectile dysfunction and metabolic syndrome to either a Mediterranean diet or a control diet. Mediterranean diet subjects were not provided food but received regular reinforcement from dietitians to consume at least 250-300 g of

fruits, 125-150 g of vegetables, 25-50 g of nuts, and 400 g of fiber-rich whole grains daily, to increase consumption of olive oil and fish, and to decrease consumption of red and processed meats. Control subjects were provided only verbal and written information about healthy food choices at visits. At 2 years, 13 men in the intervention group and 2 in the control group reported normal erectile function based on International Index of Erectile Function-5 score of 22 or higher ( $P = 0.015$ ). Measures of endothelial function and inflammatory markers (C-reactive protein) were improved in the intervention group but unchanged in the control group. In the MEditerranean DIet and Type 2 diAbetes (MEDITA) trial, a randomized controlled trial of the effects of the Mediterranean diet on sexual dysfunction in those with newly diagnosed type 2 diabetes mellitus, a Mediterranean diet significantly slowed decreases in erectile function when compared with a lower fat diet (between-group difference of 1.16,  $P = 0.024$ ).<sup>23</sup>

Based on these data, it is reasonable to counsel patients with erectile dysfunction to adhere to a Mediterranean-style dietary pattern, rich in fruits, vegetables, and whole grains and including nuts, olive oil, and fish for the purpose of slowing progression or improving erectile dysfunction.

## Observational Diet Studies

Observational studies have also supported a link between dietary components and erectile dysfunction. In a prospective cohort study of 25,096 men in the Health Professionals Follow Up Study, those in the highest quintile of fruit intake had a 14% lower risk of incident erectile dysfunction over 10 years ( $P = 0.002$ ).<sup>24</sup>

Cross-sectional and nested case-control studies have also reported an association between dietary intakes and erectile function. In a large cross-sectional study of 1500 Canadian men with diabetes, 26% of whom reported symptoms or a diagnosis of erectile dysfunction, each daily serving of fruits or vegetables as measured by a food frequency questionnaire (FFQ) was associated with a 10% decrease in the odds of self-reported erectile dysfunction.<sup>18</sup> Among 312 men with diabetes, those who reported consuming fruits seldom or weekly had a significantly higher odds ratio for erectile dysfunction of 3.2 (1.4-7.9) compared with those who consumed fruit daily.<sup>25</sup> In Italy, among 100 men with erectile dysfunction and 100 matched controls, higher intakes of fruits and nuts, and a higher monounsaturated-to-saturated fat ratio were associated with lower odds of erectile dysfunction.<sup>26</sup>

Although these studies are limited by their designs, their findings are concordant with those from randomized controlled trials of the Mediterranean diet, which emphasized fruits, vegetables, legumes, olive oil, and nuts, for the treatment of erectile dysfunction. However, not all data have been concordant. A secondary outcome analysis of the Effect of Nut Consumption on Semen Quality and Functionality in Healthy Males (FERTINUTS) study, a 14-week randomized controlled trial with 83 subjects consuming a

Western style diet, 60 g/d of nut consumption compared with control (avoiding nuts) was associated with increased orgasmic function and sexual desire, but no significant difference in erectile function. Limited statistical power, the nonprimary outcome of erectile function, and the potential inability of 60 g/d of nuts to overcome the potential deleterious effects of a Western style diet on erectile function may have contributed to their findings.<sup>27</sup> Additionally, in a cross-sectional study of 2584 Chinese men with lower urinary tract symptoms or benign prostatic hypertrophy, increased vegetable intake was associated with lower erectile function scores.<sup>28</sup> This paradoxical finding may be explained by substantial use of pesticides during the growing process or by substantial use of table salt during cooking in many regions of China.<sup>29,30</sup> Furthermore, in a cross-sectional study of 4027 men ages 18-85 from the National Health and Nutrition Examination Survey, on multivariate analysis, no difference in erectile function was observed among men consuming a Mediterranean diet, a low-fat diet, or a nonrestrictive diet.<sup>31</sup> However, the measure of erectile function used in this study had not been validated and the study is subject to limitations given its cross-sectional design.

Finally, the effect of soy foods on libido and erectile function has received attention because of the potential feminizing effects of soy isoflavones. Although a case report in which consuming large quantities of soy (containing up to 360 mg of isoflavones per day) as part of a vegan diet was temporarily associated with decreased libido and worsened erectile function,<sup>32</sup> a review of 9 studies of soy isoflavone intake in men concluded that dietary isoflavones from soy of up to 139 mg/d (about 440-610 grams of tofu) had no "feminizing effect."<sup>33,34</sup>

## POTENTIAL MECHANISMS FOR THE EFFECTS OF DIET ON ERECTILE FUNCTION

The effects of dietary patterns and components on vascular health and disease are mediated through numerous biologic pathways.<sup>35</sup> Potential mechanisms for the impact of diet on erectile function include modulation of nitric oxide, reactive oxygen species and the microbiome.

### Dietary Effects on Nitric Oxide and Reactive Oxygen Species

Nitric oxide has antiatherogenic (ie, vasodilatory, antioxidant, and anti-inflammatory) effects on vessel walls.<sup>36</sup> Plant-based foods that are high in bioactive polyphenolic compounds have been linked to increased nitric oxide bioavailability and, hence, may provide a mechanism for improved erectile function in Mediterranean and plant-based diets.<sup>37</sup> Furthermore, basic science research data have shown that consuming more plant-based foods may increase the number of endothelial progenitor cells, thereby potentially improving endothelial,<sup>38</sup> cardiovascular,<sup>39</sup> and erectile function. In animal models, data suggest that

increased intakes of marine omega-3 fatty acids (typically found in fish) may also augment nitric oxide production<sup>40</sup> and improve erectile function.<sup>41</sup>

Reactive oxygen species reduce the bioavailability of nitric oxide and promote endothelial cell dysfunction,<sup>42</sup> believed to be the root cause of vasculogenic erectile dysfunction.<sup>43</sup> Plant-based foods are protective against reactive oxygen species, given their high levels of phytochemical antioxidants. In contrast, many animal-based foods may promote reactive oxygen species formation via increasing exposure to heme iron, nitrates, advanced glycation end products (AGEs), myeloperoxidase, and N-Glycolylneuraminic acid (Neu5Gc)<sup>42</sup> and, thus, may worsen erectile function.

### Dietary Effects on the Microbiome

Recent data have shown that the population of the human microbiome, comprised of more than 100 trillion microbial cells, shifts by dietary pattern and impacts human health.<sup>44</sup> Accordingly, the microbiome of vegetarians and vegans differs from that of omnivores, influencing downstream metabolism. For instance, upon consumption of L-carnitine from red meat, vegans and vegetarians produce significantly less trimethylamine N-oxide (TMAO) than omnivores.<sup>45</sup> Trimethylamine N-oxide promotes atherosclerosis, in part, by inducing vascular inflammation and endothelial dysfunction, and higher blood levels of trimethylamine N-oxide have been associated with increased cardiovascular disease risk.<sup>46</sup> Furthermore, higher blood levels of trimethylamine N-oxide are associated with the presence of fewer and less healthful endothelial progenitor cells, as well as more reactive oxygen species, reinforcing the impact of diet on vascular health.<sup>47</sup>

In addition, unlike animal-based foods, plant-based foods provide fiber.<sup>48</sup> In animal studies, fiber consumption fosters a healthful microbiome population,<sup>49</sup> which enables the production of short-chain fatty acids, such as butyrate, which may reduce cholesterol synthesis,<sup>50,51</sup> inflammation, and the burden of atherosclerosis.<sup>52</sup>

### EFFECTS OF PHYSICAL ACTIVITY ON ERECTILE FUNCTION

A large body of evidence has shown that physical activity improves erectile function, which may be mediated by physical activity's beneficial impact on cardiovascular risk factors.<sup>53</sup> Furthermore, physical activity may also augment nitric oxide release from endothelial cells due to increasing intravascular shear stress, thereby directly improving blood flow to penile and other vascular beds.<sup>54</sup> Exercise has also been associated with a host of other vasculoprotective effects, including a decrease in serum markers of inflammation.<sup>55</sup> As such, the American Urologic Association suggests recommending exercise to patients with erectile dysfunction and comorbidities that impact erectile function.<sup>56</sup>

Importantly, cycling, although providing cardiovascular benefits,<sup>57</sup> may induce erectile dysfunction if the bicycle

seat compresses the pudendal canal, thereby injuring the pudendal nerve and artery. Proper form while cycling with positioning on the bicycle seat so as to distribute body weight over the ischial tuberosities, rather than on the perineum, as well as careful selection of a safe, comfortable bicycle seat, may help avoid this issue.<sup>58</sup>

### EFFECTS OF TOBACCO CESSATION ON ERECTILE DYSFUNCTION OUTCOMES

The American Urologic Association erectile dysfunction guidelines identify cigarette smoking as an independent risk factor for erectile dysfunction.<sup>56</sup> Cigarette smoking contributes to erectile dysfunction, in part, by reducing nitric oxide levels and by promoting both reactive oxygen species production and inflammation.<sup>59</sup> Furthermore, cigarette smoking directly damages arteries by causing calcification of medial elastic fibers, leading to arterial stiffening and a reduced response to vasodilatory signals.<sup>60</sup> Encouragingly, smoking cessation may improve erectile function. In a randomized controlled trial of smoking-cessation strategies in 719 subjects with erectile dysfunction who smoked at least 1 cigarette daily, self-reported smoking cessation, independent of strategy, was associated with significantly improved erectile function (relative risk = 2.07, 1.61-2.67) as measured by International Index of Erectile Function-5 at 6 months.<sup>61</sup> Overall, cigarette smoking is a significant risk factor for erectile dysfunction,<sup>56</sup> and smoking cessation, apart from its other numerous benefits,<sup>62</sup> is associated with improved erectile function, particularly in younger individuals. Therefore, all men with erectile dysfunction who smoke should be strongly encouraged to quit to reap benefits in both vascular and overall health.

### SUMMARY AND RECOMMENDATIONS FOR CLINICAL PRACTICE

Vasculogenic erectile dysfunction is prevalent in men by middle age and heralds an increased risk of future atherosclerotic cardiovascular disease events, including myocardial infarction and stroke. Hence, symptoms of erectile dysfunction should be elicited during the medical interview in a manner that engenders trust and demonstrates empathy toward the patient without making assumptions or value judgments about sexual orientation or number of partners.<sup>63</sup> Furthermore, in younger men, in particular, the diagnosis of erectile dysfunction should prompt heightened concern that the relative risk of future atherosclerotic cardiovascular disease events may be markedly increased. The American Urologic Association guidelines provides a framework for the evaluation of and treatment for erectile dysfunction, which includes validated questionnaires to assess erectile dysfunction severity, treatment effectiveness, and helps guide erectile dysfunction management.<sup>56</sup>

In all affected individuals, lifestyle interventions should be the cornerstone of treatment. In individuals of normal weight, a mostly plant-based Mediterranean-style diet

should be promoted. In individuals who are overweight or obese, a balanced hypocaloric diet that includes nuts, legumes, fish, and high amounts of fruits and vegetables should be advised. Consulting a registered dietitian may prove beneficial for the patient. Exercise at a level of at least 150 min/wk is recommended. Avoidance of cigarette smoking is critical. Furthermore, guideline-directed medical therapy for cardiovascular disease risk factors, including hyperlipidemia, hypertension, and diabetes should be used, recognizing that some, such as beta-blockers and thiazide diuretics have been associated with erectile dysfunction.<sup>5</sup> Finally, collaboration with experts in urologic diseases and men's health is essential, and referrals should be made in more challenging cases.

In summary, erectile dysfunction is a potent risk factor for atherosclerotic cardiovascular disease events, and erectile function is responsive to lifestyle interventions. Given erectile dysfunction's negative impact on quality of life,<sup>64</sup> its identification in clinical practice, coupled with a patient's desire to improve erectile function, may be powerful motivators for lifestyle change,<sup>65</sup> benefitting both erectile function and future atherosclerotic cardiovascular disease risk.

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