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Opinion

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Vegetarian Diets and Cardiovascular Risk Reduction: Pros

Soo Yong Lee

Division of Cardiology, Department of Internal Medicine and Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, Yangsan, Korea

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Correspondence to
Soo Yong Lee
Division of Cardiology, Department of Internal Medicine and Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, 20 Geumo-ro, Mulgeum-eup, Yangsan 50612, Korea.
Email: shonge0906@gmail.com

ORCID iDs
Soo Yong Lee
https://orcid.org/0000-0003-2616-1294

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ABSTRACT

There is an ongoing need for public health interventions aimed at further mitigating the risk of cardiovascular disease (CVD) through changes in dietary patterns and other lifestyle habits. Plant-based diets (PBDs) are effective in reducing CVD risk factors, a benefit evidenced by the favorable cardio-metabolic profiles observed in vegetarians who abstain from consuming meat, fish, and poultry compared to omnivores. Numerous studies have demonstrated that PBDs, particularly when rich in high-quality plant foods such as whole grains, fruits, vegetables, and nuts, are associated with a lower risk of adverse cardiovascular outcomes. Herein, we briefly review the current evidence regarding the relationship between CVD and PBDs, as well as the potential underlying biological mechanisms.

Keywords: Plant-based diet; Vegetarian; Cardiovascular diseases

INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of mortality worldwide, causing approximately 18 million deaths each year.[1] Therapeutic lifestyle modifications have been suggested as a key strategy that may prevent many primary and secondary cardiovascular events.[2] The current surge of public interest in adopting a healthier, plant-based eating pattern is therefore quite natural. The number of publications indexed under "vegan," "vegetarian," or "plant-based diets" (PBDs) in PubMed is increasing, reflecting growing professional interest. Furthermore, the upward trend in public interest in these dietary patterns is demonstrated by increasing Google search frequencies over time, reflecting a sustained growth in interest.[3]

Heart-healthy diets have dramatically evolved throughout the last 50 years. Starting from controlling total fat intake in the 1940s–1950s, the management of specific ingredients, such as sodium or certain types of fat, in total daily food consumption has emerged as a recent trend in strategies to manage diets in a way that promotes human health.[4] The recent primary prevention guidelines of the American College of Cardiology and American Heart Association strongly suggest "a diet emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish" to decrease atherosclerotic cardiovascular disease (ASCVD) risk for primary prevention (class I).[2] The European Society of Cardiology guidelines also recommend a healthy diet as a cornerstone of CVD prevention in all individuals (class IA).[5]

Vegetarian dietary patterns offer a variety of options, each with its own set of distinct clinical outcomes. This article aims to clarify the definitions of different vegetarian dietary patterns and to examine the existing evidence regarding the positive effects of these diets, as well as the potential biological mechanisms that lead to these benefits.

DEFINITIONS OF VEGETARIAN DIETS AND PBDs

The term "vegetarian" encompasses a broad spectrum. Various vegetarian eating patterns exist based on the exclusionary criteria that dictate specific foods to avoid (**Table1**).[3] Vegans only eat foods derived from plant sources, excluding meat or animal byproducts. Lacto-vegetarians allow dairy goods, excluding eggs, fish, or meat, while lacto-ovo-pesco-vegetarians can consume dairy, fish, and eggs excluding red meat. This classification only conveys the limitations regarding particular food items; it does not define the essential components or the ratio of each. It is important to note that not every eating pattern is inherently "healthy." The term "vegetarian" designates what someone should not eat, whereas the term "PBD" focuses on what someone should eat. A PBD embraces the basic concept of a "healthy diet" and includes "core elements," such as unprocessed whole grains, fruit, vegetables, legumes and, non-hydrogenated vegetable oils.[6] The 3 most popular heart-healthy PBDs, which are widely recommended, are the Dietary Approaches to Stop Hypertension (DASH) diet, the Mediterranean diet (MD), and the healthy vegetarian eating pattern[4] (**Table 2**). As shown in **Fig. 1**, a vegetarian diet (VD) and a PBD have overlapping characteristics with each other, and the terms are used interchangeably or ambiguously in

Table 1. Types of vegetarian diets

Types of vegetarian diets	Fruit	Vegetables	Dairy	Eggs	Seafood
Fruitarian	+				
Raw vegan	+	+			
Vegan	+	+			
Lacto-vegetarian	+	+	+		
Ovo-vegetarian	+	+		+	
Lacto-ovo-vegetarian	+	+	+	+	
Pescatarian	+	+	+	+	+
Flexitarian	+	+	+	+	+

Table 2. Currently recommended heart-healthy dietary patterns[4]

Dietary pattern	Includes	Restricts	Healthy benefits	Key differences
DASH diet	Vegetables, fruits, low-fat dairy products, whole grains, lean meats, fish, poultry, fish, beans, and nuts	Sodium intake <2,300 mg or <1,500 mg/day	• Lower BP • Lower LDL-C level • Reduced CVD risk	• More emphasis on restricting sodium intake than other diets
The Mediterranean Diet	Vegetables, fruits, nuts, legumes, whole grains, and EVOO, lean meats, fish, and poultry	Limited red meat, processed meats, and sweets intake	• Primary and secondary prevention of CVD • Reduced risk of CVD mortality • Reduced risk of MI and stroke • Reduced risk of all-cause mortality	• More emphasis on nuts, fish, and olive oil than other diets • Less emphasis on dairy than the other diets
Healthy vegetarian eating patterns	Vegetables, fruits, nuts, legumes, soy products, nuts, low-fat dairy products, and seeds	All types of meat, poultry, and seafood	• Lower BP • Lower LDL-C level • Reduced CVD risk	• More emphasis on soy products, legumes, and dairy products compared to other diets • Lean protein is entirely plant-based

This table has been modified from table 1 from reference.[4]
DASH, Dietary Approaches to Stop Hypertension; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol; CVD, cardiovascular disease; EVOO, extra-virgin olive oil; MI, myocardial infarction.

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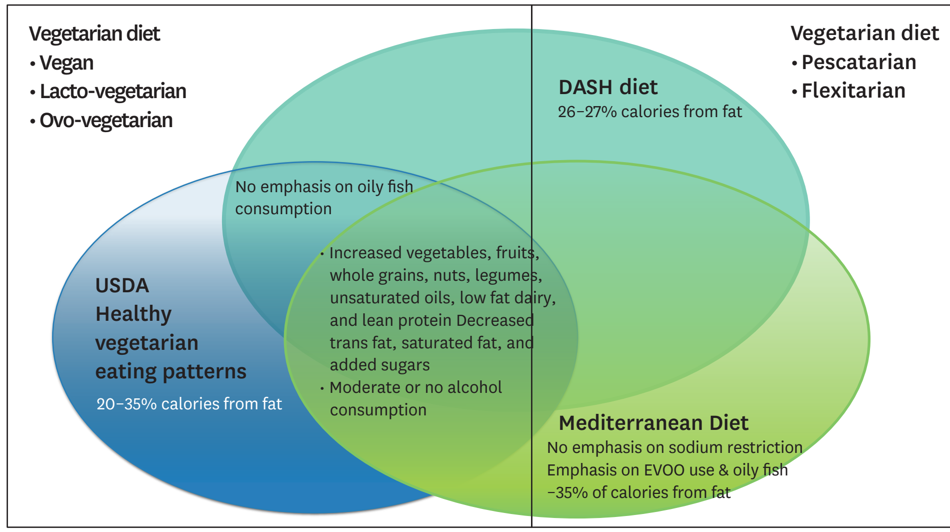

Fig. 1. Features and commonalities of the most popular plant based dietary patterns: the DASH diet, USDA healthy eating patterns, and Mediterranean diet. The relationships with various classifications of vegetarian diets care described in the diagram. In essence, the term "vegetarian" designates what someone should not eat, whereas the term "plant-based diet" focuses on what someone should eat.
DASH, Dietary Approaches to Stop Hypertension; EVOO, extra-virgin olive oil.

various research articles. In this article, both VD and PBD essentially refer to healthy eating patterns that mainly contain the above-listed "core elements."

BODY METABOLISM CHANGES IN RESPONSE TO A LOW-FAT PBD DIET

1. PBDs and microbiome changes

VDs are characterized by a higher intake of unprocessed dietary fiber, plant protein, phytochemicals, vitamin A and calcium, as well as a lower intake of fat compared to omnivorous diets.[7] These nutrients readily reach the colon intact and are efficiently utilized by its microorganisms.[8] For example, a typical VD provides the colonic microbiota with nearly 5–15 g of protein, 60 g of fermentable carbohydrates, and 5–10 g of lipids.[9] As a result, VDs have the potential to substantially influence the proportions of specific genera within the gut microbiota, leading to a notable increase in microbial diversity and abundance. This, in turn, enhances gut homeostasis. Dietary fiber-degrading bacteria, such as *Prevotella*, *Ruminococcus*, *Faecalibacterium*, *Eubacterium*, and *Lactobacillus*, have been reported to be abundant in the gut of vegetarians.[10] Additionally, microbiome-derived metabolites (postbiotics) of vegetarian dietary sources—either produced or transformed by microorganisms—play important roles in intestinal physiology.[11] These metabolites include short-chain fatty acids (SCFAs), lactate, and pyruvate derived from dietary fiber; agmatine, putrescine, spermine, and spermidine from plant proteins; and retinoic acid obtained after metabolizing vitamin A. The proposed mechanisms of action of those metabolites involve the modulation of intestinal immunity, protection of intestinal barrier integrity, and prevention of colonization by pathogens.[12] The most widely studied bacterial postbiotic SCFAs (acetate, propionate, and butyrate), which are derived from gut microbial fermentation of indigestible carbohydrates, have various protective roles in intestinal physiology. SCFA-mediated immune regulation is mainly accomplished via inhibiting histone deacetylases and activating G protein-coupled receptors present in intestinal epithelial cells and other immune cells.[13] SCFAs have also been reported to promote intestinal epithelial repair through the activation of NOD-like receptor protein 3, affecting Ca^{2+} mobilization and membrane hyperpolarization.[14] Moreover, SCFAs can directly inhibit the growth of intestinal pathogens or indirectly regulate the intestinal environment to mediate colonization resistance. For example, butyrate has been reported to restrict oxygen levels in the intestinal epithelium by stimulating the peroxisome proliferator-activated receptor γ, thereby limiting the ability of *Salmonella typhimurium*, an aerobic bacterium, to access oxygen and inhibiting its colonization.[15]

2. The benefits of reducing meat consumption

PBDs offer benefits not only from the metabolically advantageous nutrients derived from plants, but also from avoiding meat consumption. Several harmful substances are associated with meat consumption, such as endotoxin, trimethylamine N-oxide (TMAO), heterocyclic amines, advanced glycation end-products, heme iron, and Neu5GC. Among these, the association of TMAO with atherosclerosis leading to ASCVD is well established. Gut microbiotas produce trimethylamine (TMA) from the following dietary precursors: choline, L-carnitine, and betaine. These TMA precursors are most abundant in red meat and eggs.[16] TMA that has been absorbed into the circulation is immediately oxidized to TMAO by hepatic flavin-containing monooxygenase.[16] TMAO has been reported to promote the upregulation of the scavenger receptors CD36 and SR-A1, as well as induce inflammation via the MAPK/JNP pathway, which regulates the synthesis of pro-inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-6 and intercellular adhesion molecule 1.[17,18] This leads to cholesterol overload in macrophage foam cells and their faster migration and adhesion to endothelial cells. A community-based cohort study showed that higher intake of unprocessed red meat, total meat (unprocessed red meat plus processed meat), and total animal source foods were prospectively associated with a higher incidence of ASCVD during a median follow-up of 12.5 years. These associations were partly mediated by plasma levels of gut microbiota-generated metabolites, including TMAO and its 2 intermediates derived from L-carnitine, which is abundant in red meat.[19]

3. Body weight, lipid profiles, and insulin sensitivity changes in response to PBDs

There are numerous of evidence that PBD can modify potent CVD risk factors such as overweight, dyslipidemia, and insulin resistance. Kahleova et al.[20] recently conducted a randomized controlled trial (RCT) involving 122 overweight adult participants. The trial compared the effects of an intervention diet (VD, approximately 75% of energy from carbohydrates, 15% protein, and 10% fat) with a control group following a regular diet. Their body weight, insulin resistance, postprandial metabolism, and intramyocellular and hepatocellular lipid levels were evaluated. Over 16 weeks, body weight decreased in the VD group by 5.9 kg (95% confidence interval [CI], 5.0, 6.7 kg; $p<0.001$). Hepatocellular lipid levels decreased in VD group by 34.4% ($p=0.002$), and intramyocellular lipid levels decreased by 10.4% ($p=0.03$). None of these variables changed significantly in the control group after 16 weeks. The fasting plasma insulin concentration decreased by 21.6 pmol/L in the VD group, with no significant change in the control group (23.6 pmol/L; 95% CI, −5.0, 54.3 pmol/L; $p=0.006$). These results highlight how the body changes after consumption of a low-fat PBD—namely, the effects include weight reduction, a decrease in intracellular lipid concentrations, and improved insulin sensitivity.

Additionally, a recent meta-analysis of 30 trials reported that people who followed a vegan or VD had lower blood levels of low-density lipoprotein cholesterol (LDL-C), total

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cholesterol (TC), and apolipoprotein B (apoB) than omnivorous subjects.[21] Compared with the omnivorous group, PBDs reduced TC, LDL-C, and apoB levels, with mean differences of −0.34 mmol/L (95% CI, −0.44, −0.23 mmol/L; $p=1\times10^{-9}$), −0.30 mmol/L (95% CI, −0.40, −0.19 mmol/L; $p=4\times10^{-8}$), and −12.92 mg/dL (95% CI, −22.63, −3.20 mg/dL; $p=0.01$), respectively.[21] This significant overall improvement in the lipid profile could lead to a decrease in cardiovascular events.

THE CLINICAL EVIDENCE OF REDUCED CARDIOVASCULAR RISK AFTER THE ADOPTION OF A PBD

Caldwell Esselstyn is among the physicians who have aggressively argued for an association between a strict PBD and a reduction in risk for coronary artery disease. He conducted a fat-free whole-food plant-based program for 18 terminally ill coronary artery disease patients and reported the results after a 12-year follow-up in 1999.[22] The participants followed PBDs containing only 10% fat and took cholesterol-lowering medication. Before the patients participated in the program, there were 49 total coronary events, but after joining the program, the patients who adhered to a strict PBD showed no progression of clinical disease, no coronary events, and no interventions at all for 12 years.[22] After this report, there have been numerous studies examining whether a VD truly has a positive impact on CVD.

The LIFESTYLE Heart Trial by Ornish et al.[23] was the first RCT that investigated the relationship between lifestyle changes and the progression of coronary atherosclerosis without the use of lipid-lowering drugs. Intensive lifestyle changes were defined as a 10% fat whole-foods VD, aerobic exercise, stress management training, smoking cessation, and group psychosocial support for 5 years. Coronary atherosclerosis, as examined by coronary angiography, regressed constantly through 5 years in the experimental group, with relative improvements of the stenosis diameter of 4.5% at 1 year and 7.9% at 5 years. In contrast, in the control group, coronary atherosclerosis continued to progress, as shown by a relative worsening of the stenosis diameter by 5.4% at 1 year and 27.7% at 5 years. Moreover, the risk ratio of cardiac events compared to the control group was 2.47 (95% CI, 1.48, 4.20).[23]

In 2012, Huang et al.[24] found that vegetarians had a 29% lower rate of ischemic heart disease-associated mortality than non-vegetarians. In contrast, a study in 2019 revealed no significant association between a vegetarian dietary pattern and CVD or stroke mortality, yielding conflicting results.[25] However, recent studies utilizing specific indices to define food content and adherence, as a way of objectively distinguishing large-scale experimental groups, reported consistent results.[26,27] A pooled analysis combining a cohort of individuals from the Nurses' Health Study, Nurses' Health Study II, and Health Professionals Follow-up Study (165,794 women and 43,339 men) with up to 32 years of follow-up, using the Healthy Eating Index-2015, Alternative Mediterranean Diet Score, Healthful Plant-Based Diet Index, and Alternative Healthy Eating Index (AHEI), showed consistent associations between dietary scores and the risk of CVD across different subgroups. A greater adherence to healthy eating patterns was associated with a lower risk of CVD.[26]

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THE CLINICAL IMPACT OF THE DASH DIET, THE MEDITERRANEAN DIET, AND THE HEALTHY VEGETARIAN EATING PATTERN

These three popular PBDs differ slightly in terms of their constituents; however, their clinical impact has been found to be significant. Several interesting studies have compared the effects of those specific dietary patterns. The PREDIMED (Prevención con Dieta Mediterránea) study, published in 2013, was an RCT investigating the primary prevention effect of the MD on cardiovascular events.[28] In total, 7,447 participants were divided into 3 groups—MD with extra-virgin olive oil (EVOO), MD with nuts, and a control diet (low-fat diet limiting red meat)—and compared. The multivariable-adjusted hazard ratios for the primary endpoint (myocardial infarction, stroke, or death from cardiovascular causes) were 0.70 (95% CI, 0.54, 0.92) and 0.72 (95% CI, 0.54, 0.96) for the MD with EVOO and MD with nuts groups, respectively, versus the control group. The CARDIVEG (Cardiovascular Prevention with Vegetarian Diet), published in 2018 compared an MD and VD.[29] They enrolled 58 and 62 volunteers for the MD and VD groups, respectively. There were no significant differences in the reduction of body weight, body mass index, and fat mass between groups. However, VD was more effective in reducing LDL-C levels, whereas MD led to a greater reduction in triglyceride levels.[29] These results suggest that we need to choose a dietary pattern according to the lipid targets of each individual. A systematic review including six trials that compared an MD and low-fat diet reported a positive and significant association between the MD and blood pressure (BP) in adults, although the magnitude of the effect was small.[30] The study reported drops of 1.44 mmHg and 0.70 mmHg from the baselines of systolic and diastolic BP, respectively, after 1 year of adherence to the MD.[30] Meta-analyses have shown that the DASH diet, MD, and AHEI diet are associated with relative CVD risk reductions by 20%, 29%, and 26%, respectively, compared to a Western diet.[31]

THE COMPONENTS OF THE DAILY PBD AND ADHERENCE MATTER

A VD is not necessarily healthy. For instance, consuming white bread with a large amount of peanut butter at every meal would be a 100% vegan diet, but it would unlikely to be considered “'healthy” by most people. Thompson et al.[32] proved that the quality of PBD is important in a prospective cohort study using data from more than 120,000 middle-aged adults followed for over 10 years in the UK Biobank, utilizing the healthful versus unhealthful plant-based diet index. Those who consumed a healthful PBD, with higher amounts of foods such as fruits, vegetables, legumes, whole grains, and nuts and lower intakes of animal products, sugary drinks, and refined grains had a 16% lower risk of death during follow-up (10.6–12.2 years) than those with the lowest intakes of healthful plant-based foods. By contrast, an unhealthy PBD was associated with a 23% higher total mortality risk.[32] Therefore, adherence to a high-quality PBD is the key, rather than simply not eating meat.

CONCLUSION

Numerous recent experiments, RCTs, and meta-analyses have consistently conveyed clear messages regarding the link between various PBDs and reduced CVD risk. Due to

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the widespread use of potent statins and anti-dyslipidemia medications, engaging in comprehensive discussions about dietary modifications in real clinical scenarios with patients might seem useless to most clinicians. However, healthcare professionals should not overlook the significance of this evidence. It is essential to impart this important information to patients to enhance their well-being, while also aiming for savings in overall medical costs.

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