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Review Article

Stroke and diets – A review

Chin-Lon Lin[a,b]*

[a]Department of Cardiology, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chiayi, Taiwan, [b]Department of Internal Medicine, College of Medicine, Tzu Chi University, Hualien, Taiwan

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Abstract

Stroke was one of the most common causes of death and disability worldwide. In addition, there was a significant increase in the disease burden of stroke in the world over the past 25 years, especially in developing countries. We searched PubMed (National Library of Medicine, USA) and Embase (Elsevier) databases using "Stroke and diets" as strategy, and additional references were obtained from the selected articles. The risk factors of stroke include age, sex, and modifiable factors such as hypertension, smoking, diet, physical activity, diabetes mellitus, alcohol consumption, psychological factors, and cardiac causes.–together account for >90% of the population attributable risk for stroke. They were discussed individually (Hypertension, Diabetes, Dyslipidemia, Gut microbiota, Nutrition), and the dietary modifications to reduce these risks were also presented. In conclusion, besides low salt intake, plant-based dietary patterns (especially vegetarian diets) that are rich in fruit, vegetables, whole grains, legumes, seeds, nuts, and dairy and low in meat, sweets, and alcohol significantly improved risk factors for stroke, and observational studies clearly demonstrated the stroke morbidity and mortality benefits. Thus, dietary intervention should be considered as an important strategy in the prevention and management of stroke.

Keywords: *Hypertension, Microbiota, Plant-based diet, Stroke, Vegetarian diet*

Introduction

There was a significant increase in stroke burden in the world over the past 25 years, especially in developing countries [1]. Stroke was the second-most common cause of death and the third-most common cause of disability after ischemic heart disease worldwide [1]. Globally, the majority (approximately three fourth) of strokes are ischemic, followed by intracranial hemorrhage, subarachnoid hemorrhage, and cerebral venous thrombosis, etc., [2,3]. Stroke is also the most common cause of complex disability and independent risk for dementia [4]. The direct and indirect cost of stroke care is a considerable burden to both society and patients' families. Although some risk factors of stroke are nonmodifiable, such as older age and male sex, current known modifiable risk factors—hypertension, current smoking, high waist-to-hip ratio, diet, regular physical activity, diabetes mellitus, alcohol consumption, psychological factors, cardiac causes, ApoB/Apo1 ratio—together account for >90% of population attributable risk for stroke [2,5]. In addition, in the United States of America, out of the seven metrics of cardiovascular health, healthy diet score is the poorest (91.6% poor, National Health and Nutrition Examination Survey 2011–2012.) [6]; hence, diet is the worst health issues in the United States [7]. The objective of this review is to present an overview of the risk factors of stroke and how various dietary practices impact them.

We searched PubMed (National Library of Medicine, USA) and Embase (Elsevier) databases, using "Stroke and diets" as a key for peer-reviewed observational studies published in the last 5 years until June 2020. An additional manual search was also performed on the references of the studies selected from these databases. We concentrated on systemic reviews or meta-analysis with statistically significant results. We summarized our findings as follows:

Modifiable risk factors of stroke

Hypertension

The most important risk factor for stroke is hypertension, accounting for 47.9%, 45.7%, and 56.4% of the population attributable risk for overall, ischemic, and hemorrhagic strokes, respectively, in the INTERSTROKE study [2]. Diets rich in fruits, vegetables, whole grains, legumes, seeds, nuts, fish, and dairy and low in meat, sweets such as the Dietary Approaches to Stop Hypertension (DASH) diets [8], the

*Address for correspondence:
Dr. Chin-Lon Lin,
Department of Cardiology, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, 2, Minsheng Road, Dalin, Chiayi, Taiwan.
E-mail: cllinmd@tzuchi.com.tw

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Mediterranean diets (MDs) [9], the Nordic diets [10], and Vegetarian diets [11] all have been demonstrated to significantly lower systolic and diastolic blood pressures [12] and hence confer protection against stroke.

The DASH diet (diet rich in fruits, vegetables, and low-fat dairy products and with reduced saturated and total fat) reduced systolic and diastolic blood pressures by 5.5 and 3.0 mm Hg, respectively, as compared with control and It is estimated that a population-wide reduction in systolic or diastolic blood pressures of the magnitude observed would reduce stroke by approximately 27% [8], which is a very large proportion in the prevention of stroke.

After 1 year on MD, with extra virgin olive oil and mixed nuts, participants had 4.0–4.3 mm Hg lower mean systolic, and 1.9 mm Hg lower mean diastolic blood pressures on 24-h monitor than the control diet group. This reduction translated into a 30% reduction (hazard ratio [HR] 0.69) of major cardiovascular events (myocardial infarction, stroke, or death from cardiovascular causes) and 42% reduction of stroke [9].

Adherence to a healthy Nordic diet (consists of mainly whole grain and rye bread, berries, apples and pears, fish, cabbage and cruciferous vegetables, root vegetables, low-fat dairy products, potatoes, and vegetable fats) was associated with a lower risk of stroke. The HR comparing high adherence with low adherence was 0.86 (95% confidence interval [CI] 0.76–0.98) for total stroke [13]. The 15% reduction in total stroke incidence is probably an underestimate because the control is low adherence rather than no adherence.

The vegetarian diet group was also demonstrated to have a lower prevalence of hypertension than the nonvegetarian group and risk reduction in hemorrhagic, ischemic and total stroke [14]. All these studies demonstrated the significant beneficial effects of plant-based diets on hypertension and hence the risks of stroke.

Diabetes

Type 2 diabetes is a global epidemic and a rapidly rising prevalence, especially in middle-and low-income countries [15]. Diabetic patients have high rates of macro- and micro-vascular complications, including stroke, myocardial infarction, major lower-extremity amputations, end-stage renal disease, and visual impairment [16]. Increases in consumption of calorie-dense foods, including fast foods, meats and other animal fats, highly refined grains, and sugar-sweetened beverages, are thought to play a critical role in the rising rates of type 2 diabetes worldwide [17]. On the other hand, healthy diet, regular physical activity, maintaining a normal body weight, and avoiding tobacco use are ways to prevent or delay the onset of type 2 diabetes [18]. Lifestyle intervention reduced the incidence of diabetes by >50% as compared with placebo; and was even significantly more effective than metformin [19]. Plant-based diets– i.e., eating patterns that emphasize legumes, whole grains, vegetables, fruits, nuts, and seeds and discourage most or all animal products, are especially potent in preventing type 2 diabetes and have been associated with much lower rates of obesity, hypertension, hyperlipidemia, cardiovascular mortality, and cancer [20]. There is a general consensus that plant-based diets are cost-effective, low-risk interventions that are not only highly beneficial for preventing and treating type 2 diabetes and other risk factors such as obesity, hypertension, hyperlipidemia, and inflammation, and they may also reduce the number of medications needed to treat chronic diseases and lower major cardiovascular disease mortality rates [20,21]. Hence, plant-based diets are important in the prevention of stroke.

Dyslipidemia

Though the relationship between cholesterol levels and stroke has been much less clear than between cholesterol levels and coronary heart disease, recent studies provided proof that total (and low-density lipoprotein [LDL]) cholesterol-lowering, reduces stroke risk proportional to the extent of cholesterol reduction [22]. In addition, after an ischemic stroke or TIA with evidence of atherosclerosis, patients who had been treated to a LDL cholesterol level of <70 mg per deciliter had a lower risk of subsequent cardiovascular events than those who had been treated to LDL cholesterol of 90 mg to 110 mg per deciliter [23]. The Portfolio diet (a dietary portfolio of cholesterol-lowering foods such as soy protein, viscous fiber, plant sterols, and almonds), could significantly lower serum LDL-cholesterol concentrations (more than 20%) [24]. In addition, plant-based diets, such as The Mediterranean, DASH, Nordic, and the vegetarian diets, all have positive effects on various cardiometabolic risk factors (glycemic control, blood lipids, body weight and adiposity, and blood pressure) and cardiovascular disease outcomes such as myocardial infarction and stroke [25]. Thus, plant-based diets not only lower blood pressure reduces weight, improves glycemic control, they also lower total and LDL-cholesterol, and confer protection against stroke.

Gut microbiota

The gut microbiota (GM) is the community of microorganisms (bacteria, archaea, fungi, viruses) colonizing the gastrointestinal tract. GM regulates various metabolic pathways in the host, including those involved in energy homeostasis, glucose, lipid, and bile acid metabolism. GM dysbiosis has been shown to be involved in the pathogenesis of diverse diseases, such as metabolic syndrome, cardiovascular diseases, celiac disease, inflammatory bowel disease, and neurological disorders [26]. Multiple factors modulate the composition of the microbiota and its activity. The individual microbiota pattern is influenced by antibiotic use, medication (nonsteroidal anti-inflammatory drugs, proton pump inhibitors, etc.), infections, and chronic stress. However, one of the major factors triggering GM establishment is diet. Plant-based diets, with adequate fruit and vegetable intake, rich in dietary fiber, with healthy fats (monounsaturated fatty acids [MUFAs] and polyunsaturated fatty acids [PUFAs]), and a predominance of plant-derived proteins seem to be the best way to promote GM diversity and activity [26]. Vegan or vegetarian diet results in a significantly lower stool pH and shift in the microbiota, while total cell numbers remain unaltered as compared with omnivore diet [27]. Intestinal microbiota metabolism of dietary L-carnitine, trimethylamine abundant in red meat, produces trimethylamine N-oxide (TMAO) and accelerates atherosclerosis. In addition, omnivorous subjects produce

significantly more TMAO than vegans/vegetarians following the ingestion of L-carnitine through a microbiota-dependent mechanism [28]. Carnitine from meat and choline from eggs not only provide substrates for but also shift gut microbial community to enhance the production of TMAO [29], an atherosclerotic factor that has been shown to induce platelet hyperreactivity and thrombosis [30] and increase stroke incidence [31]. Thus, plant-based diets can alter the composition of intestinal microbiota and confer the protection of cardiovascular diseases through interactions with GM.

Nutrition

Salt

The close relationship between dietary sodium intake and hypertension is widely recognized. The high sodium intake in the diet increases water retention and systemic peripheral resistance, alters the endothelial function, causes changes in the structure and function of large elastic arteries, and modification in autonomic neuronal modulation of the cardiovascular system. A reduction in dietary sodium not only decreases the blood pressure and the incidence of hypertension, also is associated with a reduction in morbidity and mortality from cardiovascular diseases [32,33]. Fresh vegetables and fruits are generally low in salt content, but salt is often added in the preparation and cooking of plant-based foods and should be avoided.

Fiber

Increased fiber intake in diets lowers blood pressure and serum cholesterol levels, improves glycemic control and insulin sensitivity, enhances weight loss, and benefits a number of gastrointestinal disorders, including gastroesophageal reflux disease, duodenal ulcer, diverticulitis, constipation, and hemorrhoids [34]. Individuals with high intakes of dietary fiber appear to be at significantly lower risk for developing coronary heart disease, stroke, hypertension, diabetes, obesity [31]. In a meta-analysis, greater dietary fiber intake is significantly associated with a lower risk of first stroke [35]. Typical plant-based foods have high contents of fiber and, therefore, beneficial for the prevention of stroke.

Vitamins

Plasma homocysteine is derived from the essential amino acid methionine and its metabolic pathways are catalyzed by enzymes requiring folic acid, Vitamin B6 and Vitamin B12 (cobalamin) as essential cofactors. Hence, the total plasma concentration of total homocysteine (tHcy) is influenced by blood concentrations of the B vitamins; folic acid (B9), cyanocobalamin (B12), and pyridoxine (B6) [36]. Systematic reviews showed a strong, positive and dose-related association between the plasma concentration of tHcy and the risk of stroke, independent of other vascular risk factors [37,38]. In fact, supplementation with B vitamins (folic acid, Vitamin B12, and Vitamin B6) lower blood concentrations of tHcy by 25% and reduces the relative risk of stroke overall by about 10% compared with placebo [36]. Vegetarians tend to have a low intake of Vitamin B12, which is found mainly in animal-based foods, and this raises plasma homocysteine, leading to an increase in the risk of stroke [36]. However, the combined effect of the supposed harm of high homocysteine and the supposed benefits of low BP, glucose, and cholesterol (the unique aspect of vegetarian diets) on stroke incidence is unclear. In fact, cohort studies demonstrated that vegetarian diet is associated with a lower risk of ischemic and hemorrhagic strokes in a nonsmoking, non-drinking cohort despite higher plasma homocysteine levels [14]. Whether those on plant-based diets should receive vitamin B12 supplements remained controversial.

Nuts

Nuts have unique nutritional profiles. Nuts contain 43%–67% fat, 8%–22% protein, and only 1%-4% carbohydrate by weight and are abundant in unsaturated fatty acids (UFAs) (containing both monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA)) and only 4%–5% of saturated fatty acids. Nuts are also high in vitamins, minerals, fiber, and phytochemicals [39,40]. Recent meta-analyses found that nut consumption has beneficial effects on the cardiometabolic disease with reduced stroke incidence and mortality. It is mainly attributable to decreases in fasting glucose, total cholesterol, and LDL-C. Nuts, with its high contents of UFAs and protein are important ingredients in nutritionally balanced plant-based diets.

Epidemiological and observational studies

Various nutrients or individual foods have been studied in relation to stroke risk; whole-grain, fruit, and vegetable consumption has been found to be protective against cardiovascular mortality [41,42], and fish consumption is weakly inversely associated with the risk of stroke [43]. On the other hand, increased meat, especially processed red meat consumption, has been shown to correlate with increased stroke risk [44,45].

Dietary pattern analysis has emerged as an approach to examining the relationship between diet and the risk of chronic diseases. Instead of looking at individual nutrients or foods, pattern analysis examines the effects of overall diet and represents a broader picture of food and nutrient consumption, and maybe more predictive of disease risk than individual foods or nutrients [46]. It has also been demonstrated that the highest behavioral risk is incorrect nutrition for noncommunicable diseases, and that the choice of a balanced diet can reduce the risk of stroke [47].

After 1 year on MD supplemented with extra virgin olive oil and mixed nuts, the adjusted HRs for major cardiovascular events (myocardial infarction, stroke, or death from cardiovascular causes) were 0.70 (95% CI, 0.54–0.92, olive oil) and 0.72 (95% CI, 0.54–0.96, mixed nuts), versus the control group. Specifically, the diet also lowers the incidence of stroke by 42% and total cardiovascular mortality by 20% [9].

In the landmark "China study" [48], comparing the dietary patterns and mortality data from a large geographic area of rural China to that of the United States of America, demonstrated the link between the consumption of animal products (including dairy) and chronic illnesses such as coronary heart disease, diabetes, breast cancer, prostate cancer, and bowel cancer. The coronary artery disease mortality

rates in rural China were inversely associated with the frequency of intake of green vegetables and plasma erythrocyte MUFAs, but positively associated with salt, animal protein intake and negatively associated with plant protein, legume, and light-colored vegetable intake. The authors conclude that people who eat predominantly whole-food–avoiding animal products, including beef, pork, poultry, fish, eggs, cheese, and milk, and reducing their intake of processed foods and refined carbohydrates–will escape, reduce, or reverse the development of numerous diseases [49].

In a meta-analysis of the associations between different dietary patterns and the risk of stroke by pooling available data from 21 published studies, using a "healthy" diet scoring system on the food Frequency Questionnaire, the "healthy" dietary pattern was characterized by high intakes of vegetables, fruits, fish, low-fat milk, and whole grains. A decreased risk of stroke was demonstrated for the highest compared with the lowest categories of healthy dietary pattern (odds ratio = 0.77; 95% CI = 0.64–0.93; $P = 0.006$) [50] that translates into a 23% reduction of stroke risks.

The Adventist Health Study 2 [51] demonstrated that vegetarian groups (older, more educated, more likely to be married, drink less alcohol, smokeless, exercise more, and thinner) were associated with lower all-cause and cardiovascular mortality. The adjusted HR for all-cause mortality in all vegetarians combined versus nonvegetarians was 0.88 (95% CI, 0.80–0.97) a reduction of only 12% risk. However, they included vegan (no animal products, 7.6%), lacto-ovo–vegetarians (no animal meat, but consumes milk and eggs, 28.9%), pesco-vegetarians (consumes fish, 9.8%), semi-vegetarians (occasional meat consumption, 5.5%), in their vegetarian group. This will attenuate the true effects of vegetarian diets (meatless).

The DASH dietary pattern improves blood pressure and other cardiometabolic risk factors and is associated with decreased incidence of cardiovascular disease in people with and without diabetes [52]. Compared with lower adherence, higher adherence to the DASH diet was related to a reduced risk of developing stroke (RR 0.88, 95% CI 0.83–0.93), and there is a linear association of the DASH diet score with stroke (P for nonlinearity = 0.411), and each 4-points increment in the score conferred a risk reduction of 4% (RR 0.96, 95% CI 0.94–0.97) in total stroke events [53]. Similarly, the HR comparing high adherence to the Nordic diet with low adherence was 0.86 (95% CI 0.76–0.98) for total stroke [13]. The 12%–15% reduction in total stroke incidence is probably an underestimate because the control is low adherence rather than no adherence.

In a study comparing the stroke incidence of Buddhist volunteers, the vegetarian (meatless) diet groups (mostly ovo-lactovegetarians, few vegans) had a lower prevalence of hypertension than the nonvegetarian group and approximately, 60%, 60%, 50% risk reduction of hemorrhagic, ischemic and total stroke respectively. In addition, both the study and control groups were similar in their lifestyles (non-smoking, non-drinking, and active community volunteers). The only difference between the study and control group is the amount of meat (beef, pork, poultry, fish, etc.) they consumed; the magnitude of stroke risk reduction underscores the importance of meat abstinence in the prevention of stroke [14].

All these observational studies demonstrated the significant benefits of plant-based diets, especially vegetarian diets (no meat), on the risk of stroke.

Conclusion

In summary, besides low salt intake, plant-based dietary patterns that are rich in fruit, vegetables, whole grains, legumes, seeds, nuts, and dairy and low in meat, sweets, and alcohol, such as the DASH, Nordic, Mediterranean, and vegetarian diets significantly lowered blood pressure, diabetes and other risk factors of stroke, especially ischemic stroke. Most epidemiological or observational studies confirm such effects. As discussed in this review, plant-based diets, especially vegetarian diets (meatless), have a significant impact on major risk factors of stroke, such as hypertension, diabetes, hyperlipidemia, and GM, and should be recognized as one of the most important strategies in the prevention and management of stroke.

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Conflicts of interest

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