

# Relationship between Diet and Stroke: Review from Different Meta-Analytical Studies

Sivachidambaram Kulandaivelan<sup>1</sup>, Sonu Punia<sup>1</sup>

<sup>1,2</sup> Assistant Professor, Department of Physiotherapy, GJUS&T, Hisar

**Abstract:** ***Introduction:** Diet is one of the most important modifiable risk factors for cerebrovascular diseases, which accounts for one in every eight deaths worldwide. **Objective:** To systematically review and report the articles from world on diet modification to reduce the risk of stroke. **Methodology:** Study was done on May 2016 through various databases using search terms „Diet“ AND „Modification“ AND „Stroke“. 13 Meta analytical articles were identified for this review based on inclusion and exclusion criteria. **Results:** We selected 13 Meta analysis articles including 105 prospective studies, 8 randomized controlled trials and 36 cohort studies with 2696735 participants and 80691 stroke events for this review. All articles included in this review were from 2008 to till date. **Conclusion:** Folic acid, vitamin D, potassium and magnesium supplementation, and dietary fiber to the diet showed an inverse relationship to the stroke events. Chocolates, green and black tea and fish consumption also reduces the risk of stroke. Results from this review indicate that consumption of fresh red meat, processed red meat as well as total red meat and heavy alcohol consumption is associated with increased risk of total stroke and ischemic stroke, but not hemorrhagic stroke.*

**Keywords:** Ischemic stroke, Hemorrhagic stroke, CVD, CVA, ROL

## 1. Introduction

Stroke is the fourth leading cause of global disease burden. Over the past four decades, stroke incidence declined by 42% in high-income countries improvements in hypertension management but increased by 100% in low to middle income countries. About 87% of stroke deaths occurred in low to middle income countries, and the number of stroke deaths is projected to rise to 6.5 million in 2015 and to 7.8 million in 2030 globally without intervention<sup>6</sup>. Stroke can have a profound influence on the individual and their families.<sup>10</sup> According to American Heart Association, health behaviors nutrition, and overweight and obesity should be taken into account to reduce the risk of stroke<sup>6</sup>. Preventive strategies like diet modification have been shown to powerfully impact disease burden as well as costs.

Reduced plasma 25-hydroxyvitamin D (25-OH-vitD) concentrations, Dietary magnesium and potassium have been associated with several well-established risk factors for ischemic stroke<sup>1, 3, 11</sup>. Flavonoids in chocolate may be protective against cardiovascular disease through antioxidant, antiplatelet, and anti-inflammatory effects<sup>2</sup>. Coffee, tea and cocoa may reduce the risk of stroke through multiple mechanisms, including antihypertensive, hypocholesterolemic, antioxidant, and anti-inflammatory effects as well as through improvements of vascular endothelial function and insulin sensitivity<sup>4,5,10</sup>. Dairy foods are rich in saturated fatty acids, which can enhance cardiovascular disease by increasing cholesterol levels<sup>6</sup>. Dietary fiber intake is associated with improvements modifiable risk factors for stroke, such as hypertension, hypercholesterolaemia and hyperinsulinaemia<sup>7</sup>. Epidemiological data from studies indicate that fish consumption may be associated inversely with ischemic stroke and positively with hemorrhagic stroke<sup>9</sup>. High consumption of red meat has been associated with increased risk of type 2 diabetes cardiovascular, and cancer mortality, as well as with some types of cancers, including colorectal,

pancreatic, esophageal, and stomach cancer. Yet it is not clear that red meat consumption increases the risk of stroke.

So it is necessary to Clarify the relationship between different types of diet consumption and stroke risk because of the high incidence of stroke, the high morbidity and mortality associated with the disease. We conducted a review of different meta analytical studies done on different types of diet.

## 2. Methods

Computerized literature searches were performed using Google scholar Between January 2015 and March, 2016 and studies selected using key words “Diet” AND “modification” AND “Stroke”. Information from World Health Organization, International Classification of Diseases 8th edition: codes 431–438; and International Classification of Diseases, 10th edition: codes I60–I68 and G45), Embase, Web of Knowledge, Pubmed, The Cochrane Library, MEDLINE, MEDLINE in-process, CAB Abstracts, ISI Web of Science, and BIOSIS, Allied and Complementary Database (from 1985), Cumulative Index to Nursing and Allied Health Literature was also used. Literature from 1950 to till date through these electronic database was used.

Inclusion criteria for this study were as follows: (i) diet modification as a intervention, (ii) assessment of changes in stroke patients (iii) English-language studies published in journals, and (iv) Studies published till date. 13 articles were identified for review based on inclusion criteria.

## 3. Results

We selected 13 Meta analysis articles including 105 prospective studies, 8 randomized controlled trials and 36 cohort studies with 2696735 participants and 80691 stroke events for this review. All articles included in this review were from 2008 to till date.

**Jacobsen et al (2013)<sup>1</sup>** observed relationship between 25-Hydroxyvitamin D and Symptomatic Ischemic Stroke by an Original Study and Meta-Analysis. Individuals with 25-OH-vitD concentrations between the 1st and 24<sup>th</sup> percentiles were more often physically inactive, current smokers, and high alcohol consumers and more often had hypertension or diabetes mellitus than individuals with 25-OH-vitD concentrations above the 24th percentile. Stepwise decreasing plasma 25-hydroxyvitamin D concentrations were associated with stepwise increasing risk of ischemic stroke. 25-Hydroxyvitamin D concentrations were not associated with risk of hemorrhagic stroke. In a meta-analysis including 10 studies with a total of 58,384 participants and 2,644 ischemic stroke/stroke events, the odds ratios for ischemic stroke in the lowest versus highest quartile of 25-OH-vitD concentrations were 1.54 (95% confidence interval, 1.43–1.65; fixed effect) and 1.67 (1.43–1.96; random effect). The corresponding hazard ratios in prospective studies were 1.46 (1.35–1.58) and 1.52 (1.26–1.84). This large population-based prospective study observed stepwise increasing risk of symptomatic ischemic stroke with decreasing plasma 25-hydroxyvitamin D concentrations. This finding was substantiated in a meta-analysis.

**Susanna C. Larsson et al (2012)<sup>2</sup>** had done a prospective cohort of men and meta-analysis on Chocolate consumption and risk of stroke. This Meta analysis included 5 article (1,995 incident stroke cases, including 1,511 cerebral infarctions, 321 hemorrhagic strokes, and 163 unspecified strokes). Stroke risk estimate was calculated after consumption of chocolate in grams was computed by multiplying the frequency of chocolate consumption by 4 age-specific portion sizes (43–54 years, 42 g; 55–63 years, 34 g; 64–71 years, 27 g; 72–77 years, 26 g). High chocolate consumption was associated with a lower risk of stroke. The multivariable relative risk of stroke comparing the highest quartile of chocolate consumption (median 62.9 g/week) with the lowest quartile (median 0 g/week) was 0.83 (95% CI 0.70–0.99). The overall relative risk of stroke for the highest vs lowest category of chocolate consumption was 0.81 (95% CI 0.73–0.90), without heterogeneity among studies ( $p = 0.47$ ). The RR of stroke for a 50 g/week increment of chocolate consumption was 0.86 (95% CI 0.76–0.97). These findings suggest that moderate chocolate consumption may lower the risk of stroke.

**Susanna C Larsson, et al<sup>3</sup>** had done a meta-analysis of prospective studies on Dietary magnesium intake and risks of stroke. Seven prospective studies, with 6477 cases of stroke and 241,378 participants, were eligible for inclusion in the meta-analysis. Meta analysis observed a modest but statistically significant inverse association between magnesium intake and risk of stroke. An intake increment of 100 mg Mg/d was associated with an 8% reduction in risk of total stroke (combined RR: 0.92; 95% CI: 0.88, 0.97), without heterogeneity among studies ( $P = 0.66$ ,  $I^2 = 0\%$ ). Magnesium intake was inversely associated with risk of ischemic stroke (RR: 0.91; 95% CI: 0.87, 0.96) but not intracerebral hemorrhage (RR: 0.96; 95% CI: 0.84, 1.10) or subarachnoid hemorrhage (RR: 1.01; 95% CI: 0.90, 1.14). Combined RRs of stroke for an increment in intake of 100 mg Mg/d were 0.91 (95% CI: 0.85, 0.96) in studies

conducted in the United States and 0.95 (95% CI: 0.88, 1.02) in the European studies. Dietary magnesium intake is inversely associated with risk of stroke, specifically ischemic stroke.

**Susanna C. Larsson et al (2011)<sup>4</sup>** had done Systematic Reviews and Meta- and Pooled Analyses Coffee Consumption and Risk of Stroke. 11 Prospective Studies (with 10,003 cases of stroke and 479,689 participants) were used. Compared with no coffee consumption, the relative risks of stroke were 0.92 (95% confidence interval (CI): 0.89, 0.96) for 1 cup of coffee per day, 0.86 (95% confidence interval (95% CI): 0.78, 0.94) for 2 cups of coffee per day, 0.83 (95% CI: 0.74, 0.92) for 3–4 cups/day, 0.87 (95% CI: 0.77, 0.97) for 6 cups/day, and 0.93 (95% CI: 0.79, 1.08) for 8 cups/day. When we pooled the relative risks for comparable categories of coffee consumption, the relative risks of stroke were 0.88 (95% CI: 0.86, 0.90) for <3 cups/day, 0.88 (95% CI: 0.77, 1.01) for 3–5 cups/day, 0.87 (95% CI: 0.75, 1.02) for 5–7 cups/day, and 0.93 (95% CI: 0.76, 1.12) for ≥7 cups/day. Findings from this meta-analysis indicate that moderate coffee consumption may be weakly inversely associated with risk of stroke.

**D. Hu et al (2014)<sup>5</sup>** had done a meta-analysis from 15 prospective cohort studies, with 28 138 stroke events among 764 635 participants on Dairy foods (Butter, cream, ice cream and whole/high-fat milk were included in the whole/high-fat dairy foods group) and risk of stroke. Random-effect model was used to combine the results. Total dairy [relative risk (95% CI): 0.88 (0.82–0.94)], low-fat dairy [0.91 (0.85–0.97)], fermented milk [0.80 (0.71–0.89)] and cheese [0.94 (0.89–0.995)] were significantly associated with reduced risk of stroke, but whole/high-fat dairy, nonfermented milk, butter and cream were not significantly associated with risk of stroke.

Stronger association was found with risk of stroke mortality [0.80 (0.76–0.84)] was stronger ( $P = 0.01$ ) than incidence [0.95 (0.87–1.03)]. The combined RR (95%CI) of stroke for highest vs. lowest milk consumption (10 results) was 0.91 (0.82–1.01). Cheese, butter and cream Highest vs. lowest cheese consumption (6 results) conferred an RR (95%CI) of 0.94 (0.89–0.995), Butter [0.95 (0.85–1.07), 4 results] and cream [0.97 (0.88–1.06), 3 results] was not associated with risk of stroke. Dairy foods might be inversely associated with the risk of stroke.

**Diane E. Threapleton et al (2013)<sup>6</sup>** had done a Systematic Review and Meta-Analysis (8 cohort studies) on Dietary Fiber Intake and Risk of First Stroke. Total dietary fiber intake was inversely associated with risk of hemorrhagic plus ischemic stroke, with some evidence of heterogeneity between studies ( $I^2$ ; relative risk per 7 g/day, 0.93; 95% confidence interval, 0.88–0.98;  $I^2=59\%$ ). Soluble fiber intake, per 4 g/day, was not associated with stroke risk reduction with evidence of low heterogeneity between studies, relative risk 0.94 (95% confidence interval, 0.88–1.01;  $I^2=21\%$ ). There were few studies reporting stroke risk in relation to insoluble fiber or fiber from cereals, fruit, or vegetables. Greater dietary fiber intake is significantly associated with lower risk of first stroke. Overall, findings support dietary recommendations to increase intake of total

dietary fiber. However, a paucity of data on fiber from different foods precludes conclusions regarding the association between fiber type and stroke. There is a need for future studies to focus on fiber type and to examine risk for ischemic and hemorrhagic strokes separately.

**Susanna C. Larsson et al (2011)**<sup>7</sup> had done a Dose-Response Meta-Analysis on Fish Consumption and the Risk of Stroke using 15 prospective studies (with 9360 stroke events among 383 838 participants). An increment of 3 servings/week in fish consumption was associated with a 6% reduction in risk of total stroke (relative risk, 0.94; 95% CI, 0.89–0.99). Among 9 studies with results for stroke subtypes, the relative risks were 0.90 (95% CI, 0.84–0.97) for ischemic stroke and 0.90 (95% CI, 0.76–1.06) for hemorrhagic stroke. When the RR for each study for the highest versus lowest category of fish consumption was combined, the RR was 0.88 (95% CI, 0.81–0.96). These findings indicate that fish consumption is weakly inversely associated with the risk of stroke.

**Ka He, MD et al (2004)**<sup>8</sup> had done a Meta-Analysis of Cohort Studies on Fish Consumption and Incidence of Stroke. 9 independent cohorts (from 8 studies) were included. Beneficial effects on stroke risk appeared to increase with greater fish intake. Compared with those who never consumed fish or ate fish less than once per month, the pooled RRs for total stroke were 0.91 (95% CI, 0.79 to 1.06), for individuals with fish intake 1 to 3 times per month, 0.87 (95% CI, 0.77 to 0.98) for once per week, 0.82 (95% CI, 0.72 to 0.94) for 2 to 4 times per week, and 0.69 (95% CI, 0.54 to 0.88) for  $\geq 5$  times per week ( $P$  for trend 0.06). The pooled RR for those who consumed fish at least once per month were 0.85 (95% CI, 0.79 to 0.91) for total stroke, 0.67 (95% CI, 0.58 to 0.78) for ischemic stroke, and 1.06 (95% CI, 0.82 to 1.37) for hemorrhagic stroke. These results suggest that intake of fish is inversely related to risk of stroke, particularly ischemic stroke. Fish consumption as seldom as 1 to 3 times per month may protect against the incidence of ischemic stroke.

**Lenore Arab et al (2009)**<sup>9</sup> observed relationship between Green and Black Tea Consumption and Risk of Stroke. A Meta-Analysis from 9 studies involving 4378 strokes among 194 965 individuals was done. Relative risk or risk ratio was used as the primary effect estimate. Results showed that regardless of their country of origin, individuals consuming 3 cups of tea per day had a 21% lower risk of stroke than that consuming 1 cup per day (absolute risk reduction, 0.79; CI, 0.73 to 0.85). This meta-analysis suggests that daily consumption of either green or black tea equaling 3 cups per day could prevent the onset of ischemic stroke.

**Lanfranco D'Elia et al (2011)**<sup>10</sup> had done a Meta-Analysis of 11 Prospective Studies (247,510 male and female participants (follow-up 5 to 19 years), 7,066 strokes, 3,058 coronary heart disease (CHD) events, and 2,497 total CVD events) on relationship between Potassium Intake, Stroke, and Cardiovascular Disease. In the pooled analysis, a 1.64-g (42 mmol) per day higher potassium intake was associated with a 21% lower risk of stroke (RR: 0.79; 95% CI: 0.68 to 0.90;  $p=0.0007$ ). Sensitivity analysis showed that the risk of stroke did not vary substantially with the exclusion of any

individual study. Higher dietary potassium intake is associated with lower rates of stroke and might also reduce the risk of CHD and total CVD. These results support recommendations for higher consumption of potassium-rich foods to prevent vascular diseases.

**Joanna Kaluza et al (2012)**<sup>11</sup> investigated relationship between Red Meat Consumption and Risk of Stroke through a Meta-Analysis of 6 Prospective Studies (10 630 cases of stroke and 329 495 participants). For each serving per day increase in fresh red meat, processed meat, and total red meat consumption, the RR (95% CI) of total stroke were 1.11 (1.03–1.20), 1.13 (1.03–1.24), and 1.11 (1.06–1.16), respectively. Among 4 articles with results for stroke subtypes, the risk of ischemic stroke was positively associated with consumption of fresh red meat (RR, 1.13; 95% CI, 1.00–1.27), processed meat (RR, 1.15; 95% CI, 1.06–1.24), and total red meat (RR, 1.12; 95% CI, 1.05–1.19). There was no significant association between hemorrhagic stroke and consumption of fresh red meat (RR, 1.08; 95% CI, 0.84–1.39), processed meat (RR, 1.16; 95% CI, 0.92–1.46), or total red meat (RR, 1.13; 95% CI, 0.94–1.35). Results from this meta-analysis indicate that consumption of fresh red meat and processed red meat as well as total red meat is associated with increased risk of total stroke and ischemic stroke, but not hemorrhagic stroke.

**Krish Reynolds et al (2003)**<sup>12</sup> had done a meta-analysis on Alcohol consumption and risk of stroke from 35 observational studies (19 cohorts or 16 case controls). Alcohol consumption (5 subgroups: none, less than 12g, 12 to 23, 24 to 60 and more than 60g/day) was used as intervention. Consumption of more than 60 g of alcohol per day was associated with an increased relative risk of total stroke, 1.64 (95% CI, 1.39–1.93), consumption of less than 12 g/d was associated with reduced relative risk of total stroke, 0.83 (95% CI, 0.75–0.91), ischemic stroke, 0.80 (95% CI, 0.67–0.96) and consumption of less than 12g/d to 24g/d was associated with ischemic stroke, 0.72 (95% CI, 0.57–0.91). These results indicate that heavy alcohol consumption increase the RR of stroke while light or moderate level may be protective against total and ischemic stroke.

**Xiaobin Wang et al (2007)**<sup>13</sup> investigated Efficacy of folic acid supplementation in stroke prevention through a Meta analysis from 8 randomized controlled trials (16841 individuals). Folic acid supplementation significantly reduced the risk of stroke by 18 % (RR 0.82, 95% CI, 0.68–1.00,  $P=0.045$ ). In the stratified analysis, a greater beneficial effect was seen in those trials with a treatment duration of more than 36 month (RR 0.71, 95% CI, 0.57–0.87,  $P=0.001$ ), a decrease in the concentration of homocysteine of more than 20 % (RR 0.77, 0.63–0.94,  $P=0.012$ ), no fortification or partly fortified again (RR 0.82, 0.62–0.90,  $P=0.03$ ), with fortification of grain 0.89 (95% CI, 0.55–1.42,  $P=0.62$ ), with history of stroke 1.04 (0.84–1.29,  $p=0.71$ ) and with no history of stroke (RR 0.75, 0.62–0.90,  $P=0.02$ ). In the corresponding comparison group, the estimated RR was attenuated and insignificant. These findings indicate that folic acid supplementation can effectively reduced the RR of stroke in primary prevention.

#### 4. Discussion

This review including a large number of stroke cases showed that diet is a modifiable risk factor for total stroke, hemorrhagic and ischemic stroke events.

The large population-based prospective study observed stepwise increasing risk of symptomatic ischemic stroke with decreasing plasma 25-hydroxyvitamin D concentrations<sup>1</sup>. Current evidence from experimental studies in animals and humans along with findings from prospective studies indicates beneficial effects of green and black tea as well as chocolate on cardiovascular health, and that tea and chocolate consumption may reduce the risk of stroke. The strongest evidence exists for beneficial effects of tea and cocoa on endothelial function, total and LDL cholesterol (tea only), and insulin sensitivity (cocoa only). The majority of prospective studies have reported a weak inverse association between moderate consumption of coffee and risk of stroke. Flavonoids in chocolate may also decrease blood concentrations of low density lipoprotein (LDL) cholesterol and reduce LDL oxidation as well as improve endothelial function and reduces blood pressure. Fish contains long-chain omega-3 polyunsaturated fatty acids including eicosapentaenoic acid and docosahexaenoic acid, which have been demonstrated to have anti atherosclerotic and antithrombotic effects that help in reducing the risk of stroke<sup>8</sup>. Many cross-sectional and longitudinal prospective studies have detected an inverse relationship between dietary potassium, magnesium intake and BP which is indirectly related to stroke events.<sup>11</sup>

#### 5. Conclusion

Folic acid, vitamin D, potassium and magnesium supplementation, and dietary fiber to the diet showed an inverse relationship to the stroke events. Chocolates, green and black tea and fish consumption also reduces the risk of stroke.

Results from this review indicate that consumption of fresh red meat, processed red meat as well as total red meat and heavy alcohol consumption is associated with increased risk of total stroke and ischemic stroke, but not hemorrhagic stroke.

#### References

- [1] P. B. Jacobsen, B. G. Nordestgaard, P Schnohr, M. Benn, "25-Hydroxyvitamin D and Symptomatic Ischemic Stroke: An Original Study and Meta-Analysis," ANN NEUROL, vol. 73, pp.38-47, 2013.
- [2] S.C. Larsson, J. Virtamo, A. Wolk, "Chocolate consumption and risk of stroke: A prospective cohort of men and meta-analysis," Neurology, vol. 79 pp.1223, 2012.
- [3] S. C. Larsson, N. Orsini, A Wolk, "Dietary magnesium intake and risk of stroke: a meta-analysis of prospective studies," Am J Clin Nutr, vol. 95, pp. 362-6, 2012.
- [4] S. C. Larsson, N. Orsini, "Systematic Reviews and Meta- and Pooled Analyses Coffee Consumption and Risk of Stroke: A Dose-Response Meta-Analysis of Prospective Studies," Am J Epidemiol, vol. 174, no.9, pp. 993-1001, 2011.
- [5] D. Hu , J. Huang , Y. Wang , D. Zhang , Y. Qu, "Dairy foods and risk of stroke: A meta-analysis of prospective cohort studies," Nutrition, Metabolism & Cardiovascular Diseases, vol. 24, pp. 460-469, 2014.
- [6] D. E. Threapleton et al, "Dietary Fiber Intake and Risk of First Stroke: A Systematic Review and Meta-Analysis," Stroke, vol. 44, pp. 1360-1368, 2013.
- [7] S. C. Larsson, N. Orsini, "Fish Consumption and the Risk of Stroke: A Dose-Response Meta-Analysis," Stroke, vol. 42, pp. 3621-3623, 2011.
- [8] K. He, Y. Song, M. L. Daviglius, K. Liu, L. V. Horn, A. R. Dyer, U. Goldbourt, P. Greenland, "Fish Consumption and Incidence of Stroke: A Meta-Analysis of Cohort Studies," Stroke, vol. 35 pp. 1538-1542, 2004.
- [9] L. Arab, W. Liu, D. Elashoff, "Green and Black Tea Consumption and Risk of Stroke: A Meta-Analysis," Stroke, vol. 40, pp. 1786-1792, 2009.
- [10] L. D'Elia, G. Barba, F. P. Cappuccio, P. Strazzullo, "Potassium Intake, Stroke, and Cardiovascular Disease: A Meta-Analysis of Prospective Studies," J Am Coll Cardiol, vol. 57, pp. 1210-9, 2011.
- [11] J. Kaluza, A. Wolk, S. C. Larsson, "Red Meat Consumption and Risk of Stroke: A Meta-Analysis of Prospective Studies" Stroke, vol. 43, pp. 2556-2560, 2012.
- [12] K. Reynolds et al, "Alcohol consumption and risk of stroke: a meta-analysis," JAMA, vol. 289, no. 5, 2003.
- [13] Xiaobin Wang et al, "Efficacy of folic acid supplementation in stroke prevention: A Meta analysis," Lancet, vol. 369, pp. 1876-82, 2007.
- [14] S. C. Larsson, "Coffee, Tea, and Cocoa and Risk of Stroke," Stroke, vol. 45, pp. 309-314, 2014.