Review Article

Nutrition and stroke

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Stroke is one of the leading causes of death and certainly the major cause of disability in the world. WHO has estimated that between 1990 to 2020 the world will witness an increase in stroke mortality of 78% in woman and 106% in man. Much of this increase will be in developing countries which are witnessing rapid change in lifestyle and nutrition, hypertension, diabetes mellitus, smoking, atrial fibrillation, hyperlipidemia, Homocysteinemia, and alcohol are the most significant modifiable risk factors of stroke. Of these, hypertension, diabetes, smoking, hyperlipidemia, homocysteinemia and alcoholism are obviously affected by lifestyle and nutrition. However, whilst epidemiology studies have noted an association of nutritional practice with stroke risk, further research is needed to show how nutritional interventions can be effective in stroke prevention.

Key Words: cerebrovascular disease, nutrition, cerebral ischemia, cerebral hemorrhage, hypertension

Introduction

Stroke is one of the leading causes of death and disability in the world. WHO has estimated that between 1990 to 2020 the world will witness an increase in stroke mortality of 78% in woman and 106% in man. Stroke mortality is affected by stroke incidence, the mortality rate of stroke subtypes and the level of stroke care. Cerebral hemorrhage have a much higher mortality rate than ischemic stroke, and therefore better control of hypertension is likely to lead to decrease in its incidence, and result in a fall in stroke mortality. Stroke incidence therefore reflects better the actual trend in stroke occurrence. A stable stroke incidence may harbour, however, improving or deteriorating stroke morbidity since lacunar infarcts and partial strokes have less disabling strokes. A shift to a subtype of less disabling stroke, can only be captured by studies on stroke subtypes and outcomes. This data is however rarely available in the literature. In general, within the developed countries, stroke incidence is declining or remaining stable. However in the developing countries, stroke is still increasing.

The major determinant for both ischemic and hemorrhagic stroke is hypertension. In addition, diabetes, hyperlipidemia, hyperhomocysteinemia, smoking, all further increases the risk of atherosclerotic ischemic stroke. Cardioembolic disease from non valvular atrial fibrillation is an important cause of ischemic stroke, especially in the aged population. The risk of atrial fibrillation is also increased by hypertension, diabetes, and ischemic heart disease. Thus, many of the common risk factors for stoke can be affected by diet and nutrition.

Diet and nutritional pattern is however not static, and in the past fifty years, there has been remarkable changes in the nutritional pattern. The increase of stroke in developing countries has been ascribed both to population aging, and change in lifestyle and diet which increases the risk of stroke. As national income rise, dietary animal fat and protein have increased whilst carbohydrate and fiber have decreased.[1]

Whilst many countries have undergone a "westernization" of their diet, the western diets has been characterized as contributing to hypertension, obesity and therefore increase stroke risk. An analysis of randomized controlled trials of dietary and lifestyle factors suggested for example that for Finland, Italy, The Netherlands, UK and USA, overweight made a substantial contribution to the population attributable risk percentages for hypertension (PAR%: 11-17%), as was the case for excessive sodium intake (9-17%), low potassium intake (4-17%), physical inactivity (5-13%), and low intake of fish oil (3-16%).[2]

The relationship between dietary change and stroke is however complex. Many observational studies have been based on stroke mortality. However, mortality is affected by both changes in incidence, subtype of stroke, and level of stroke care. Thus mortality may not reflect change in incidence. For example, in Korea, there is an increase in serum total cholesterol level and intake of total fat (albeit still low in amount) along with a high salt intake and a high, although decreasing, prevalence of cigarette smoking. During the 15-year period investigated, 1984-1999, the age-adjusted mortality from stroke decreased while the proportion of ischemic strokes among total stroke deaths actually increased.[3]

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Westernization of the lifestyle in Japan has led to dramatic rise in the Per capita consumption of meat, milk, and dairy products, resulting in increase in animal protein animal fat intake. Nevertheless, the mean animal protein intake and mean saturated fat intake in Japan still only correspond to the low consumption categories in Western countries. At the same time there has been a decline of salt consumption. During this time, there has been a decline in the stroke mortality, as well as ischemic stroke and hemorrhagic stroke incidence. But the pattern is not consistent for all types of ischemic stroke, the age-standardized incidence of lacunar infarction has been reported to significantly decline whilst atherothrombotic infarction has remained steady after an initial decline and cardioembolic infarction remains unchanged.[4]

In France on the other hand, whilst the proportion of hypercholesterolemia and diabetes significantly increased, lacunar strokes incidence has significantly increased, cardioembolic stroke significantly decreased and atherothrombotic strokes remained steady.[5]

In China, the diet is rapidly increasing in saturated fat and animal protein content. Obesity and smoking has increased. Both in Hong Kong and in China, cerebral hemorrhage is on the decline, and ischemic stroke is increasing.[6,7]

Salt and hypertension
Hypertension is the most important determinant of stroke. Analysis of cohort and randomized studies indicate that each 10 mm Hg lower systolic BP is associated with a decrease in risk of approximately one third in subjects aged 60 to 79 years. The association is continuous down to levels of at least 115/75 mm Hg and is consistent across sexes, regions, and stroke subtypes and for fatal and nonfatal events.[8]

Observation studies have repeatedly shown an association between blood pressure levels and dietary sodium chloride, and an inverse relationship to dietary potassium, calcium and magnesium.[9]

High salt intake has been associated with increased stroke risk in previous observational studies.[10] More recent studies have confirmed this association[11], although in the US NHANES follow-up study, higher salt intake was associated with stroke in overweight persons but not in those of normal weight.[12] Negative finding in one study is possibly because of the small number of stroke cases. (HR 1.13, 0.84-1.51)[13]

Short term intervention studies have shown that increased intake of fruit, vegetables, poultry, fish, and low-fat dairy products, and reduced intake of red meats, fats, cholesterol, and sweets, as well as additional reduced salt intake can indeed reduce blood pressure, substantially (by 6.7 mm Hg, 5.4 to 8.0 mm Hg) and therefore would reduces stroke risk.[14, 15]

However, the DASH trial required intensive measures, which included provision of all food, and there are few trials which have examined the effect of longer term effect of dietary control of blood pressure. These have shown that the blood pressure reduction have been much more modest. Thus, Hooper et al found in a review of three trials in normotensives (n=2326), five in untreated hypertensives (n=387) and three in treated hypertensives

(n=801) with follow up from six months to seven years, that there was only small reduction in systolic blood pressure (1.1 mm Hg, 1.8 to 0.4).[16]

In a later meta-analysis of seventeen trials in individuals with elevated blood pressure (n=734) and 11 trials in individuals with normal blood pressure (n=2220), He and McGregor found that modest reduction of salt lasting a duration of 4 or more weeks, of about 4.5 g/day could achieve in individuals with elevated blood pressure a mean reduction in systolic blood pressure was -4.97 mmHg (95%CI:-5.76 to -4.18), and mean reduction in diastolic blood pressure was -2.74 mmHg (95% CI:-3.22 to -2.26). In individuals with normal blood pressure there is also reduction to a lesser degree in both the systolic and diastolic blood pressure. There was also a correlation between the magnitude of salt reduction and the magnitude of blood pressure reduction.[17]

Unfortunately, the efficacy of such dietary intervention seems to wane with time in the American population. While the lifestyle modifications and the DASH diet tested over six months, in free-living persons, was still effective, the effect was less than in the short term study, achieving 4.3 mmHg in the established plus DASH group.[18] A more extended study to 11 months did even worse, failing to modify the blood pressure despite significantly reducing body weight and salt intake.[19] A recent report from Japan however reported a decrease of 2.7 mmHg systolic blood pressure one year after moderately intense dietary counselling for salt reduction in free-living healthy subjects.[20]

Whilst lowering salt intake appears to be sensible and possibly effective on a population basis, salt intake is often linked to dietary preferences and how to alter this effectively remains problematic. In Japan, the decline in stroke mortality and general reduction in the mean blood pressure has been ascribed to dietary changes, including public campaigns to reduce salt. Despite a reduction of salt intake however, substitution and change in salt sources have been noted, which attenuate the effectiveness of such campaign. Few of these trials reported on clinical endpoints so there is currently no reliable data on whether these measures can actually achieve clinically useful goals.

A lower stroke mortality rate has been found with higher potassium intake, and higher stroke rate with low potassium intake.[21, 22, 23, 24, 25] There are no specific interventional studies on whether stroke incidence could be affected by potassium supplementation. Since serum potassium is kept within a narrow range, it may be clinically difficult to monitor whether potassium supplement is adequate for an individual. However, Low potassium intake in those not taking diuretics was associated with increased stroke incidence among older individuals, whilst those taking diuretics and have a serum potassium ≤4.0 mEq/L. have a higher stroke rate.[26]

If this is confirmed in other studies, then keeping the serum potassium level to above 4.0 mEq/L may be a feasible target for clinical trials.

Vegetables and fruits
Epidemiology studies suggest that intake of green yellow vegetables, fruits, fibre or whole grain but not refined

grain is protective against ischemic stroke.

The protective effect of vegetables and fruits occur irrespective of the background of fat or protein consumption. Daily consumption of green-yellow vegetables and fruits is associated with a lower risk of mortality from total stroke, intracerebral hemorrhage, and cerebral infarction amongst Japanese who have a lower animal protein and fat intake. The protective effects are similar in both men and women. Adjustment for animal product attenuated but did not invalidate the findings.[27]

Joshipura examined the associations between fruit and vegetable intake and ischemic stroke with data from 2 prospective American cohort studies, including 75,596 women aged 34 to 59 years in the Nurses' Health Study with 14 years of follow-up (1980-1994), and 38,683 men aged 40 to 75 years in the Health Professionals' Follow-up Study with 8 years of follow-up (1986-1994). After controlling for standard cardiovascular risk factors, persons in the highest quintile of fruit and vegetable intake (median of 5.1 servings per day among men and 5.8 servings per day among women) had a relative risk (RR) of 0.69 (95% confidence interval [CI], 0.52-0.92) compared with those in the lowest quintile. Cruciferous vegetables, green leafy vegetables, and citrus fruit were found to contribute most to the effect. There was 15.6% unknown type of stroke in this population. There were too few cerebral hemorrhages to be analyzed.[28]

Fung et al reported also that in American women, a diet higher in fruits and vegetables, fish, and whole grains may protect against ischemic stroke whereas a dietary pattern typified by higher intakes of red and processed meats, refined grains, and sweets and desserts may increase ischemic stroke risk, especially in those with a history of hypertension, There was no observed effect on cerebral hemorrhage. However, 17% of all cases had only a probable diagnosis of stroke, creating a huge uncertainty as to the effect on stroke subtype.[29]

Similar benefit has been observed for man. In the Framingham Heart Study, a significant inverse association was observed also between total vegetable and fruit consumption and incidence of ischemic stroke among 832 men [multivariate RR of stroke for each increment of 3 servings per day of fruit and vegetables was 0.75 (95% CI: 0.57, 1.00)].[30]

In a study on 9608 adults aged 25–74 y participating in the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study and free of cardiovascular disease at the time of their baseline examination between 1971 and 1975, consuming fruit and vegetables ≥ 3 times/d compared with <1 time/d was associated with a lower total stroke incidence [relative risk (RR): 0.73; 95% CI: 0.57, 0.95; *P* for trend = 0.01], and a lower stroke mortality (0.58; 0.33, 1.02; *P* for trend = 0.05).[31] The protective effect on ischemic stroke was noted for fruit but not vegetables in a Danish study.[32] This study also found that there was most pronounced risk reduction for the small vessel infarcts with the highest quintile of fruit consumption. This though not statistically significant because of the small number is consistent with another Korean study which found that lesser amount of fruit consumption favoured definite small vessel ischemic stroke over distal large vessel ischemic stroke.[33]

An interesting observation is that in a follow up study of 1352 families living in 16 areas of England and Scotland surveyed between 1937 and 1939, higher childhood intake of vegetables was associated with lower risk of stroke death during adulthood. It is possible that this effect may not be a residual childhood effect but is due to associated adult vegetable intake, or other associated adult lifestyle behaviours or material circumstances. As this is based on mortality, it is not known whether stroke incidence is also altered.[34]

Different mechanisms have been postulated to explain the association between intake of fruit, vegetables and stroke. The effect of vegetable and fruit may be partly due at least to effect on the blood pressure. Meta-analysis of randomized controlled trials show that increased intake of dietary fiber may reduce BP in patients with hypertension.[35, 36]

One recent interesting suggestion is that increased intake of salicylates may be another benefit of fruit and vegetable consumption.[37] The presence of naturally occurring salicylates in fruits, vegetables, and spices, has been confirmed by several research groups, it is plausible that dietary salicylates may contribute to the beneficial effects of a vegetarian diet, although it seems unlikely that most people who consume a mixed diet will achieve sufficient dietary intake of salicylates to have a therapeutic effect.

The above finding that vegetables and fruits may have a protective effect against stroke is however on a background of continuous animal product consumption. It is also unclear how much of this effect is due to the dietary intake and how much is attributable to the lifestyle and other risk profile of such persons, The observed effect of vegetable and fruit intake must be tempered with the possibility of confounding factors associated with such diet. Those who take high vegetable and fruit diet may have different lifestyles including smoking and exercise habits as well as education and social background.

A recent meta-analysis further concluded that whilst there is good evidence that fruits protect against ischemic stroke, the effect of vegetables alone was statistically non significant.[38]

Consistent with this view, is an analysis of 5 studies on pure vegetarians in Europe and America versus non vegetarians with similar lifestyle which shows that after 5 years, there is significant reduction by 24% in ischemic heart disease but no effect on stroke mortality (0.92, 0.68-1.24), the cholesterol levels were detected to be lowered in three of the studies amongst the vegetarians by 0.33 to 0.61 mmol/L.[39]

Even at 21 years follow up, although German vegetarians had lowered ischemic heart and stroke mortality than the general population, when compared with non vegetarians who had a similar healthy lifestyle, pure vegetarians had lowered ischemic heart disease but not reduced stroke mortality. Thus, a purely vegetarian diet did not seem to confer any advantage on stroke when compared with the healthy conscious who consume occasional meat. However no breakdown in the stroke incidence or subtype, or stroke incidence was available, so it is not known whether there was any effect on non fatal stroke subtype and outcome indicating a change to less disabling forms

of stroke, or whether the incidence of intracerebral hemorrhage could have altered because of the diet, and thus offsetting the advantage on ischemic stroke.[40]

Since vegetable types, consumption pattern and cooking methods vary world-wide, it is uncertain also how far the European-American experience applies. Increased vegetarian intake when salted, or the use of sauce to improve taste varieties may mean increased salt intake. Chinese vegetarians tend to cook with lots of oil, frequently consume fried vegetable items, and develop higher blood pressure because of use of processed protein substitutes, oyster sauce and tomato sauce which result in a higher salt intake. Vegetarians are also known often to have hyperhomocysteinemia because of low B12 intake subsequent to a lower intake of dairy products or fortified cereal products than omnivorous. Thus, depending on the consumption pattern, a vegetarian diet may have opposing effect on the vascular system, which loses the benefits of vegetables and fruits on a normal diet.[41]

Whole grain
The effect of grain on ischemic stroke is less certain. Whole grain was reported to decrease ischemic stroke in a prospective study by Mozaffarian and colleagues, who followed 3588 men and women aged 65+ years at baseline for 8.6 years to determine the association between fiber consumption from fruit, vegetables and cereal sources and incident cerebrovascular disease, defined as combined incident stroke, fatal and nonfatal myocardial infarction, and coronary heart disease death. In secondary analyses, they found that higher cereal fiber intake was associated with lower risk of total stroke and ischemic stroke when comparing the 80th percentile with the 20th percentile (HR 0.76, 0.60-0.95). It is worth noting that in this study, subjects who took more cereal also tend to take more fish and less of beef and pork.[42]

However, no effect was found between while grain intake and the risk of ischemic stroke when adjusted for potential confounders by Liu, and Steffen.

Liu and colleagues observed an inverse relationship between whole grain, but not refined grain intake with the risk of ischemic stroke during a 12-year follow-up of the Nurses Health Study involving 75 521 women between 38 and 63 years. However when adjustment is made for the effect of specific constituents (folate, potassium, magnesium, vitamin E and fiber), although the inverse relation remained, it was no longer statistically significant suggesting that other constituents may confer important additional protection. No such inverse relationship was observed for refined grain intake.[43]

Steffen also failed to find any effect on ischemic stroke after adjustment for potential confounders (RR 0.75, 0.46-1.22) amongst 11 940 African Americans men and women from four US cities, aged 45–64 years, and followed up over 11 years, despite a beneficial effect on mortality and coronary heart disease.[44]

Micronutrients
As discussed above, it is possible that some of the beneficial effect of whole grain relates to the folic acid intake. Folate may be beneficial both because of effect on the blood pressure and on homocysteine.[45] In a prospective, nested case-referent study plasma folate was statistically significantly associated with risk of hemorrhagic stroke in an inverse linear manner, both in univariate analysis and after adjustment for conventional risk factors including hypertension. There was no relationship with ischemic stroke.[46]

Homocyteine has been recognized as a risk factor for the development of atherosclerotic vascular disease. In the United States and Canada, folic acid fortification of enriched grain products was fully implemented by 1998. The resulting population-wide reduction in blood homocysteine concentrations might be expected to reduce stroke mortality if high homocysteine levels are an independent risk factor for stroke. A study found that the ongoing decline in stroke mortality observed in the United States between 1990 and 1997 accelerated in 1998 to 2002 in nearly all population strata, In contrast, the decline in stroke mortality in England and Wales did not change significantly between 1990 and 2002.[47]

However, there was no consistent trend in the USA population homocysteine levels during 1997-2001.[48] Thus the decline of stroke in the American population within a few years of folic acid supplementation does not appear likely to be attributable to the supplementation alone.

Recent study on folic acid, B12 and B6 supplementation showed that despite reduction of homocysteine level, stroke was not significantly reduced.[49] However, there was only 1.5μmol/L reduction of homocysteine. With a lowering of 3.2μmol/L there was a 24 % reduction of ischemic stroke, without reduction in TIA, and significant reduction in nonfatal stroke in the Hope 2 study.[50] The total number of ischemic strokes were relatively small however (81 in the treatment arm and 117 in the placebo arm) in the study. Thus no firm conclusion can be reached on whether micronutrient supplement can be clinically effective in preventing ischemic stroke.

Cerebral venous thrombosis is an uncommon disorder which often occurs in pregnant woman. Apart from increased risk form genetic based thrombophilic abnormalities, and oral contraceptives, recent case-control studies have reported an association of cerebral venous thrombosis with hyperhomocysteinemia.[51] Despite the fact that factor V Leiden mutation is absent in Asians, the occurrence of cerebral venous thrombosis is not uncommon in this population. There is increased demand for folic acid during pregnancy and low folate level has been found to be associated in cases of cerebral venous thrombosis and hyperhomocysteinemia.[52] Moreover, hyperhomocysteinemia and low folic and B12 intake is known to exist in many parts of Asia. Whether cerebral venous thrombosis during pregnancy in these patients is due to poor folate intake during pregnancy, and whether folate supplement would be useful in preventing this kind of stroke deserve investigation.

Other micronutrients
A subgroup analysis of the vitamin E And Beta carotene supplement trial suggest that vitamin E 50mg daily may reduce ischemic stroke among hypertensives. However, 600 IU of natural-source vitamin E taken every other day provided no overall benefit for ischemic or hemorrhagic stroke.[53] There was also an association of vitamin E

supplementation with increased risk of subarachnoid hemorrhage in a trial (relative risk [RR], 2.45; 95% confidence interval [CI], 1.08-5.55)[54]

Protein

Animal products such as eggs, dairy products, and fish have been found to decrease mortality due to cerebral hemorrhage but not cerebral infarction, amongst Japanese and adjustment for vegetables and fruits did not alter the finding.[55] This finding has been confirmed in another study which showed that low intake of saturated fat and animal protein is associated with increased cerebral haemorrhage among Japanese man, irrespective of whether hypertensives or nonhypertensives.[56] Consistent with this finding, even amongst Americans who have a higher protein intake, a low intake of saturated fat and animal protein has been reported to be associated with an increased risk of cerebral hemorrhage in women with history of hypertension.[57]

The blood pressure in these studies was however based on baseline values, and therefore would have underestimated the impact if any of hypertension. Furthermore, the ascertainment rate of the diagnosis of cerebral hemorrhage, by CT/MRI or autopsy was not reported.

Protein intake has been associated with lowering of blood pressure.[58, 59] It is possible therefore, that if confirmed by more rigorous studies, the observed association is due to blood pressure changes.

In a randomized trial also, 40 g of isolated soybean protein supplements per day for 12 weeks also resulted in a reduction in systolic and diastolic blood pressure. The trial did not examine whether the blood pressure reduction was due to protein or isoflavones in soybean.[60]

Cholesterol and fat

High cholesterol is a risk factor for ischemic stroke. A recent Asian study found that for people in the highest categories of both total cholesterol and SBP (i.e., with measured total cholesterol $\geq$6.25 mmol/L and measured SBP $\geq$160 mm Hg), ischemic stroke risk 8 times higher than among people in the lowest categories of both (i.e., measured values of total cholesterol and SBP of <4.75 mmol/L and 130 mm Hg, respectively). This study however found no evidence of a particular increase in hemorrhagic stroke with the combination of low cholesterol and high SBP, suggesting that if there is an association, it is smaller than indicated in other cohorts.[61]

Since dietary fat can affect the blood cholesterol level, it can be expected to contribute towards a high cholesterol level and thereby increased stroke risk. Consistent with this is the adverse effect of dietary fat on stroke mortality, reported by Sasaki et al who examined population dietary and mortality data. The intake levels of dietary saturated fatty acid correlated independently, significantly, and positively with log-stroke mortality rates except in both sexes in the age class 45-54, when urinary-Na was included in the multiple regression analysis.[62] Except for Japan, the data used were from Western Europe or America.

In contrast, this effect has not been noted with specific prospective studies. No relationship between dietary fat and ischemic or hemorrhagic stroke was found in 40000 men followed up for 4 years. Intakes of red meats, high fat dairy products, nuts, and eggs were also not appreciably related to risk of stroke.[63]

On the other hand, as part of the Framingham Heart Study, Gillman et al found instead that intakes of fat, saturated fat, and monounsaturated fat were associated with reduced risk of ischemic stroke in men. Adjustment for cigarette smoking, glucose intolerance, body mass index, blood pressure, blood cholesterol level, physical activity, and intake of vegetables and fruits and alcohol did not materially change the results. Too few cases of hemorrhagic stroke (n=14) occurred to draw inferences.[64]

This finding is similar to that reported by Sauvaget in Japan, where animal product and fat intake is lower than in Western countries, a high consumption of animal fat and cholesterol was also associated with a reduced risk of cerebral infarction death. The risk of death from infarction was reduced by 63% (CI, 82% to 22%) in the high cholesterol consumption group, compared with the low consumption group. A significant linear dose-response relationship was observed.[65] This was however a death certificate based study with uncertainty regarding ascertainment of diagnosis and interaction with blood pressure.

Consistent with the above two studies, the Asia Pacific Cohort Studies Collaboration found there was a clear trend (P<0.007 for the likelihood ratio test of linear interactions) toward steeper associations of systolic blood pressure with stroke in those with low values of cholesterol (and vice versa) For example, with regard to risk of total ischemic stroke, a 10–mm Hg–higher SBP was associated with hazard ratios of 40% (95% CI, 36 to 43), 39% (95% CI, 33 to 45), 37% (95% CI, 29 to 43), and 29% (95% CI, 21 to 37) in cholesterol groups of <4.75, 4.75 to 5.49, 5.50 to 6.24, and $\geq$6.25 mmol/L, respectively. This suggests therefore that an excessively low cholesterol level might be detrimental for ischemic stroke when hypertension is present. Unfortunately there is no information on this correlation in the two dietary studies.

There has been controversy on whether a low cholesterol level will increase cerebral hemorrhage risk. However, there is insufficient data correlating cerebral hemorrhage risk and dietary fat.

While the use of statins have been shown to lower the risk of ischemic stroke,
there is insufficient data what effect interventional trials of low fat diet may have on stroke.

The Lyon Diet Heart Study is a randomized secondary prevention trial aimed at testing whether a Mediterranean-type diet may reduce the rate of recurrence after a first myocardial infarction. A protective effect was found for myocardial infarction and coronary death. However there were too few stroke events in this study even after 4 years of follow up. (4 for control, none in the Mediterranean diet group).[66]

Fish intake

An analysis of 5 prospective cohort studies and one case control study with regard to the effect of fish intake on stroke incidence shows that fish intake is associated with less ischemic stroke.[67]

However in the GISSI prevention trial, a Mediterranean diet and 850 mg of omega 3 fatty acid showed a benefit

for combined non fatal myocardial infarction, death, and stroke, but the number of stroke in the trial was small and no effect demonstrated specifically, Nor did supplement with linoleic acid have an effect.[68]

Cerebral embolic stroke is mainly related to atrial fibrillation. Consumption of tuna and other broiled or baked fish, but not fried fish or fish sandwiches, is associated with lower incidence of atrial fibrillation among older adults and therefore reduced risk from cerebral embolism.[69]

Other prospective studies[70, 71] however have failed to show any effect of fish intake on atrial fibrillation. Mozzaffarin has emphasized that the way the fish is eaten may be significant. But adjustment for taking of fried fish did not alter the findings in the Rotterdam study.

A randomized control trial has shown recently however that preoperative and postoperative treatment with n-3 polyunsaturated fatty acids was effective in preventing the occurrence of atrial fibrillation after coronary artery bypass graft surgery; giving credence to the possibility that fish intake may be useful.[72]

In contrast to the above studies which suggest that fish intake may be beneficial against ischemic stroke, there are some reports suggesting that there may be instead an increase of hemorrhagic stroke with fish consumption.[73] In a recent report, higher intake of fish during childhood was associated with higher risk of stroke during adulthood. The fully adjusted rate ratio between the highest and lowest quartile of fish intake was 2.01 (95% confidence interval 1.09 to 3.69, p for trend 0.01). Whether this higher risk of stroke death associated with increased fish intake is a residual effect from childhood consumption or due to adult fish intake is however unknown.[74]

Carbohydrate

As a result of over-nutrition, there has been a worldwide increase of obesity. Obesity is a risk factor for developing type II diabetes and diabetes is a known risk factor for stroke.

In the Nurses Health Study, total Carbohydrate intake was associated with elevated risk of hemorrhagic stroke when the extreme quintiles were compared (relative risk = 2.05, 95% confidence interval: 1.10, 3.83; p (trend) = 0.02). Glycemic load or index however did not have any significant relationship. The positive association between carbohydrate intake and stroke risk was most evident among women with a body mass index of > or =25 kg/m. although curiously BMI itself was inversely related to hemorrhagic stroke, In this study, the higher qintiles of carbohydrate intake however also has less saturated and trans fat intake. On the other hand, higher consumption of cereal fiber though not total fibre was associated with lower risk of total and hemorrhagic stroke.[75] The authors suggested that this pattern of high carbohydrate intake may explain the increase of hemorrhagic stroke in the Asian population. However, the authors did not give the actual carbohydrate intake of their study population. Comparison of carbohydrate intake as percentage of energy intake or total amount between Asian population and Australian population[76] where the cerebral hemorrhage incidence is close to American incidence, however does not suggest this alone is a likely explanation. Unfortu-

nately also, medical record was only available for 74% of the non fatal stroke cases and 68% of the fatal strokes in this study.

BMI was a strong risk factor for total and ischemic stroke but not for hemorrhagic stroke. The association was highly mediated by hypertension, diabetes, and elevated cholesterol. Several studies have found positive associations between body mass index (BMI) and stroke in men.[77] Both cross-sectional and longitudinal studies have consistently identified an association between overweight and hypertension independent of other risk factors for hypertension. Several clinical trials also have shown a BP-lowering effect of weight loss. These data indicate that weight loss is an important approach for primary prevention of hypertension and thereby reduce stroke risk.

Very few patients with general obesity have none of the components of the metabolic syndrome, a clustering of disturbed glucose and insulin metabolism, obesity and abdominal fat distribution, dyslipidemia, and hypertension and associated with an increased risk for acute ischemic/non-embolic stroke.[78] In the presence of metabolic syndrome, HDL cholesterol loses its protective role against ischemic stroke.[79] The risk of any stroke is increased in men with metabolic syndrome, even if stroke, diabetes and cardiovascular disease is absent at baseline.[80] A dose effect is also seen with more ischemic stroke seen with more components of the metabolic syndrome present. It remains uncertain however, whether obesity and excessive caloric intake, will have additional effect on stroke risk, in the absence of hypertension, diabetes or hyperlipidemia. The fact that obesity have markedly increased in America since the 1980's but stroke incidence has not, would suggest otherwise however.

Lifestyle and nutrition

Instead of a single component of nutritional intake, the entire lifestyle and dietary pattern may be more important. Finland had one of the highest reported incidences of stroke in the world. There has been however a highly significant downward trend in both the incidence and mortality of stroke. A major reason for the decline in stroke incidence and mortality is believed to be that the cardiovascular risk factor levels, which used to be very unfavourable in Finland, have improved considerably. This is been attributed to a public campaign aimed at changing the type of fat used, to lower sodium intake, and to increase vegetable and fruit consumption, strive for better blood pressure control, and stop smoking, Of the 4 main risk factors (high blood pressure, elevated blood lipids, smoking, and obesity), the only one that has not been reduced by these health-promoting campaigns is obesity.[81]

In a large prospective cohort of 37 636 apparently healthy women, a healthy lifestyle consisting of abstinence from smoking, low body mass index, moderate alcohol consumption, regular exercise, and healthy diet was associated with a significantly reduced risk of total and ischemic stroke but not of hemorrhagic stroke.[82]

However, stroke was not reduced in a randomized controlled trial involving 48,835 postmenopausal women aged 50 to 79 years, of diverse backgrounds and ethnicities, randomly assigned to an intervention or comparison group in a free-living setting. Mean follow-up in this

analysis was 8.1 years. Intensive behaviour modification in group and individual sessions were designed to reduce total fat intake to 20% of calories and increase intakes of vegetables/fruits to 5 servings/d and grains to at least 6 servings/d. The intervention however reduce dietary fat intake by 8% and achieved only modest effects on CVD risk factors, Low-density lipoprotein cholesterol levels, diastolic blood pressure, and factor VIIc levels were significantly reduced by 3.55 mg/dL, 0.31 mm Hg, and 4.29%, respectively; levels of high-density lipoprotein cholesterol, triglycerides, glucose, and insulin did not significantly differ in the intervention vs. comparison groups.[83]

Conclusion

Observational studies have shown that stroke risk factors can be altered by nutritional intake. Most interventional studies however have so far failed to achieve meaningful clinical outcomes. We therefore do not have at present evidence that dietary or lifestyle interventions in the absence of pharmacological therapy can effectively prevent stroke. It may not however be that such interventions will not work, but that the dose of intervention was insufficient, or that the knowledge of how to make these interventions achieve a clinically significant impact is still deficient. Alternatively, the experience from Japan and Finland suggest that change in lifestyle and dietary habits may be more successful if carried out as a societal effort, rather than by individual coaching. Further investigations on the methodology of nutritional and lifestyle interventions are clearly needed.

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