

## Intakes of Vegetables and Fruits are Negatively Correlated with Risk of Stroke in Iran

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### ABSTRACT

**Background:** Stroke is a leading cause of death. Current therapeutic strategies have been unsuccessful. Several studies have reported benefits on reducing stroke risk and improving the poststroke associated functional declines in patients who ate foods rich in fruits and vegetables. Their potential protective effects may be due to their antioxidants, calcium, potassium, riboflavine, peridoxin, riboflavin contents. Folic acid, peridoxin, and riboflavin are all cofactors in hyperhomocysteinemia as a stroke risk factor. Studies suggest that oxidative stress plays important roles in pathogenesis of ischemic cerebral injury and higher intake of antioxidants has been associated with a lower stroke risk. The aim of this study was to examine if the dietary intake of vegetables and fruits in patients with stroke were comparatively worse than those in patients without stroke.

**Methods:** In this case control study, 93 stroke patients admitted to Alzahra hospital were matched for age and sex with 60 patients who were not affected with acute cerebrovascular diseases and did not have a history of stroke. Dietary intake was assessed with a validated food frequency questionnaire. Food intakes were compared between two groups and with recommended value.

**Results:** Mean daily intake of vegetable and fruits was more in male with stroke than male without stroke as well as calorie intake from vegetables and fruit was higher in male with stroke. Mean daily intake of vegetable and fruits were lower in women with stroke than women without stroke as well as calorie intake from vegetables and fruit was lower in women with stroke.

**Conclusions:** Our findings suggest that increased vegetable and fruits intake may be associated with decreased risk of stroke.

**Keywords:** Dietary quality, fruit, stroke, vegetable

### INTRODUCTION

According to the World Health Organization (WHO), stroke and other cerebrovascular diseases are the second highest causes of mortality worldwide at 9.7% of the total

mortality rate.<sup>[1]</sup> Over 85% of these deaths occur in low- and middle-income countries.<sup>[2]</sup> Stroke is a major public health problem in developing countries.<sup>[3]</sup> According to a recent well-designed population-based study in Mashhad, Iran, incidence of stroke in Iran is considerably higher than in most of the Western countries.<sup>[4]</sup>

Risk factors associated with stroke have been divided into two main categories non-modifiable and modifiable. Advanced age, gender, race, and genetic susceptibility are the most prominent non-modifiable risk factors; while lifestyle risk factors such as diet, exercise, and use of tobacco and alcohol are considered as modifiable risk factors.<sup>[5]</sup> An increase has been observed in the number of cerebrovascular events in developing countries that matches with food and lifestyle changes arising from industrialization and urbanization.<sup>[6]</sup>

Meta-analysis of cohort studies show that increased intake of fruits and vegetables is associated with a reduced risk of stroke, and provides support for the recommendation to consume more than five servings of fruits and vegetables per day, which is likely to cause a major reduction in stroke.<sup>[7]</sup> The potential protective effects of fruits and vegetables may be due to their antioxidant vitamins,<sup>[8]</sup> folic acid contents, and metabolically related B vitamins such as vitamin B12, vitamin B6, and riboflavin.<sup>[9]</sup>

Six prospective cohort studies have examined the relationship between fruit and vegetable intake and risk of stroke. The risk of ischemic stroke with fruit and vegetable intake was evaluated jointly among 75,596 women aged 34-59 years from the Nurses' Health Study (NHS), who were followed up for 14 years, and 38,683 men aged 40-75 years from the Health Professionals' Follow-up Study (HPFS), who were followed up for 8 years. Ischemic stroke was documented among 366 women and 204 men. An inverse relationship was detected among the group in the highest quintile of fruit and vegetable consumption (RR, 0.69; 95% confidence interval (CI), 0.52-0.92). In particular, high consumption of cruciferous vegetables, green leafy vegetables, citrus fruits, and vitamin C-rich fruits carried the lowest risk for both cohorts, with significance remaining intact after adjustment for potential confounders. Similar results were seen for total fruits and total vegetables when computed separately.<sup>[10]</sup>

Vitamin C,  $\beta$ -carotene, and vitamin E in fruits and vegetables scavenge free radicals, and

vitamin C protects membranes from peroxidation by regenerating their  $\alpha$ -tocopherol components.<sup>[11]</sup> Free radical oxidation of LDL is thought to be an important contributor to the development of atherosclerosis, and thus antioxidants may slow or prevent this process and thereby decrease the risk of stroke. Observational studies have shown that decreased risk of stroke is associated with increased antioxidant intake.<sup>[12]</sup> There has been growing interest in protection against stroke by intake of folic acid and related B vitamins from fruits and vegetables.<sup>[13,14]</sup> These effects may be mediated via homocysteine, the metabolism of which requires adequate status of all four relevant B vitamins.<sup>[9]</sup> Higher folic acid intakes were associated with reduced stroke risk in studies of Health Professionals,<sup>[15]</sup> male Swedish smokers,<sup>[13]</sup> and male Finnish smokers,<sup>[10]</sup> but not in the Nurses Health study.<sup>[16]</sup> Thus, the role of folic acid in stroke has yet to be established, and data on the intake of other B vitamins and stroke are sparse. The aim of this study was to examine if the dietary intake of vegetables and fruits in patients with stroke were comparatively worse than those in patient without stroke.

## METHODS

In this case-control study, 93 stroke patients (46 male, age =  $56 \pm 18$  and 23 female, age =  $52 \pm 7$ ) admitted to Alzahra hospital between April 2009 and May 2010 were matched for age and sex with 60 patients (30 male and 30 female) from the same hospital who were not affected with acute cerebrovascular diseases and did not have a history of stroke. Informed consent was obtained from all stroke patients or their family member and all healthy controls.

Dietary intake was assessed with a validated self-administered food frequency questionnaire that included 168 food items and mixed dishes commonly consumed in Iran. FFQ was collected by face-to-face interview with one of their close relative. It was used with a portion-size color picture booklet of 122 photographs of foods, each with 3-5 different portion sizes. Participants were asked to report their average consumption and portion size for each food/dish during the previous year. Frequencies were reported as the number of times per month, week, or day. A dietitian provided verbal

and written instruction on how to record food consumption. Intake of nutrients was calculated by use of the food composition database.

FFQ categorized the food items into six food groups: (i) Mixed dishes (cooked or canned); (ii) grains (different types of bread, cakes, biscuits, and potato); (iii) dairy products (dairies, butter and cream); (iv) fruits and vegetables; (v) meat and protein (meat, fish, turkey, legume, and eggs); (vi) miscellaneous food items and beverages (including sweets, fast foods, nuts, desserts, and beverages).

The statistics in this study were done by SPSS (version 16.0) software. Results are expressed as mean  $\pm$  SD. Student's *t*-tests were performed to compare the means of two groups. Statistical significance was defined as  $P < 0.05$ .

## RESULTS

Age, waist, BMI, and WHR in stroke patients are shown in Table 1. Mean daily intake of vegetable and fruits were more in male with stroke than male without stroke as well as calorie intake from vegetables and fruit was higher in male with stroke [Table 2]. Mean daily intake of vegetable and fruits were lower in women with stroke than women without stroke as well as calorie intake from vegetables and fruit was lower in women with stroke [Table 3].

## DISCUSSION

This is the first study to investigate the diet quality of patients with stroke in Iran. This study revealed that patients with stroke had lower dietary quality than patients without stroke.

The results from this study reveal that mean daily intake of vegetable and fruits in women with stroke (440 and 170 g/day respectively) was lower than patients

without stroke (620 and 208 g/day, respectively). However, mean daily intake of vegetable and fruits in men with stroke (340 and 253 g/day, respectively) was higher than men without stroke (320 and 213 g/day, respectively).

Vegetables and fruits contain many vitamins, minerals, and antioxidants having effects in preventing stroke:

### Flavonoids

Flavonoids (flavonols, flavones, and isoflavones) are dietary antioxidant compounds commonly found in concentrated amounts in multiple fruits, vegetables including apples, berries, grapes, and onions.<sup>[17]</sup> They are characterized by their inherent potent antioxidant effects with a range of biochemical properties, such as antioxidant, anti-inflammatory, and antithrombotic effects;<sup>[18]</sup> inhibiting lipid peroxidation; preventing atherosclerosis; promoting vascular relaxation; and with antihypertensive properties that may explain beneficial effects on stroke. Hollman and colleagues<sup>[18]</sup> have conducted a meta-analysis of six prospective cohort studies to assess quantitatively the strength of the association between flavonol intake and stroke incidence. A high intake of flavonols when compared with a low intake was inversely associated with nonfatal and fatal stroke, suggesting that flavonols may reduce stroke risk.

### Carotenoids

Carotenoids, the pigments responsible for the yellow to red color of some fruits and vegetables have been implicated as beneficial substances. They are found in the human diet and primarily derived from plants, found in their roots, leaves, shoots, seeds, fruit, and flowers.<sup>[19]</sup> Various biological effects have been attributed to carotenoids. A possible mechanism of action is through the antioxidant activity, but other mechanisms of protection may exist.<sup>[19]</sup> The currently dietetic recommendation to increase consumption of fruits and vegetables rich in antioxidants has generated interest in the role of

**Table 1:** General characteristics of the subjects

BMI(kg/m <sup>2</sup> )	Waist (cm)	WHR	Age (year)
25/5 $\pm$ 3/5	92 $\pm$ 8	0/9 $\pm$ 0/1	52 $\pm$ 7

BMI=Body mass index, WHR=Waist to hip ratio

**Table 2:** Mean of daily fruits and vegetable intake in men

Food Items	Kcal/day from vegetables or fruits in men without stroke	Grams per day for men without stroke	Kcal/day from vegetables or fruits in men with stroke	Grams per day for men with stroke
Fruits	96	213	114	253
Vegetables	80	320	85	340

**Table 3:** Mean of daily fruits and vegetable intake in women

Food Items	Kcal/day from vegetables or fruits in women without stroke	Grams per day for women without stroke	Kcal/day from vegetables or fruits in women with stroke	Grams per day for women with stroke
Fruits	94	208	80	177
Vegetables	155	620	100	440

carotenoids.<sup>[20]</sup> However, the mechanisms are not clearly known. Some researchers have evaluated their effect in preventing cardiovascular disease.

Prospective studies have shown the association between plasma levels of carotenoids and markers of inflammation, oxidative stress, endothelial dysfunction,<sup>[21,22]</sup> and arterial stiffness.<sup>[23]</sup> Their many conjugated double bonds give them an antioxidant potential. Lycopene is the most powerful antioxidant among plasma carotenoids.<sup>[23]</sup> Its effects have been related to decreased risk of cardiovascular disease,<sup>[24,25]</sup> including atherosclerosis<sup>[26]</sup> and myocardial infarction.<sup>[27]</sup> These nutrients can affect the risk of stroke.

There are a few studies associating carotenoids with stroke. Rissanen and colleagues,<sup>[28]</sup> in the Kuopio Ischaemic Heart Disease Risk Factor Study, examined 725 men during 6 years for associated serum lycopene levels and risk of coronary heart disease and stroke. Men in the lowest quarter of serum lycopene levels had a 3.3-fold risk of acute coronary heart events and stroke. These findings suggest that lycopene might have a role in the prevention of coronary events and stroke.

### B vitamins

The potential protective effect of vegetables and fruits on stroke is thought to be mediated through reductions in homocysteine concentration. Elevated homocysteine concentration is considered a risk factor for arterial endothelial dysfunction.<sup>[27]</sup> Plasma homocysteine is very responsive to intervention with B vitamins required for its metabolism: Folate, and to a lesser extent, vitamin B6, and riboflavin.<sup>[9,29]</sup> Previous studies have shown that intake of folate between 300 and 821 µg reduced the risk of stroke.<sup>[10,14,16,30,31]</sup> There is growing evidence that niacin inhibits vascular inflammation by decreasing endothelial reactive oxygen species production and subsequent LDL oxidation and inflammatory cytokine production, key events involved in atherogenesis.<sup>[32]</sup>

Another B vitamin, vitamin B12 may also

protect against stroke by mediating homocysteine metabolism.

### Calcium and potassium

Vegetables are also rich sources of potassium and calcium, which have been shown to lower blood pressure. Since high blood pressure is the major cause of stroke, the effects of potassium and calcium on blood pressure may contribute to the reduced risk of stroke with an increased vegetable intake.<sup>[33]</sup> Higher dietary calcium and potassium intake are inversely correlated with the risk of stroke or stroke mortality,<sup>[34,35]</sup> and the Systolic Hypertension in the Elderly Study indicated that low serum potassium was associated with increased stroke incidence.<sup>[36]</sup> Randomized controlled trials have shown fruit and vegetable consumption to significantly lower systolic and diastolic blood pressure,<sup>[37,38]</sup> and thus possibly preventing stroke.

## CONCLUSIONS

Our findings seem to suggest that vegetables and fruits may play a role in reducing the risk of stroke. As already noted and our patients especially women with stroke indicate a more insufficient intake of beneficial food groups, which results in a low nutrition density diet and poor overall dietary quality, than subjects without stroke. A large-scale prospective study to identify the dietary patterns of patients with stroke in Iran should be conducted.

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## REFERENCES

1. Lim H, Choue R. Dietary pattern, nutritional density, and dietary quality were low in patients with cerebral infarction in Korea. *Nutr Res* 2011;31:601-7.
2. Delbari A, Salman Roghani R, Tabatabaei SS, Rahgozar M, Lökk J. Stroke epidemiology and one-month



- fatality among an urban population in Iran. *Int J Stroke* 2011;6:195-200.
3. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global burden of disease study. *Lancet* 1997;349:1269-76.
4. Azarpazhooh MR, Etemadi MM, Donnan GA, Mokhber N, Majidi MR, Ghayour-Mobarhan M, *et al.* Excessive incidence of stroke in Iran: Evidence from the Mashhad stroke incidence study (MSIS), a population-based study of stroke in the middle East. *Stroke* 2010;41:e3-10.
5. Romero JR, Morris J, Pikula A. Stroke prevention: Modifying risk factors. *Ther Adv Cardiovasc Dis* 2008;2:287-303.
6. Dans A, Ng N, Varghese C, Tai ES, Firestone R, Bonita R. The rise of chronic non-communicable diseases in southeast Asia: Time for action. *Lancet* 2011;377:680-9.
7. He FJ, Nowson CA, MacGregor GA. Fruit and vegetable consumption and stroke: Meta-analysis of cohort studies. *Lancet* 2006;367:320-6.
8. Spence JD. Nutrition and stroke prevention. *Stroke* 2006;37:2430-5.
9. McNulty H, Scott JM. Intake and status of folate and related B-vitamins: Considerations and challenges in achieving optimal status. *Br J Nutr* 2008;99:S48-54.
10. Joshipura KJ, Ascherio A, Manson JE, Stampfer MJ, Rimm EB, Speizer FE, *et al.* Fruit and vegetable intake in relation to risk of ischemic stroke. *JAMA* 1999;282:1233-9.
11. Sies H, Stahl W. Vitamins E and C, beta-carotene, and other carotenoids as antioxidants. *Am J Clin Nutr* 1995;62:1315S-21S.
12. Davi GL, Orenstein AJ, Dyer AR, Liu K, Morris DK, Persky V, *et al.* Dietary vitamin C, beta-carotene and 30-year risk of stroke: Results from the Western Electric Study. *Neuroepidemiology* 1997;16:69-77.
13. Van Guelpen B, Hulthén J, Johansson I, Stegmayr B, Hallmans G, Nilsson TK, *et al.* Folate, vitamin B12, and risk of ischemic and hemorrhagic stroke: A prospective, nested case-referent study of plasma concentrations and dietary intake. *Stroke* 2005;36:1426-31.
14. Weng LC, Yeh WT, Bai CH, Chen HJ, Chuang SY, Chang HY, *et al.* Is ischemic stroke risk related to folate status or other nutrients correlated with folate intake? *Stroke* 2008;39:3152-8.
15. Gillman MW, Cupples LA, Gagnon D, Posner BM, Ellison RC, Castelli WP, *et al.* Protective effect of fruits and vegetables on development of stroke in men. *JAMA* 1995;273:1113-7.
16. Al-Delaimy WK, Rexrode KM, Hu FB, Albert CM, Stampfer MJ, Willett WC, *et al.* Folate intake and risk of stroke among women. *Stroke* 2004;35:1259-63.
17. Kizhakekuttu TJ, Widlansky ME. Natural antioxidants and hypertension: Promise and challenges. *Cardiovasc Ther* 2010;28:e20-32.
18. Hollman PC, Geelen A, Kromhout D. Dietary flavonol intake may lower stroke risk in men and women. *J Nutr* 2010;140:600-4.
19. Voutilainen S, Nurmi T, Mursu J, Rissanen TH. Carotenoids and cardiovascular health. *Am J Clin Nutr* 2006;83:1265-71.
20. Agarwal S, Rao AV. Tomato lycopene and its role in human health and chronic diseases. *CMAJ* 2000;163:739-44.
21. Hozawa A, Jacobs DR Jr, Steffen MW, Gross MD, Steffen LM, Lee DH. Relationships of circulating carotenoid concentrations with several markers of inflammation, oxidative stress, and endothelial dysfunction: The coronary artery risk development in young adults (CARDIA)/Young adult longitudinal trends in antioxidants (YALTA) study. *Clin Chem* 2007;53:447-55.
22. van Herpen-Broekmans WM, Klöpping-Ketelaars IA, Bots ML, Kluft C, Princen H, Hendriks HF, *et al.* Serum carotenoids and vitamins in relation to markers of endothelial function and inflammation. *Eur J Epidemiol* 2004;19:915-21.
23. Markovits N, Ben Amotz A, Levy Y. The effect of tomato-derived lycopene on low carotenoids and enhanced systemic inflammation and oxidation in severe obesity. *Isr Med Assoc J* 2009;11:598-601.
24. Sesso HD, Buring JE, Norkus EP, Gaziano JM. Plasma lycopene, other carotenoids, and retinol and the risk of cardiovascular disease in women. *Am J Clin Nutr* 2004;79:47-53.
25. Sesso HD, Liu S, Gaziano JM, Buring JE. Dietary lycopene, tomato-based food products and cardiovascular disease in women. *J Nutr* 2003;133:2336-41.
26. Klipstein-Grobusch K, Launer LJ, Geleijnse JM, Boeing H, Hofman A, Witteman JC. Serum carotenoids and atherosclerosis. The Rotterdam Study. *Atherosclerosis* 2000;148:49-56.
27. Kohlmeier L, Kark JD, Gomez-Gracia E, Martin BC, Steck SE, Kardinaal AF, *et al.* Lycopene and myocardial infarction risk in the EURAMIC Study. *Am J Epidemiol* 1997;146:618-26.
28. Rissanen TH, Voutilainen S, Nyyssönen K, Lakka TA, Sivenius J, Salonen R, *et al.* Low serum lycopene concentration is associated with an excess incidence of acute coronary events and stroke: The Kuopio Ischaemic heart disease risk factor study. *Br J Nutr* 2001;85:749-54.
29. Keli SO, Hertog MG, Feskens EJ, Kromhout D. Dietary flavonoids, antioxidant vitamins, and incidence of stroke: The Zutphen study. *Arch Intern Med* 1996;156:637-42.
30. Bazzano LA, He J, Ogden LG, Loria C, Vupputuri S,

- Myers L, *et al.* Dietary intake of folate and risk of stroke in US men and women: NHANES I Epidemiologic follow-up study. National health and nutrition examination survey. *Stroke* 2002;33:1183-8.
31. Woo KS, Sanderson JE, Sun YY, Chook P, Cheung AS, Chan LT, *et al.* Hyperhomocyst(e) inemia is a risk factor for arterial endothelial dysfunction in humans. *Circulation* 2000;101:E116.
  32. Ganji SH, Qin S, Zhang L, Kamanna VS, Kashyap ML. Niacin inhibits vascular oxidative stress, redox-sensitive genes, and monocyte adhesion to human aortic endothelial cells. *Atherosclerosis* 2009;202:68-75.
  33. Savage GS. Candidate foods in the Asia-Pacific region for cardiovascular protection: Fish, fruit and vegetables. *Asia Pac J Clin Nutr* 2001;10:134-7.
  34. Ascherio A, Rimm EB, Hernán MA, Giovannucci EL, Kawachi I, Stampfer MJ, *et al.* Intake of potassium, magnesium, calcium, and fiber and risk of stroke among US men. *Circulation* 1998;98:1198-204.
  35. Umesawa M, Iso H, Date C, Yamamoto A, Toyoshima H, Watanabe Y, *et al.* Dietary intake of calcium in relation to mortality from cardiovascular disease: The JACC Study. *Stroke* 2006;37:20-6.
  36. Franse LV, Pahor M, Di Bari M, Somes GW, Cushman WC, Applegate WB. Hypokalemia associated with diuretic use and cardiovascular events in the systolic hypertension in the elderly program. *Hypertension* 2000;35:1025-30.
  37. John JH, Ziebland S, Yudkin P, Roe LS, Neil HA; Oxford Fruit and Vegetable Study Group. Effects of fruit and vegetable consumption on plasma antioxidant concentrations and blood pressure: A randomised controlled trial. *Lancet* 2002;359:1969-74.
  38. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, *et al.* A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;336:1117-24.

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