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META-ANALYSIS

Nut consumption and risk of stroke

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Abstract Nut consumption has been inconsistently associated with risk of stroke. Our aim was to carry out a meta-analysis of prospective studies to assess the relation between nut consumption and stroke risk and mortality. Pertinent studies were identified by a search of PubMed and Embase through June 2014 and by reviewing the references of retrieved articles. Prospective cohort studies that reported relative risks (RRs) with 95 % confidence intervals (CIs) for the association between nut consumption and risk of stroke were included. Six articles including nine independent prospective cohorts with 476,181 participants were included in the meta-analysis. The pooled RR of stroke was 0.90 (95 % CI 0.83–0.98) comparing the highest with the lowest nut consumption. Stratifying by gender, significant inverse association was observed for females (RR 0.88; 95 % CI 0.78–0.98). Sensitivity analysis restricted to studies with adjustment for common confounding factors showed similar results, strengthening the association between nut consumption and stroke risk. Moreover, we observed a trend toward an inverse association between higher nut consumption and stroke mortality (RR 0.86; 95 % CI 0.69–1.06), although it is not significant. Current evidence indicated that nut consumption is inversely associated with risk of stroke.

Keywords Nut · Stroke · Prospective studies

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Introduction

Stroke is the second leading cause of death worldwide, which is a huge public health problem [1]. Diet is one of the key lifestyle factors involved in the prevention of stroke, among which nut consumption has received considerable attention. Nuts are rich in vitamins, minerals, unsaturated fatty acids, fiber, and many other bioactive substances [2, 3]. Studies have shown that nuts may have beneficial effects on lipids [4], blood pressure [5], and insulin sensitivity [6]. Moreover, nuts are an important constituent of the Mediterranean diet and studies have indicated that Mediterranean diet supplemented with nuts could reduce the risk of stroke [7, 8].

A recent meta-analysis [9] reported that nut consumption was not associated with stroke risk (RR 0.89; 95 % CI 0.74–1.05). However, the evidence was limited because only 4 studies (155,685 participants) were included. In addition, gender may modify the effects of nut consumption on stroke risk [10, 11], examining the gender differences in the nut consumption-stroke association is of interest. Moreover, there is still no definite conclusion between nut consumption and stroke mortality.

To fill these gaps, we systematically evaluated the association between nut consumption and stroke risk and mortality by conducting a meta-analysis.

Methods

Literature search and selection

We conducted this meta-analysis according to the checklist of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [12]. We performed literature search

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in PubMed and Embase through June 2014 using the key words "nut" combined with "stroke", "cerebrovascular disease", and "cerebrovascular disorder". Then, we reviewed the references of retrieved publications to identify any relevant articles that were not identified in the preliminary literature searches.

For inclusion, studies had to meet the following criteria: (1) published in the English language; (2) a prospective cohort design; (3) the exposure of interest was nut consumption; (4) the outcome of interest was stroke; and (5) relative risk (RR) with 95 % confidence intervals (CIs) was provided. We excluded retrospective studies, randomized controlled trials, non-human studies, non-original research (editorials, reviews, or commentaries), and duplicated studies. Three authors (ZZ, GX, and XL) evaluated the retrieved studies independently and discrepancies were resolved by discussion.

Data extraction and quality assessment

Data we collected included the name of first author, publication year, country, characteristics of study population, follow-up time, methods for assessment of nut consumption, total number of individuals and cases, confounding factors, and the RRs with corresponding 95 % CIs. If necessary, we contacted authors to request additional data. To assess the study quality, a 9-star system based on the Newcastle–Ottawa Scale [13] was adopted. The score ranges from 0 to 9 with a higher score indicating higher study quality.

Statistical analysis

Statistical heterogeneity from primary studies was tested with the Q and I^2 statistic [14]. Given the absence of heterogeneity, we combined RR estimates using fixed-effects models. Publication bias was evaluated with Egger regression test. Subgroup analyses were also conducted to test the robustness of the association.

Sensitivity analysis was conducted to examine the influence of diverse exclusion criteria on the overall outcome. We also evaluated whether the overall results could have been affected by a single study using knock-1-out analysis in sequence.

Then we assessed the dose–response relationship based on the dose–response meta-analysis method proposed by Orsini et al [15]. We assigned the median or mean level of nut consumption for each category to the corresponding RR for each study. If the linear dose–response result was provided by the included study already, it was used directly. Potential nonlinear relationship between nut consumption and study outcomes was examined using restricted cubic splines with knots fixed at percentiles 25, 50, and 75 % of the distribution [16]. All statistical analyses were two-sided and performed with STATA version 12 (StataCorp, College Station, TX). $P < 0.05$ was considered significant.

Results

Literature search and study characteristics

The initial search identified 239 potentially relevant citations. Of these, 18 articles were identified for detailed evaluation (Fig. 1). Among the 18 articles, 13 were further excluded: review (n = 8); no RR or 95 % CI reported (n = 5). One additional article was included from the reference review. Thus, six articles [17–22] with nine independent cohorts remained in this meta-analysis.

The characteristics of the selected studies are shown in the Table 1. These studies were published between 2000 and 2013. The duration of follow-up ranged from 7.6 to 30 years and cohort sizes ranged from 21,078 to 87,025 (total 476,181). Quality scores of each study are shown in Table 2. The included studies met the quality score of 7–9.

Nut consumption and risk of stroke

The association between nut consumption and risk of stroke was shown in Fig. 2. For the 9 cohorts, 6 detected an inverse association between nut consumption and stroke risk, with 1 [20] reaching statistical significance. Overall, participants with the highest nut consumption, compared with the lowest, had a significant decreased stroke risk (-combined RR 0.90; 95 % CI 0.83–0.98) without heterogeneity among studies ($P = 0.751$; Table 3). Beginning with the first published study, we computed the cumulative combined RR. As a result, the pooled RR reached statistical significance since 2012 and showed a trend of association as published studies increased (Fig. 3).

Subgroup analysis

Stratifying by subtype, the RRs were 0.90 (95 % CI 0.74–1.09) for ischemic stroke, and 1.53 (95 % CI 0.97–2.41) for hemorrhagic stroke. Stratifying by gender, significant inverse association was observed for females (RR 0.88; 95 % CI 0.78–0.98; Fig. 4). In the subgroup analyses by sample size, the protective effect of nut consumption was stronger in studies with larger sample size (≥50,000). Moreover, we also observed significant association in high quality studies (≥8 stars) (Table 3).

Dose–response analysis

Five studies [17, 19–22] were eligible for the dose–response analysis. We did not observe a nonlinear

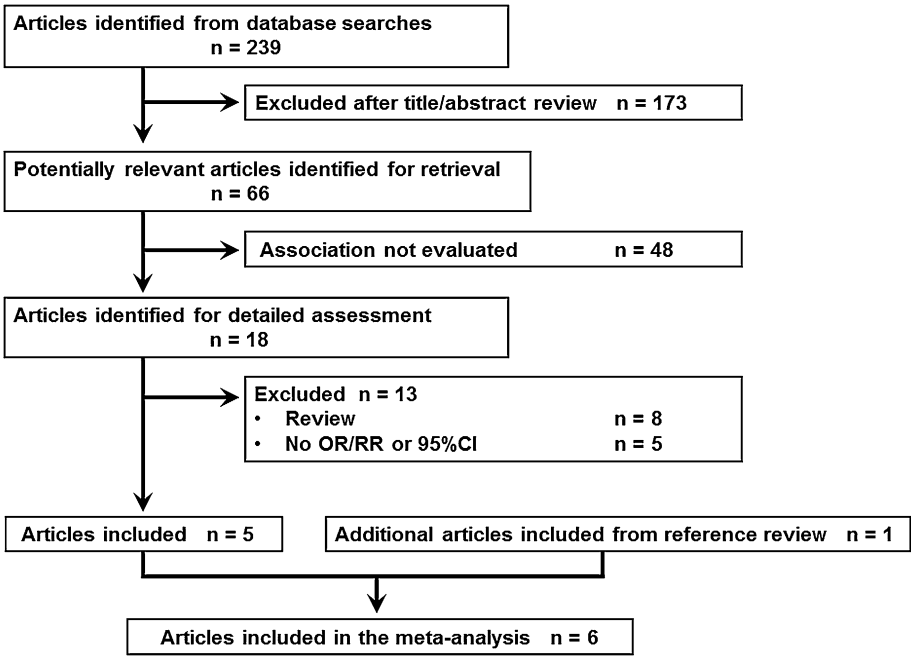

Fig. 1 Flowchart of study selection

relationship between nut consumption and risk of stroke (P for nonlinearity >0.05). The dose–response analysis indicated that a 1 serving/day increment of nut consumption was associated with 6 % lower risk of stroke (RR 0.94; 95 % CI 0.82–1.08).

Sensitivity analyses

Sensitivity analyses were conducted to examine the influence of different exclusion criteria on the pooled result. Exclusion of one study [18] that were did not adjust for age yielded an RR of 0.89 (95 % CI 0.82–0.97), without heterogeneity ($P = 0.711$). The results persisted when we excluded one study [20] that did not adjust for hypertension (RR 0.92; 95 % CI 0.81–1.06), without heterogeneity ($P = 0.620$). Further analyses testing the influence of any single study on the overall results by removing a study at each turn yielded a range of RR from 0.88 to 0.92.

Nut consumption and stroke mortality

Of the included studies, two [17, 22] reported the association between nut consumption and stroke mortality. In the combined analysis, there was a trend toward an inverse association between higher nut consumption and lower stroke mortality (RR 0.86; 95 % CI 0.69–1.06, $P = 0.16$).

Publication bias

Egger test indicated no evidence of publication bias among the included studies ($P = 0.40$, Fig. 5).

Comment

There is rapidly increasing interest in the association between nut consumption and risk of stroke. In this meta-analysis, we found that high nut consumption was significantly associated with a reduced risk of stroke. The protective effects of nut on stroke have a strong biological basis. Although nuts are high in fat, they contain mostly unsaturated fats, which have beneficial effects on blood lipids [4]. Randomized controlled study indicated that men in the nut diet decreased total and low-density lipoprotein cholesterol (LDL-C) levels by 12 and 16 %, respectively, compared with the control diet [23]. In addition, nuts are also rich in arginine. Arginine is the precursor of nitric oxide (NO), which is an effective vasodilator and can restrain platelet aggregation and adhesion. Therefore, the anti-atherogenic effect of nuts might be in part connected with the arginine–NO pathway [24]. Moreover, nuts are rich sources of potassium, magnesium, folate, fiber [25, 26]. Meta-analyses of randomized controlled trials show that supplementation with potassium alone or in combination with other minerals such as magnesium and calcium results in a reduction in blood pressure [27, 28]. Studies also suggest that higher dietary fiber and protein intake could lower blood pressure and are associated with decreased stroke risk [29–32]. Since hypertension is an important risk factor for stroke, the blood pressure-lowering effect of major components in nuts could be one of the major mechanisms contributing to a reduced risk of stroke with increased nut consumption. Another important nutrient in nut is folate. Folate is a crucial regulator of the

Table 1 Characteristics of the included studies

References	Country	Age (year)	Sex	Study period	No. of cohort	Follow up (year)	Nut intake assessment	Intake comparison	Outcome	Adjusted or matched variables
Yochum [17]	United States	55–69	F	1986–1997	34,492	11	FFQ	>4 versus 0 /month	Fatal stroke	Age, total energy intake, BMI, waist-to-hip ratio, high blood pressure, diabetes, use of estrogen replacement therapy, alcohol intake, education, marital status, pack-years of smoking, physical activity level, intakes of cholesterol, saturated fat, fish, vitamin C, arotenoids, dietary fiber, and whole grains
He [18]	United States	40–75	M	1986–2000	43,732	14	FFQ	≥1/day versus <1/week	Fatal/nonfatal stroke	BMI, physical activity, history of hypertension, smoking, aspirin use, multivitamin use, alcohol consumption, potassium, fibre, and vitamin E, total servings of fruit and vegetables, total energy intake, and hypercholesterolaemia at baseline
Djoussé [19]	United States	41–87	M	1982–2008	21,078	21.1	FFQ	≥7 versus 0 /week	Fatal/nonfatal stroke	Age, aspirin assignment, BMI, alcohol consumption, smoking, fruit and vegetable intake, regular exercise, breakfast cereal, red meat, fish, dairy consumption, and prevalent hypertension, diabetes, atrial fibrillation, coronary heart disease
Bernstein [20]	United States	30–75	M/F	1980–2008	127,160	26	FFQ	Quintile (V vs. I)	Fatal/nonfatal stroke	Age, time period, BMI, smoking, physical exercise, parental history of early MI, menopausal status in women, multivitamin use, vitamin E supplement use, aspirin use, total energy, cereal fiber, alcohol, trans fat, fruit, vegetables, and other protein sources
Yaemsiri [21]	United States	50–79	F	1993–2005	87,025	7.6	FFQ	Continuous variable	Fatal/nonfatal stroke	Age, race, education, family income, years as a regular smoker, hormone replacement therapy use, total metabolic equivalent task hours per week, alcohol intake, history of coronary heart disease, history of atrial fibrillation, history of diabetes, aspirin use, use of antihypertensive medication, use of cholesterol-lowering medication, BMI, systolic blood pressure, total energy intake, dietary vitamin E, fruits and vegetable intake, and fiber
Bao [22]	United States	46–74	M/F	1980–2010	118,962	30	FFQ	≥5 versus 0 /week	Fatal stroke	Age, race, BMI, physical activity, status with regard to smoking, whether a physical examination was performed for screening purposes, current multivitamin use, current aspirin use, status with regard to a family history of diabetes mellitus, MI, or cancer, status with regard to a history of diabetes mellitus, hypertension, or hypercholesterolemia, intake of total energy, alcohol, red or processed meat, fruits, vegetables, menopausal status and hormone use

BMI body mass index, *F* female, *FFQ* food frequency questionnaire, *M* male, *MI* myocardial infarction

Table 2 Methodologic quality of cohort studies included in the meta-analysis

References	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Control for important factors[a]	Assessment of outcome	Follow-up long enough for outcomes to occur[b]	Adequacy of follow up of cohorts[c]	Total quality scores
Yochum [17]	☆	☆	☆	☆	☆☆	☆	☆	–	8
He [18]	–	☆	☆	☆	☆	☆	☆	☆	7
Djoussé [19]	–	☆	☆	☆	☆☆	☆	☆	☆	8
Bernstein [20]	–	☆	☆	☆	☆☆	☆	☆	☆	8
Yaemsiri [21]	☆	☆	☆	☆	☆☆	☆	–	☆	8
Bao [22]	☆	☆	☆	☆	☆☆	☆	☆	☆	9

[a] A maximum of 2 stars could be awarded for this item. Studies that controlled for age received one star, whereas studies that controlled for intake of other nutrients received an additional star

[b] A cohort study with a follow-up time >10 year was assigned one star

[c] A cohort study with a follow-up rate >80 % was assigned one star

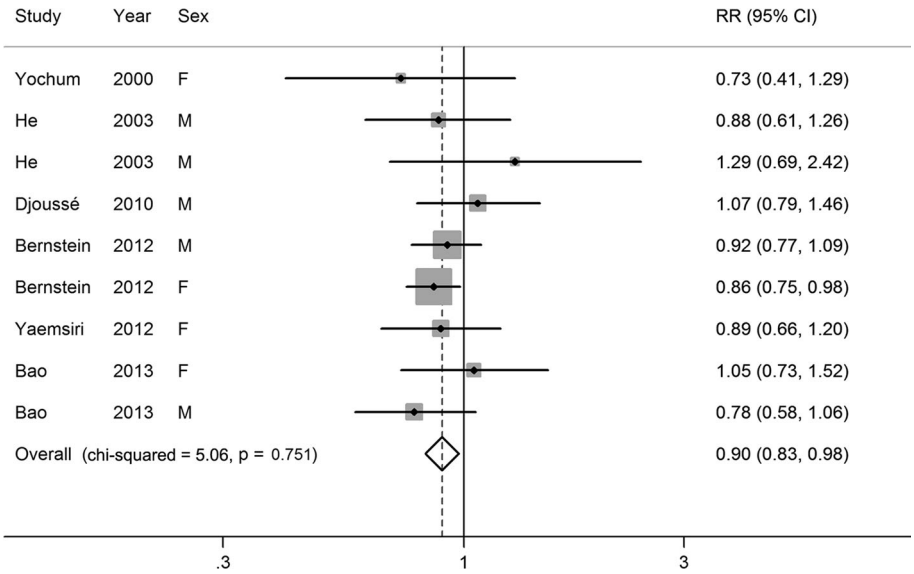

Fig. 2 Nut consumption and risk of stroke

metabolism of homocysteine, and studies have indicated that dietary supplementation with folate reduces blood levels of homocysteine and is inversely related to the risk of stroke [33].

In this study, the protective effect of nut consumption was stronger in females than in males. One possible explanation is the different self-reporting of dietary habits between genders as well as the higher awareness of healthy dietary patterns among females than males. Compared with females, males tended to be more likely to be smokers, consume more calories, alcohol and caffeine, which may diminish the benefit of nut on stroke. Moreover, because of the small sample size for subgroup analysis and the observational nature of the included studies, this result should be interpreted with caution. Further well-designed large prospective studies and randomized clinical trials for nut supplementation are warranted to confirm this association and to establish the gender effects on nut-stroke relationship.

Our present study is robust because the prospective design of included study could eliminate recall bias and selection bias. In addition, the studies included in this meta-analysis had relatively large sample size (476,181 subjects) and long period of follow-up (mean follow-up duration: 21.1 years). Meta-analysis of these prospective studies is a potentially powerful method to evaluate the long-term effects of nut consumption on stroke risk. Our study also has several limitations. First, because of the observational design, the possibility that other factors may

Table 3 Stratification analyses of nut consumption and stroke risk

Group	No. of studies	RR (95 % CI)	Heterogeneity test		
			χ^2	P	I^2 (%)
Total	9	0.90 (0.83–0.98)	5.06	0.751	0.0
Subtype					
Ischemic stroke	3	0.90 (0.74-1.09)	0.05	0.975	0.0
Hemorrhagic stroke	2	1.53 (0.97–2.41)	0.58	0.445	0.0
Gender					
Male	5	0.92 (0.82–1.05)	3.25	0.517	0.0
Female	4	0.88 (0.78–0.98)	1.41	0.703	0.0
Sample size					
<50,000	6	0.92 (0.81–1.03)	3.87	0.568	0.0
≥50,000	3	0.88 (0.78–0.99)	1.01	0.604	0.0
Publication year					
<2010	3	0.91 (0.69–1.20)	1.79	0.409	0.0
≥2010	6	0.90 (0.82–0.98)	3.27	0.659	0.0
Duration of follow-up					
<20 years	4	0.90 (0.73–1.10)	1.80	0.616	0.0
≥20 years	5	0.90 (0.82–0.98)	3.26	0.515	0.0
Quality score					
<8 stars	2	0.97 (0.71–1.33)	1.07	0.301	6.5
≥8 stars	7	0.89 (0.82–0.97)	3.75	0.711	0.0

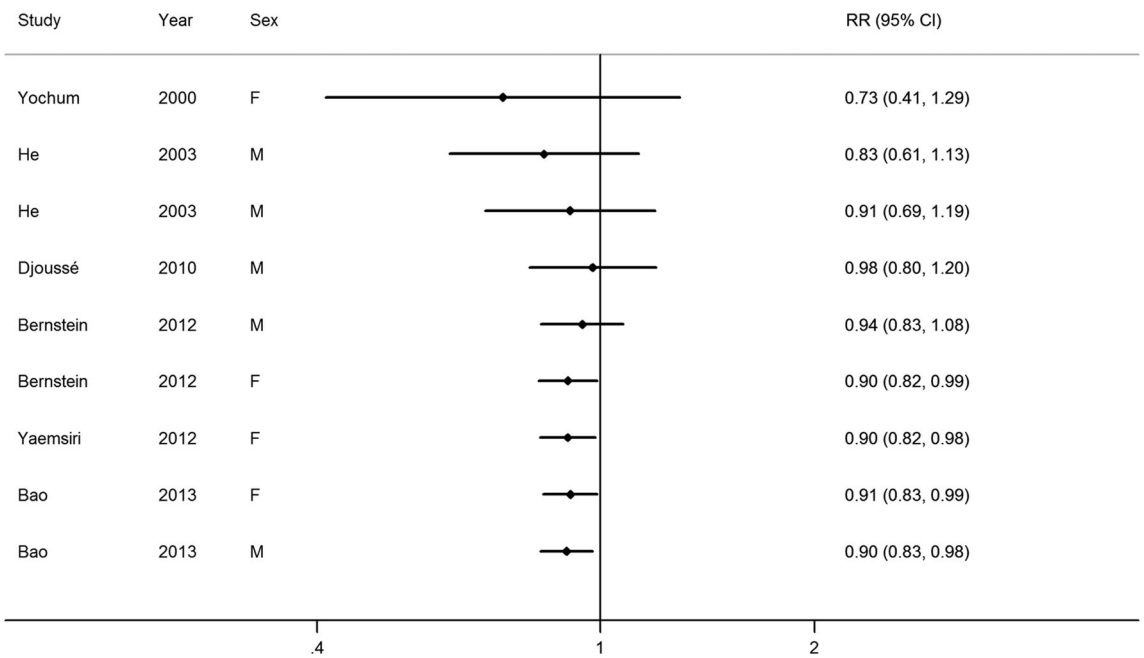

Fig. 3 Cumulative meta-analysis. Evaluation of time trends (year of publication) in relation between nut consumption and risk of stroke

account for the observed results could not be eliminated. Nut consumption tends to be associated with healthy lifestyles that may be protective against stroke, such as higher fruit or vegetables intake and less smoking. However, most included studies have adjusted for these major confounders, which should decrease the potential bias due to these lifestyle factors. Second, all included studies used food frequency questionnaires to evaluate levels of nut consumption. As a result, measurement error was inevitable, which may lead to attenuation of true associations in

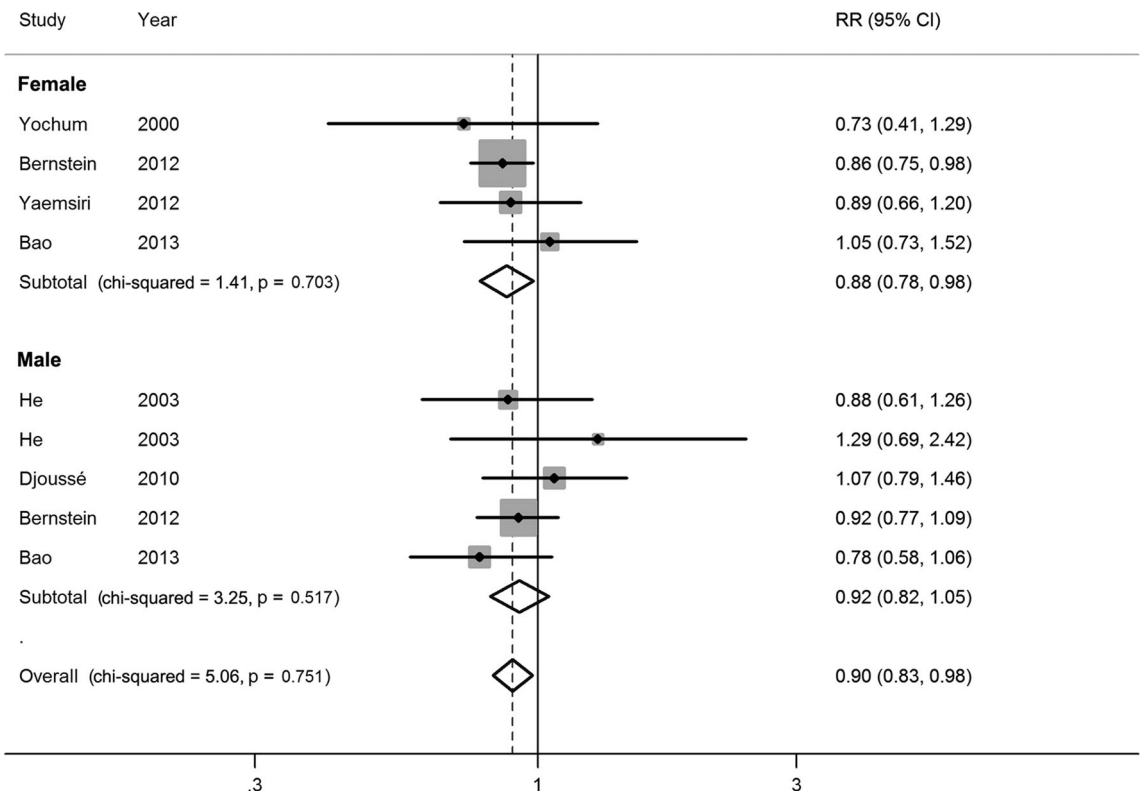

Fig. 4 Nut consumption and risk of stroke stratified by gender

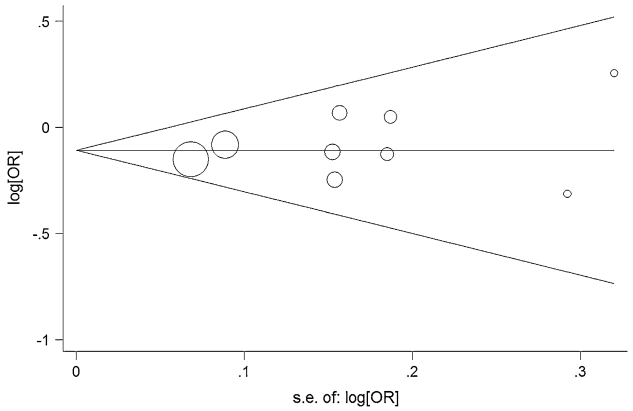

Fig. 5 Funnel plot for the publication bias

a prospective study, especially when the exposure was evaluated before outcome. Thus, further study should update the assessment of nut consumption termly during the follow-up. Third, the unit/serving and the range between the lowest and highest categories for nut consumption was not consistent among the studies and the information on type of nuts was lacking in some studies, which may have contributed to the heterogeneity in the pooled analysis. Future studies should use uniform criteria for nut consumption and consider type of nuts in the analysis. Fourth, in a meta-analysis of published studies, publication bias could be of concern because small studies with negative results tend not to be published. In this meta-analysis, no evidence of publication bias was found.

Implications

Stroke is a main cause of permanent disability and death, with huge economic losses due to functional impairments. The epidemiologic evidence on the relation between nut consumption and stroke risk remain inconsistent. Findings from our meta-analysis of prospective cohort studies indicate that nut consumption is inversely associated with risk of stroke. Thus, future guidelines should recommend nut consumption for stroke prevention.

Conclusions

Our meta-analysis demonstrates that high nut consumption was significantly associated with a reduced risk of stroke. The findings from these observational studies need to be further confirmed in well-designed large randomized clinical trials of nut supplementation.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380:2095–128.
2. Kris-Etherton PM, Hu FB, Ros E, Sabate J. The role of tree nuts and peanuts in the prevention of coronary heart disease: multiple potential mechanisms. J Nutr. 2008;138:1746S–51S.
3. Gonzalez CA, Salas-Salvado J. The potential of nuts in the prevention of cancer. Br J Nutr. 2006;96(Suppl 2):S87–94.
4. Grundy SM, Denke MA. Dietary influences on serum lipids and lipoproteins. J Lipid Res. 1990;31:1149–72.
5. Myers VH, Champagne CM. Nutritional effects on blood pressure. Curr Opin Lipidol. 2007;18:20–4.
6. Jiang R, Manson JE, Stampfer MJ, Liu S, Willett WC, Hu FB. Nut and peanut butter consumption and risk of type 2 diabetes in women. JAMA. 2002;288:2554–60.
7. Psaltopoulou T, Sergentanis TN, Panagiotakos DB, Sergentanis IN, Kosti R, Scarmeas N. Mediterranean diet, stroke, cognitive impairment, and depression: a meta-analysis. Ann Neurol. 2013; 74:580–91.
8. Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, Gomez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013;368:1279–90.
9. Afshin A, Micha R, Khatibzadeh S, Mozaffarian D. Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis. Am J Clin Nutr. 2014;100:278–88.
10. Misirli G, Benetou V, Lagiou P, Bamia C, Trichopoulos D, Trichopoulou A. Relation of the traditional Mediterranean diet to cerebrovascular disease in a Mediterranean population. Am J Epidemiol. 2012;176:1185–92.
11. Eguchi E, Iso H, Tanabe N, Wada Y, Yatsuya H, Kikuchi S, Inaba Y, Tamakoshi A. Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study. Eur Heart J. 2012;33:467–77.
12. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000;283:2008–12.
13. Stang A. Critical evaluation of the Newcastle–Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25:603–5.
14. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21:1539–58.
15. Orsini N, Bellocco R, Greenland S. Generalized least squares for trend estimation of summarized dose–response data. Stata J. 2006;6:40–57.
16. Orsini N, Li R, Wolk A, Khudyakov P, Spiegelman D. Meta-analysis for linear and nonlinear dose-response relations: examples, an evaluation of approximations, and software. Am J Epidemiol. 2012;175:66–73.
17. Yochum LA, Folsom AR, Kushi LH. Intake of antioxidant vitamins and risk of death from stroke in postmenopausal women. Am J Clin Nutr. 2000;72:476–83.
18. He K, Merchant A, Rimm EB, Rosner BA, Stampfer MJ, Willett WC, Ascherio A. Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study. BMJ. 2003;327:777–82.
19. Djousse L, Gaziano JM, Kase CS, Kurth T. Nut consumption and risk of stroke in US male physicians. Clin Nutr. 2010;29:605–9.
20. Bernstein AM, Pan A, Rexrode KM, Stampfer M, Hu FB, Mozaffarian D, Willett WC. Dietary protein sources and the risk of stroke in men and women. Stroke. 2012;43:637–44.
21. Yaemsiri S, Sen S, Tinker L, Rosamond W, Wassertheil-Smoller S, He K. Trans fat, aspirin, and ischemic stroke in postmenopausal women. Ann Neurol. 2012;72:704–15.
22. Bao Y, Han J, Hu FB, Giovannucci EL, Stampfer MJ, Willett WC, Fuchs CS. Association of nut consumption with total and cause-specific mortality. N Engl J Med. 2013;369:2001–11.
23. Sabate J, Fraser GE, Burke K, Knutsen SF, Bennett H, Lindsted KD. Effects of walnuts on serum lipid levels and blood pressure in normal men. N Engl J Med. 1993;328:603–7.
24. Cooke JP, Tsao P, Singer A, Wang BY, Kosek J, Drexler H. Antiatherogenic effect of nuts: is the answer NO? Arch Intern Med. 1993;153:896–99, 902.
25. Dreher ML, Maher CV, Kearney P. The traditional and emerging role of nuts in healthful diets. Nutr Rev. 1996;54:241–5.
26. Fraser GE. Diet and coronary heart disease: beyond dietary fats and low-density-lipoprotein cholesterol. Am J Clin Nutr. 1994; 59:1117S–23S.
27. Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, Klag MJ. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. JAMA. 1997; 277:1624–32.
28. Beyer FR, Dickinson HO, Nicolson DJ, Ford GA, Mason J. Combined calcium, magnesium and potassium supplementation for the management of primary hypertension in adults. Cochrane Database Syst Rev. 2006;19:CD004805.
29. Streppel MT, Arends LR, van 't Veer P, Grobbee DE, Geleijnse JM. Dietary fiber and blood pressure: a meta-analysis of randomized placebo-controlled trials. Arch Intern Med. 2005;165: 150–6.
30. Appel LJ. The effects of protein intake on blood pressure and cardiovascular disease. Curr Opin Lipidol. 2003;14:55–9.
31. Zhang Z, Xu G, Liu D, Zhu W, Fan X, Liu X. Dietary fiber consumption and risk of stroke. Eur J Epidemiol. 2013;28: 119–30.
32. Zhang Z, Xu G, Yang F, Zhu W, Liu X. Quantitative analysis of dietary protein intake and stroke risk. Neurology. 2014;83:19–25.
33. Wang X, Qin X, Demirtas H, Li J, Mao G, Huo Y, Sun N, Liu L, Xu X. Efficacy of folic acid supplementation in stroke prevention: a meta-analysis. Lancet. 2007;369:1876–82.