Spicy food consumption and risk of vascular disease: Evidence from a large-scale Chinese prospective cohort of 0.5 million people

Dongfang You[1], Dianjianyi Sun[2,3,4], Ziyu Zhao[1], Mingyu Song[2], Lulu Pan[1], Yaqian Wu[1], Yingdan Tang[1], Mengyi Lu[1], Fang Shao[1], Sipeng Shen[1], Jianling Bai[1], Honggang Yi[1], Ruyang Zhang[1,5,6], Yongyue Wei[2], Hongxia Ma[7,8], Hongyang Xu[9], Canqing Yu[2,3,4], Jun Lv[2,3,4,10], Pei Pei[3], Ling Yang[11,12], Yiping Chen[11,12], Zhengming Chen[12], Hongbing Shen[7,8], Feng Chen[1,5,6,8], Yang Zhao[1,5,6,8], Liming Li[2,3,4]; On behalf of the China Kadoorie Biobank Collaborative Group

[1]Department of Biostatistics, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China;
[2]Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing 100191, China;
[3]Peking University Center for Public Health and Epidemic Preparedness & Response, Beijing 100191, China;
[4]Key Laboratory of Epidemiology of Major Diseases, Ministry of Education, Peking University, Beijing 100191, China;
[5]China International Cooperation Center for Environment and Human Health, Center for Global Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China;
[6]The Center of Biomedical Big Data and the Laboratory of Biomedical Big Data, Nanjing Medical University, Nanjing, Jiangsu 211166, China;
[7]Department of Epidemiology, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China;
[8]Jiangsu Key Lab of Cancer Biomarkers, Prevention and Treatment, Collaborative Innovation Center for Cancer Personalized Medicine, Nanjing Medical University, Nanjing, Jiangsu 211166, China;
[9]Department of Critical Care Medicine, Wuxi People's Hospital Affiliated to Nanjing Medical University, Wuxi, Jiangsu 214023, China;
[10]State Key Laboratory of Vascular Homeostasis and Remodeling, Peking University, Beijing 100191, China;
[11]Medical Research Council Population Health Research Unit at the University of Oxford, Oxford OX3 7LF, United Kingdom;
[12]Clinical Trial Service Unit & Epidemiological Studies Unit (CTSU), Nuffield Department of Population Health, University of Oxford, Oxford OX3 7LF, United Kingdom.

Abstract

Background: Spicy food consumption has been reported to be inversely associated with mortality from multiple diseases. However, the effect of spicy food intake on the incidence of vascular diseases in the Chinese population remains unclear. This study was conducted to explore this association.

Methods: This study was performed using the large-scale China Kadoorie Biobank (CKB) prospective cohort of 486,335 participants. The primary outcomes were vascular disease, ischemic heart disease (IHD), major coronary events (MCEs), cerebrovascular disease, stroke, and non-stroke cerebrovascular disease. A Cox proportional hazards regression model was used to assess the association between spicy food consumption and incident vascular diseases. Subgroup analysis was also performed to evaluate the heterogeneity of the association between spicy food consumption and the risk of vascular disease stratified by several basic characteristics. In addition, the joint effects of spicy food consumption and the healthy lifestyle score on the risk of vascular disease were also evaluated, and sensitivity analyses were performed to assess the reliability of the association results.

Results: During a median follow-up time of 12.1 years, a total of 136,125 patients with vascular disease, 46,689 patients with IHD, 10,097 patients with MCEs, 80,114 patients with cerebrovascular disease, 56,726 patients with stroke, and 40,098 patients with non-stroke cerebrovascular disease were identified. Participants who consumed spicy food 1–2 days/week (hazard ratio [HR] = 0.95, 95% confidence interval [95% CI] = [0.93, 0.97], P <0.001), 3–5 days/week (HR = 0.96, 95% CI = [0.94, 0.99], P = 0.003), and 6–7 days/week (HR = 0.97, 95% CI = [0.95, 0.99], P = 0.002) had a significantly lower risk of vascular disease than those who consumed spicy food less than once a week (P_{trend} <0.001), especially in those who were younger and living in rural areas. Notably, the disease-based subgroup analysis indicated that the inverse associations remained in IHD (P_{trend} = 0.011) and MCEs (P_{trend} = 0.002) risk. Intriguingly, there was an interaction effect between spicy food consumption and the healthy lifestyle score on the risk of IHD ($P_{interaction}$ = 0.037).

Access this article online

Quick Response Code:

Website:
www.cmj.org

DOI:
10.1097/CM9.0000000000003177

Dongfang You, Dianjianyi Sun, and Ziyu Zhao contributed equally to this work.

Correspondence to: Yang Zhao, Department of Biostatistics, School of Public Health, Nanjing Medical University, 101 Longmian Avenue, Nanjing, Jiangsu 211166, China
E-Mail: yzhao@njmu.edu.cn;
Liming Li, Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, No. 38, Xueyuan Road, Beijing 100191, China
E-Mail: lmlee@bjmu.edu.cn;
Dongfang You, Department of Biostatistics, School of Public Health, Nanjing Medical University, 101 Longmian Avenue, Nanjing, Jiangsu 211166, China
E-Mail: youdongfang@njmu.edu.cn

Chinese Medical Journal 2025;138(14)

Received: 13-09-2023; **Online:** 19-07-2024 **Edited by:** Xiangxiang Pan

Conclusions: Our findings support an inverse association between spicy food consumption and vascular disease in the Chinese population, which may provide additional dietary guidance for the prevention of vascular diseases.
Keywords: Prospective cohort studies; Spicy food consumption; Vascular disease; Healthy lifestyle; China Kadoorie Biobank; Stroke; Ischemic heart disease; Major coronary events

Introduction

Vascular diseases, including cardiovascular and cerebrovascular diseases, are becoming increasingly prevalent and have become the main cause of morbidity and mortality worldwide.[1–5] Especially in China, vascular disease-specific deaths account for more than 40% of the total deaths each year.[6–8] Therefore, exploring the risk factors related to vascular diseases is needed for early prevention.

As an important part of the human diet worldwide, spicy food has a long history of use.[9–11] Interestingly, cumulative evidence has demonstrated that capsaicin, the main nutrient component of spicy food, is helpful in improving vascular function,[12–14] as well as vascular disease prognosis, which was found in a previous study.[15] Most studies of European populations have reported that spicy food consumption is associated with a decreased risk of multiple diseases, such as hypertension, diabetes, vascular diseases, and obesity.[11,16–18] However, due to ethnic differences in diet and lifestyle, it may be inappropriate to extrapolate the findings in European populations to Chinese population. Hence, the relationship between spicy food consumption and vascular diseases in the Chinese population remains unclear.

Therefore, we aimed to investigate the association between spicy food consumption and the incidence of vascular disease, ischemic heart disease (IHD), major coronary events (MCEs), cerebrovascular disease, stroke, and non-stroke cerebrovascular disease in the prospective China Kadoorie Biobank (CKB) cohort of 486,335 participants, which may provide additional dietary guidance for the prevention of vascular diseases.

Methods

Ethical approval

This research was conducted using CKB Resource (application ID: DAR-2020-00120). The use of the CKB cohort was approved by the Ethical Review Committee of the Chinese Center for Disease Control and Prevention (Beijing, China) and the Oxford Tropical Research Ethics Committee, University of Oxford (Oxford, UK), and all participants provided written informed consent before taking part in the study. Access to CKB data was granted under Project Number DAR-2020-00120.

Study design and participants

This study was performed using the large-scale CKB prospective cohort of 512,723 participants from 10 different geographical regions in China who were aged 30–79 years at enrollment. Participants have been followed up until December 31, 2018. Further details of the CKB study design have been described elsewhere.[19–21] Additional information on the subjects is presented in the Supplementary Material, http://links.lww.com/CM9/C41.

Participants with a self-reported history of cancer or vascular disease (n = 26,344), those with negative values for the duration of spicy food consumption (n = 42), and those with missing body mass index (BMI) data (n = 2) were excluded from the study, and 486,335 participants were ultimately included in the study [Supplementary Figure 1, http://links.lww.com/CM9/C41].

Assessment of spicy food consumption

The variables regarding spicy food consumption were derived from the following: (1) consumption frequency: never/almost never and only occasionally (i.e., <1 day/week), 1–2 days/week, 3–5 days/week, and 6–7 days/week; (2) strength of spice: weak, moderate, and strong; and (3) the main sources of spice usually used: chili sauce, chili oil, dried chili pepper, fresh chili pepper, and others or unknown. Participants who ate spicy food more than once a week were defined as regular consumers. Additionally, we included 1603 participants who completed the same questionnaire twice within 1.5 years from baseline to the first resurvey. The Spearman's coefficient of the frequency of spicy food consumption in the two questionnaires completed within 1.5 years was 0.73, indicating good reproducibility of spicy food consumption [Supplementary Table 1, http://links.lww.com/CM9/C41]. Detailed information on the assessment of spicy food consumption is provided in the Supplementary Material, http://links.lww.com/CM9/C41.

Follow-up and outcome measures

Participants were followed up periodically to minimize loss to follow-up. All fatal and non-fatal disease outcomes were obtained by linkage, using the unique national identification number of each participant, with disease registries and national health insurance claim databases. The national health insurance claim databases, which cover 96% of CKB participants, helped to improve the accuracy of diagnosis and further data collection.

The primary outcomes of this study were vascular disease (I00–I99), IHD (I20–I25), MCEs (I20–I25 [fatal], I21–I23), cerebrovascular disease (I60–I69), stroke (subarachnoid stroke [I60], hemorrhagic stroke [I61], ischemic stroke [I63], other or unspecified stroke [I64]), and non-stroke cerebrovascular disease (I62, I65–I69), as defined by the International Classification of Disease, 10th Edition (ICD-10). Additional information is presented in the Supplementary Material, http://links.lww.com/CM9/C41.

Statistical analysis

Consumption frequency was the main exposure variable. A Cox proportional hazards regression model was used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between spicy food consumption and the risk of vascular disease. After adjusting for potential risk factors, the following multivariable models were established: (1) model 1: unadjusted; (2) model 2: adjusted for sex, age, and study site; (3) model 3: additionally adjusted for educational level, marital status, alcohol consumption, smoking status, physical activity, household income, BMI, intake frequencies of red meat, fruits, and vegetables, and diagnosis of hypertension at baseline.

Subgroup analysis was also performed to evaluate the heterogeneity of the association between spicy food consumption and the risk of vascular disease stratified by several basic characteristics, including sex, age, physical activity in metabolic equivalent of task (MET), BMI, urban and rural area, smoking status, and drinking status.

In addition, we calculated healthy lifestyle scores by aggregating eight dietary and lifestyle factors, including smoking status (health level: no current smoking or having stopped smoking ≥15 years), alcohol consumption (health level: <25 g/day and <15 g/day for men and women, respectively), physical activity (health level: ≥20 MET h/day), BMI (health level: 18.5–23.9 kg/m^2), waist-to-hip ratio (WHR) (health level: <0.90 and 0.85 for men and women, respectively), red meat consumption (health level: <5 days/week), preserved vegetable consumption (health level: <3 days/week), and fresh fruit/vegetable consumption (health level: >5 days/week). Participants were classified into three groups: a favorable lifestyle (including 6–8 healthy factors), an intermediate lifestyle (including 4–5 healthy factors), and an unfavorable lifestyle (including 0–3 healthy factors) group. We then evaluated the joint effects of spicy food consumption and the healthy lifestyle score on the risk of vascular disease.

In addition, several sensitivity analyses were performed to assess the reliability of the association results: (1) an analysis in which participants who developed an event of interest during the first two years of follow-up were excluded; (2) an analysis in which additional seasonal adjustments were made; (3) an analysis in which additional adjustments were made for women's menarche age, number of pregnancies, and menopause status; and (4) an analysis in which additional adjustment was made for diabetes. Moreover, we also explored the associations of the age at which spicy food began to be eaten regularly, the strength of spicy food eating, and the main sources of spice with vascular diseases risk, respectively.

All statistical analyses were performed using R Statistical Software (v4.2.2, R Foundation, Vienna, Austria). *P* values (two-sided) <0.05 were considered significant.

Results

Baseline characteristics of participants

A total of 486,335 participants were included in the current analysis, 59.07% of whom were women and 43.13% of whom were from urban areas, with a mean age of 51.53 years at baseline [Table 1]. Overall, 42.84% (208,331/486,335) of the participants were regular spicy food consumers; among these participants, 15.20% (31,657/208,331), 13.66% (28,459/208,331), and 71.14% (148,215/208,331) reported consuming spicy food 1–2 days/week, 3–5 days/week, and 6–7 days/week, respectively. The frequency of spicy food consumption varied greatly across the 10 study areas [Figure 1]. For example, in Hunan and Sichuan, 99.7% (56,738/56,912) and 77.9% (42,716/54,859) of participants consumed spicy food more than one day per week. Compared with participants consuming spicy foods less than once a week, those regular consumers were more likely to be current smokers and alcohol drinkers, to consume red meat and preserved vegetables more frequently, and to have lower levels of systolic blood pressure (SBP). Among regular consumers, those who consumed spicy foods almost every day (6–7 days/week) preferred a stronger spice intensity, consumed spice starting at an early age, and had a high proportion intake of fresh chili pepper and dried chili pepper.

Association between spicy food consumption and vascular diseases

During a median follow-up time of 12.1 years, 136,125 patients with vascular disease, 46,689 patients with IHD, 10,097 patients with MCEs, 80,114 patients with cerebrovascular disease, 56,726 patients with stroke, and 40,098 patients with non-stroke cerebrovascular disease were identified. Compared with participants who consumed spicy food less than once a week, for those who consumed spicy food 1–2 days/week, 3–5 days/week, and 6–7 days/week, the adjusted HRs for vascular disease were 0.95 (0.93, 0.97; P <0.001), 0.96 (0.94, 0.99; P = 0.003), and 0.97 (0.95, 0.99; P = 0.002), respectively (P_{trend} <0.001; Table 2, Supplementary Figure 2, http://links.lww.com/CM9/C41). Interestingly, a negative association was also observed in the risk of IHD, with corresponding HRs of 0.95 (0.91, 0.99), 0.98 (0.94, 1.03), and 0.96 (0.93, 0.99), respectively (P_{trend} = 0.011) and in the risk of MCEs, with corresponding HRs of 0.96 (0.87, 1.06), 0.87 (0.78, 0.96), and 0.91 (0.84, 0.98), respectively (P_{trend} = 0.002; Table 2, Supplementary Figure 2, http://links.lww.com/CM9/C41). However, no significant association was found between cerebrovascular disease, stroke, and non-stroke cerebrovascular disease risk and spicy food consumption (P_{trend} >0.05).

Subgroup and sensitivity analyses

Furthermore, in the stratification analysis, we evaluated the heterogeneity of associations based on different demographic characteristics. As shown in Figure 2, when stratified by BMI, smoking, and drinking status, there was no significant heterogeneity in the association between spicy food consumption and vascular disease risk ($P_{\text{heterogeneity}}$ >0.05). However, compared with participants who consumed spicy food less than once a week, a stronger association with vascular disease risk was observed in individuals who were female (HR = 0.94, 0.92–0.96, $P_{\text{heterogeneity}}$ = 0.038), younger (<65 years, HR = 0.87, 0.85–0.88, $P_{\text{heterogeneity}}$ <0.001), had less physical activity (<10.76 MET h/day, HR = 0.92, 0.90–0.95,

Table 1: Baseline characteristics of the participants according to weekly spicy food consumption.

Characteristics	Frequency of spicy food consumption per week <1 day (*n* = 278,004)	1–2 days (*n* = 31,657)	3–5 days (*n* = 28,459)	6–7 days (*n* = 148,215)	All participants (*n* = 486,335)
Age (years)	52.75 ± 10.67	49.14 ± 10.01	49.08 ± 9.81	50.24 ± 10.22	51.53 ± 10.55
Female	167,118 (60.11)	17,458 (55.15)	15,749 (55.34)	86,969 (58.68)	287,294 (59.07)
Urban	148,771 (53.51)	18,268 (57.71)	16,537 (58.11)	26,197 (17.67)	209,773 (43.13)
Education level					
Primary school or lower	140,524 (50.55)	12,973 (40.98)	11,297 (39.70)	82,355 (55.56)	247,149 (50.82)
Middle school	77,014 (27.70)	9422 (29.76)	8691 (30.54)	43,184 (29.14)	138,311 (28.44)
High school or higher	60,466 (21.75)	9262 (29.26)	8471 (29.77)	22,676 (15.30)	100,875 (20.74)
Household income (CNY/year)					
<20,000	147,011 (52.88)	16,254 (51.34)	15,131 (53.17)	99,753 (67.30)	278,149 (57.19)
20,000–34,999	74,233 (26.70)	8410 (26.57)	6892 (24.22)	30,639 (20.67)	120,174 (24.71)
≥35,000	56,760 (20.42)	6993 (22.09)	6436 (22.61)	17,823 (12.03)	88,012 (18.10)
Smoking status					
Non-current	204,401 (73.52)	20,816 (65.75)	18,448 (64.82)	97,274 (65.63)	340,939 (70.10)
Current	73,603 (26.48)	10,841 (34.25)	10,011 (35.18)	50,941 (34.37)	145,396 (29.90)
Drinking status					
Non-current	131,481 (47.29)	12,003 (37.92)	10,355 (36.39)	68,224 (46.03)	222,063 (45.66)
Current	146,523 (52.71)	19,654 (62.08)	18,104 (63.61)	79,991 (53.97)	264,272 (54.34)
SBP (mmHg)					
<120	86,654 (31.17)	11,318 (35.75)	10,332 (36.30)	49,780 (33.59)	158,084 (32.51)
120–139	109,744 (39.48)	12,626 (39.88)	11,378 (39.98)	62,371 (42.08)	196,119 (40.33)
≥140	81,606 (29.35)	7713 (24.36)	6749 (23.71)	36,064 (24.33)	132,132 (27.17)
BMI (kg/m^2)					
<18.5	11,430 (4.11)	1022 (3.23)	935 (3.29)	8027 (5.42)	21,414 (4.40)
18.5–23.9	140,267 (50.46)	16,156 (51.03)	14,217 (49.96)	84,987 (57.34)	255,627 (52.56)
24.0–27.9	95,325 (34.29)	10,891 (34.40)	9892 (34.76)	43,527 (29.37)	159,635 (32.82)
≥28.0	30,982 (11.14)	3588 (11.33)	3415 (12.00)	11,674 (7.88)	49,659 (10.21)
Physical activity (MET h/day)	21.13 ± 14.47	23.70 ± 13.36	23.75 ± 13.48	21.50 ± 12.89	21.56 ± 13.90
Weekly consumption* (days)					
Red meat	3.60 ± 2.64	3.86 ± 2.74	3.94 ± 2.70	3.66 ± 2.52	3.66 ± 2.62
Fresh vegetables	6.86 ± 0.70	6.46 ± 1.52	6.64 ± 1.09	6.90 ± 0.60	6.84 ± 0.79
Fresh fruits	2.44 ± 2.69	2.91 ± 2.80	2.79 ± 2.78	2.08 ± 2.39	2.38 ± 2.62
Preserved vegetables	1.88 ± 2.60	2.62 ± 2.68	2.68 ± 2.67	1.98 ± 2.35	2.01 ± 2.55
Strength of spicy food eating					
Weak	–	21,660 (68.42)	15,370 (54.01)	23,413 (15.80)	60,443 (12.43)
Moderate	–	9043 (28.57)	10,263 (36.06)	53,356 (36.00)	72,662 (14.94)
Strong	–	954 (3.01)	2826 (9.93)	71,446 (48.20)	75,226 (15.47)
Age started to eat spicy food regularly (years)	–	25.39 ± 13.42	23.81 ± 13.40	11.63 ± 9.38	15.39 ± 12.22
Types of spicy food eating commonly†	–				
Fresh chili pepper	–	19,596 (61.90)	19,441 (68.31)	131,031 (88.41)	170,068 (34.97)
Dried chili pepper	–	11,894 (37.57)	13,265 (46.61)	115,591 (77.99)	140,750 (28.94)
Chili sauce	–	13,678 (43.21)	13,165 (46.26)	62,876 (42.42)	89,719 (18.45)
Chili oil	–	15,467 (48.86)	15,383 (54.05)	63,201 (42.64)	94,051 (19.34)
Others or don't know	–	7894 (24.94)	7106 (24.97)	33,890 (22.87)	48,890 (10.05)
Diseases					
Vascular disease	80,172 (28.84)	7615 (24.05)	7166 (25.18)	41,172 (27.78)	136,125 (27.99)
IHD	28,369 (10.20)	2747 (8.68)	2617 (9.20)	12,956 (8.74)	46,689 (9.60)
MCEs	6060 (2.18)	535 (1.69)	452 (1.59)	3050 (2.06)	10,097 (2.08)
Cerebrovascular disease	46,855 (16.85)	4328 (13.67)	4167 (14.64)	24,764 (16.71)	80,114 (16.47)
Stroke	35,607 (12.81)	3172 (10.02)	3098 (10.89)	14,849 (10.02)	56,726 (11.66)
Non-stroke cerebrovascular disease	21,564 (7.76)	2026 (6.40)	1880 (6.61)	14,628 (9.87)	40,098 (8.24)

Data are presented as mean ± standard deviation or *n* (%). *Average weekly consumptions of red meal, fresh fruit, fresh vegetables, and preserved vegetables were calculated by assigning participants to the midpoint of their consumption category. †Each individual may choose multiple types. BMI: Body mass index; IHD: Ischemic heart disease; MCEs: Major coronary events; MET: Metabolic equivalent of task; SBP: Systolic blood pressure. –: Not application.

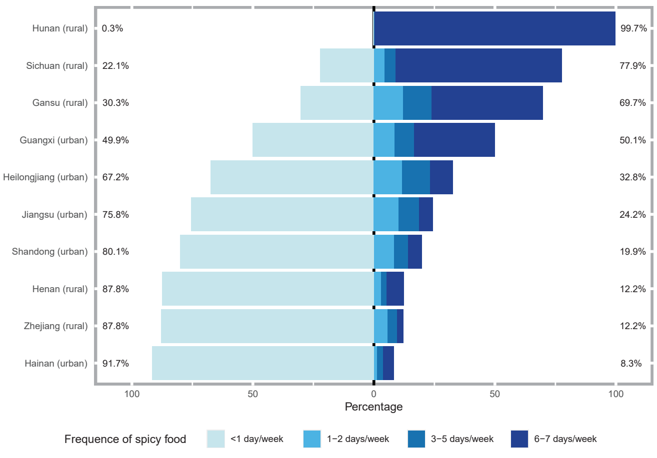

Figure 1: Frequency of spicy food consumption.

$P_{heterogeneity}$ <0.001), and lived in rural areas (HR = 0.94, 0.92–0.96, $P_{heterogeneity}$ <0.001).

Interestingly, the heterogeneity among different age groups was also observed in individuals with IHD ($P_{heterogeneity}$ = 0.006; Supplementary Figure 3, http://links.lww.com/CM9/C41), cerebrovascular disease ($P_{heterogeneity}$ <0.001; Supplementary Figure 4, http://links.lww.com/CM9/C41), stroke ($P_{heterogeneity}$ <0.001; Supplementary Figure 5, http://links.lww.com/CM9/C41), and non-stroke cerebrovascular disease ($P_{heterogeneity}$ <0.001; Supplementary Figure 6, http://links.lww.com/CM9/C41), but not in those with MCEs ($P_{heterogeneity}$ = 0.100; Supplementary Figure 7, http://links.lww.com/CM9/C41). People living in rural areas also had a lower risk of IHD ($P_{heterogeneity}$ = 0.002; Supplementary Figure 3, http://links.lww.com/CM9/C41), MCEs ($P_{heterogeneity}$ = 0.001; Supplementary Figure 7, http://links.lww.com/CM9/C41), and non-stroke cerebrovascular disease ($P_{heterogeneity}$ =

Table 2: The association between spicy food consumption and the risk of vascular disease.

Items	No. of participants	Frequency of spicy food consumption per week				
		<1 day	1–2 days	3–5 days	6–7 days	P_{trend}
No. of participants	486,335					
Vascular disease						
No. of events[*]	136,125	80,172	7615	7166	41,172	
Model 1[†]		1.00	0.80 (0.78, 0.81)	0.84 (0.82, 0.86)	0.93 (0.92, 0.94)	<0.001
Model 2[‡]		1.00	0.97 (0.94, 0.99)	0.98 (0.96, 1.01)	0.98 (0.96, 1.00)	0.035
Model 3[§]		1.00	0.95 (0.93, 0.97)	0.96 (0.94, 0.99)	0.97 (0.95, 0.99)	<0.001
IHD						
No. of events[*]	46,689	28,369	2747	2617	12,956	
Model 1[†]		1.00	0.83 (0.80, 0.86)	0.88 (0.85, 0.92)	0.84 (0.82, 0.85)	<0.001
Model 2[‡]		1.00	0.97 (0.93, 1.01)	1.01 (0.96, 1.05)	0.97 (0.94, 1.01)	0.152
Model 3[§]		1.00	0.95 (0.91, 0.99)	0.98 (0.94, 1.03)	0.96 (0.93, 0.99)	0.011
MCEs						
No. of events[*]	10,097	6060	535	452	3050	
Model 1[†]		1.00	0.76 (0.70, 0.83)	0.72 (0.65, 0.79)	0.93 (0.89, 0.97)	<0.001
Model 2[‡]		1.00	0.98 (0.89, 1.08)	0.87 (0.78, 0.96)	0.88 (0.82, 0.95)	<0.001
Model 3[§]		1.00	0.96 (0.87, 1.06)	0.87 (0.78, 0.96)	0.91 (0.84, 0.98)	0.002
Cerebrovascular disease						
No. of events[*]	80,114	46,855	4328	4167	24,764	
Model 1[†]		1.00	0.78 (0.76, 0.81)	0.84 (0.82, 0.87)	0.97 (0.95, 0.98)	<0.001
Model 2[‡]		1.00	0.96 (0.93, 0.99)	0.99 (0.95, 1.02)	1.00 (0.98, 1.03)	0.873
Model 3[§]		1.00	0.94 (0.91, 0.97)	0.96 (0.93, 0.99)	0.99 (0.96, 1.01)	0.079
Stroke						
No. of events[*]	56,726	35,607	3172	3098	14,849	
Model 1[†]		1.00	0.76 (0.73, 0.79)	0.83 (0.80, 0.86)	0.76 (0.74, 0.77)	<0.001
Model 2[‡]		1.00	0.96 (0.92, 0.99)	0.99 (0.95, 1.03)	1.01 (0.98, 1.04)	0.599
Model 3[§]		1.00	0.94 (0.90, 0.98)	0.96 (0.92, 1.00)	1.00 (0.97, 1.03)	0.444
Non-stroke cerebrovascular disease						
No. of events[*]	40,098	21,564	2026	1880	14,628	
Model 1[†]		1.00	0.80 (0.77, 0.84)	0.83 (0.80, 0.87)	1.27 (1.24, 1.29)	<0.001
Model 2[‡]		1.00	0.96 (0.92, 1.01)	0.98 (0.93, 1.03)	1.00 (0.96, 1.04)	0.679
Model 3[§]		1.00	0.94 (0.90, 0.99)	0.95 (0.91, 1.00)	0.97 (0.94, 1.01)	0.064

[*]During a median follow-up time of 12.1 years. [†]Model 1: The HRs (95% CIs) were estimated using Cox proportional hazard model without adjustment for any covariate. [‡]Model 2: The HRs (95% CIs) were estimated using Cox proportional hazard model adjusted for sex, study site, and age. [§]Model 3: The HRs (95% CIs) were estimated using Cox proportional hazard model additionally adjusted for educational level (no formal school, primary school, middle school, high school, college, or university or higher); marital status (married, widowed, divorced or separated, or never married); alcohol consumption (never, formerly regular, occasional, or currently regular); smoking status (non-current smoker, occasional, most days, or daily); physical activity (MET, h/day); household income (<20,000 CNY/year, 20,000–34,999 CNY/year, ≥35,000 CNY/year); BMI; intake frequencies of red meat, fruits, and vegetables (rarely/never or monthly, 1–3 days/week, 4–6 days/week, daily); diagnosis of hypertension in the baseline (no or yes). BMI: Body mass index; CIs: Confidence intervals; HRs: Hazard ratios; IHD: Ischemic heart disease; MCEs: Major coronary events; MET: Metabolic equivalent of task.

Subgroup	No. of participants (No. of events)	Hazard ratio (95%CI)	Heterogeneity tests I^2	P-value
Sex			0.77	0.038
Male	199,041 (57,068)	0.97 (0.95–0.99)		
Female	287,294 (79,057)	0.94 (0.92–0.96)		
Age (years)			0.92	<0.001
<65	421,703 (100,012)	0.87 (0.85–0.88)		
≥65	64,632 (36,113)	0.93 (0.90–0.96)		
Physical activity(MET h/day)			0.83	<0.001
<10.76	121,221 (49,264)	0.92 (0.90–0.95)		
10.76 to 18.09	121,819 (38,106)	0.95 (0.93–0.98)		
18.10 to 30.58	121,689 (27,377)	1.00 (0.97–1.03)		
≥30.59	121,606 (21,378)	0.97 (0.94–1.00)		
Body mass index (kg/m^2)			0.00	0.548
<18.5	21,414 (6471)	0.92 (0.85–0.99)		
18.5 to 23.9	255,627 (62,758)	0.96 (0.94–0.98)		
24.0 to 27.9	159,635 (48,367)	0.97 (0.94–0.99)		
≥28.0	49,659 (18,529)	0.95 (0.91–0.98)		
Urban and rural			0.92	<0.001
Rural	276,562 (75,773)	0.94 (0.92–0.96)		
Urban	209,773 (60,352)	0.99 (0.97–1.01)		
Smoking status			0.00	0.541
Non–current	340,939 (96,295)	0.95 (0.93–0.97)		
Current	145,396 (39,830)	0.96 (0.93–0.98)		
Drinking status			0.59	0.117
Non–current	222,063 (61,883)	0.94 (0.92–0.96)		
Current	264,272 (74,242)	0.96 (0.95–0.98)		

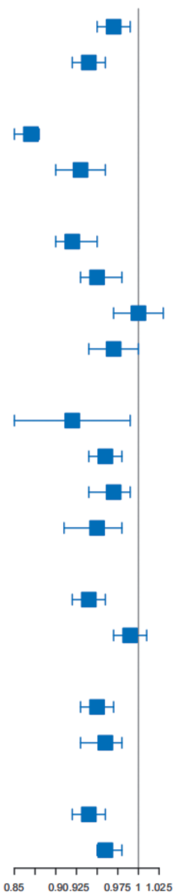

Figure 2: Subgroup analysis of the associations between regular consumption of spicy food and vascular disease risk. The HRs (95% CIs) for the risk of vascular disease were used to compare participants who ate spicy foods ≥1 day a week with those who ate spicy foods less than once a week. Estimates were made using Cox proportional hazard models with stratification for age, sex, region, and adjustment for educational level, marital status, alcohol consumption, smoking status, physical activity, household income, BMI, intake frequencies of red meat, fruits, and vegetables, diagnosis of hypertension in the baseline. BMI: Body mass index; CIs: Confidence intervals; HRs: Hazard ratios; MET: Metabolic equivalent of task.

0.017; Supplementary Figure 6, http://links.lww.com/CM9/C41).

In the sensitivity analysis, the associations of spicy food consumption with the risk of each event did not materially change after further adjusting for diabetes [Supplementary Table 2, http://links.lww.com/CM9/C41]. However, when participants who developed an event of interest during the first two years of follow-up were excluded, spicy food consumption was no longer associated with IHD risk (P_{trend} = 0.100), but was significantly associated with a decreased risk of cerebrovascular disease (P_{trend} = 0.013) and non-stroke cerebrovascular disease (P_{trend} = 0.008). After additional adjustment for season, spicy food consumption was significantly negatively associated with cerebrovascular disease risk (HR = 0.95 [0.92–0.98], 0.95 [0.92–0.99], and 0.96 [0.93–0.98] among individuals who consumed spicy food 1–2 days/week, 3–5 days/week, and 6–7 days/week, respectively; P_{trend} <0.001), which may imply that season is one of the factors of cerebrovascular disease. In addition to the frequency of spicy food consumption, the age when one started to eat spicy food, the strength of spicy food eating, and the main source of spice also had a significant inverse association with the risk of vascular disease [Supplementary Table 3, http://links.lww.com/CM9/C41].

Joint effects of spicy food consumption and the healthy lifestyle score

Subsequently, eight lifestyle factors were used to construct a healthy lifestyle score, which was significantly associated with a lower risk of vascular disease (P_{trend} <0.001, Supplementary Table 4, http://links.lww.com/CM9/C41). By integrating spicy food consumption and the healthy lifestyle score, we found that among participants eating spicy food 3–5 days/week, those who lived in a favorable lifestyle had stronger inverse associations with the risk of cerebrovascular disease ($P_{heterogeneity}$ = 0.039) and stroke ($P_{heterogeneity}$ = 0.045, Figure 3). In addition, there was an interaction effect between spicy food consumption and the healthy lifestyle score on the risk of IHD ($P_{interaction}$ = 0.037, Supplementary Table 5, http://links.lww.com/CM9/C41).

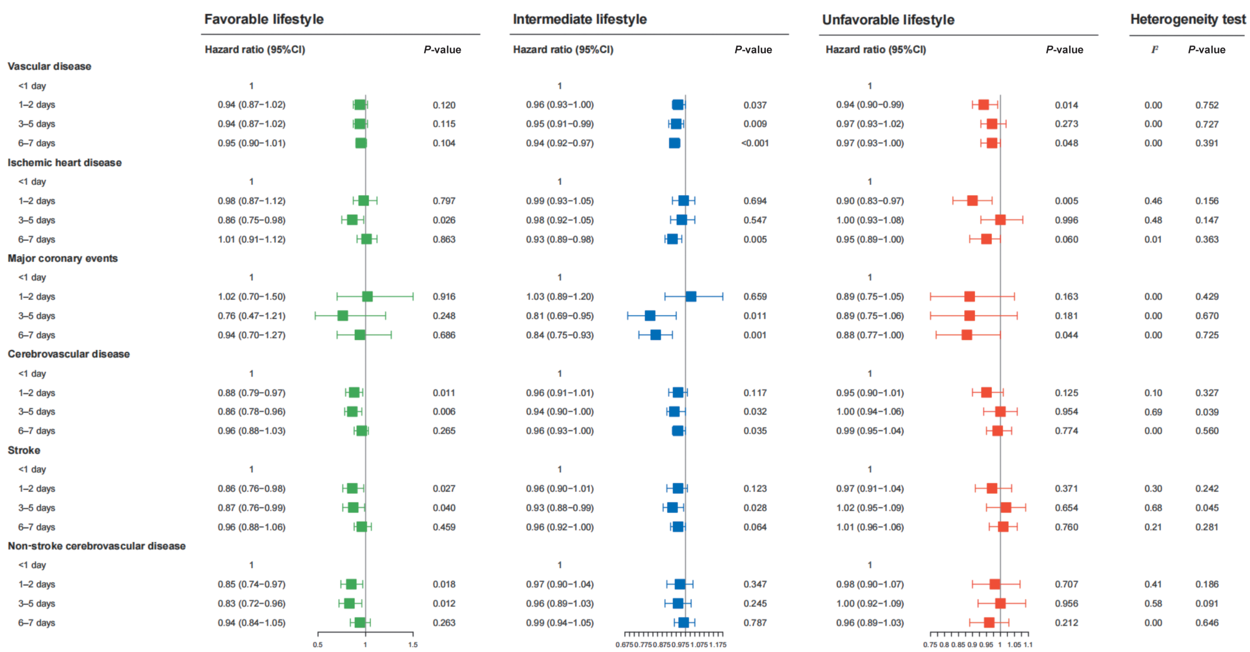

Figure 3: The association between spicy food consumption and vascular disease risk stratified by healthy lifestyle categories. The HRs (95% CIs) were estimated using Cox proportional hazard models with stratification for age, sex, region, and adjustment for household income, marital status, and education level. CIs: Confidence intervals; HRs: Hazard ratios.

Discussion

In this large prospective study of the Chinese population, a significant inverse association between spicy food consumption and the risk of vascular disease was found, especially in young people and individuals living in rural areas. The inverse association remained in the risk of IHD and MCEs. Intriguingly, there was an interaction effect between spicy food consumption and the healthy lifestyle score on the risk of IHD.

Previous studies showed the evidence that spicy food intake had beneficial effects on cardiovascular and cerebrovascular diseases.[11,22–25] However, the association between eating spicy food and the risk of vascular diseases has not been well studied in large population-based observational studies. Population studies in other countries have focused on the mortality of diseases.[11,25] In the Chinese population, most researches were limited in specific regions, diseases, or age groups.[22–24] Using a larger sample size with more factors and vascular diseases considered, we obtained favorable evidence of the inverse association between spicy food consumption and the risk of vascular diseases.

The protective effect of spicy food consumption against vascular diseases is attributed to capsaicin, the major pungent bioactive component of chili pepper.[13,26] Previous studies have shown that capsaicin affects vascular function through several pathways.[27–29] First, capsaicin can upregulate the messenger RNA (mRNA) and protein levels of cytochrome P450 family 7 subfamily A member 1 (CYP7A1), which mediates the regulatory mechanism of cholesterol and bile acid homeostasis, and leads to the cholesterol-lowering effects.[27] Second, capsaicin can regulate the vascular tone by activating transient receptor potential vanilloid 1 (TRPV1), and thus increasing endothelial nitric oxide synthase (eNOS) phosphorylation and nitric oxide (NO) production.[28] Third, capsaicin can increase the antioxidant capacity of blood vessels by reducing the level of malondialdehyde (MDA, a marker of oxidative stress) and increasing the activity of superoxide dismutase (SOD, an enzyme that mitigates oxidative stress).[29] Consistent with previous evidence, we found a significant inverse association between spicy food consumption and the risk of vascular disease. Similar trends were observed in the risk of IHD (HR ranged from 0.95 to 0.98) and MCEs (HR ranged from 0.87 to 0.96).

The protective effect of spicy food against vascular disease may be affected by several factors, especially lifestyle factors and dietary habits. Previous randomized controlled studies indicated that capsaicin showed effects including anti-atherosclerotic, anti-obesogenic,[30,31] and appetite-reducing effects.[32,33] However, these studies did not account for the differences in lifestyles and changes in eating habits. For these participants, pepper, as an essential seasoning, can improve dietary flavor and increase appetite. Due to the special Chinese food culture, most consumers who eat spicy food daily are smokers and/or drinkers, and their diet mostly includes foods that are high in salt, oil, and high energy.[34] Therefore, we constructed a healthy lifestyle score[35] and classified the study population into three groups (the favorable, intermediate, and unfavorable lifestyle groups). The inverse associations of spicy food with the risk of vascular disease, IHD, and MCEs were almost observed among participants with different healthier lifestyle scores.

In addition, the bioavailability and bioaccessibility of capsaicin may also be involved. The pharmacological effects of capsaicin depend on several factors, the most important being its concentration in the target tissues. Low doses of capsaicin displayed various preventive effects, which were not observed in participants with long-term high-dose capsaicin exposure.[36] This may also partly explain why the apparent protective association between spicy food consumption and vascular disease risk was restricted to participants consuming spice with weak or moderate intensity in the present study.

This is a large-scale study to examine the association between spicy food consumption and the risk of vascular diseases in the Chinese population. It is important to note that our prospective study was performed with a sufficient sample size, with adjustment for several established and potential confounders to obtain reliable estimation, as well as with more analyses (e.g., joint analysis with the healthy lifestyle score). However, several limitations need to be noted. First, the impact of the level of spicy food intake and different peppers (e.g., red pepper) should be further refined. Second, more potential confounding factors (e.g., energy intake, oil and salt intake, triglycerides, cholesterol, and socioeconomic status) need to be considered in the future. Third, several biases (e.g., population selection, recall bias, self-reported dietary intake, and outcome capture) limited the reliability of our study, which needs to be considered in the further research.

In conclusion, this study found a significant inverse association between spicy food consumption and the risk of vascular disease, especially in those who were younger and living in rural areas. The disease-based subgroup analysis indicated that the inverse associations remained in IHD and MCEs risk. Intriguingly, there was an interaction effect between spicy food consumption and the healthy lifestyle score on the risk of IHD. Overall, this large-scale study examined the association between spicy food consumption and the risk of vascular diseases in the Chinese population, which may provide additional dietary guidance for the prevention of vascular diseases. Nevertheless, further in-depth studies are needed to elucidate the causal roles and mechanisms of spicy food intake in reducing the risk of vascular disease.

Acknowledgments

We thank the Chinese Center for Disease Control and Prevention, Chinese Ministry of Health, National Health and Family Planning Commission of China, and 10 provincial/regional Health Administrative Departments. The most important acknowledgment is to the participants in the study and the members of the survey teams in each of the 10 regional centers, as well as to the project development and management teams based at Beijing, Oxford, and the 10 regional centers.

Funding

This work was supported by the National Natural Science Foundation of China (Project Nos. 82173620 and 82373690 to Y.Z. and 82204156 to D.Y.). This study was also funded by the Priority Academic Program Development of Jiangsu Higher Education Institution (PAPD).

Conflicts of interest

None.

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How to cite this article: You DF, Sun DJY, Zhao ZY, Song MY, Pan LL, Wu YQ, Tang YD, Lu MY, Shao F, Shen SP, Bai JL, Yi HG, Zhang RY, Wei YY, Ma HX, Xu HY, Yu CQ, Lv J, Pei P, Yang L, Chen YP, Chen ZM, Shen HB, Chen F, Zhao Y, Li LM; On behalf of the China Kadoorie Biobank Collaborative Group. Spicy food consumption and risk of vascular disease: Evidence from a large-scale Chinese prospective cohort of 0.5 million people. Chin Med J 2025;138:1696–1704. doi: 10.1097/CM9.0000000000003177