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Original article

Spicy food and self-reported fractures

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SUMMARY

Background & aims: Population-based evidence that suggests health effects of spicy consumptions on fracture was scant. The study aimed to explore the association of spicy food intake with self-reported history of fractures in the Chinese populations.

Methods: Data was drawn from the baseline survey of a large cohort study conducted in China between 2004 and 2008. A total of 512,891 adults (including 302,632 females) were included. Frequency, strength and duration of spicy food consumption were assessed using a survey questionnaire. Fracture history was self-reported based on physician's diagnoses. Multivariate logistic regression models stratified by socio-economic factors, body mass index and other lifestyle factors were performed adjusting for potential confounders.

Results: The prevalence of daily spicy food intake was 30.32% in males and 29.90% in females. The adjusted odds ratios for fractures were 1.04 (95% CI: 1.01–1.07) for those who ate spicy food occasionally, 1.10 (95% CI: 1.05–1.16) for those who ate one or two days a week, 1.15 (95% CI: 1.09–1.20) for three to five days a week, and 1.12 (95% CI: 1.07–1.17) for daily consumers, compared to participants who never ate spicy food. Participants who ate weak spicy food (OR: 1.10, 95% CI: 1.14–1.23), moderate spicy food (OR: 1.11, 95% CI: 1.06–1.15) and strong spicy food (OR: 1.18, 95% CI: 1.12–1.25) were more strongly associated with self-reported history of fracture. In addition, the strengths of associations were consistently stronger with the duration of spicy food exposure. In stratified analyses, the strength of such an association appeared stronger in rural areas (OR: 1.14, 95% CI: 1.09–1.20) than urban (OR: 1.09, 95% CI: 1.05–1.12). The correlation was consistently stronger in males than in females.

Conclusions: Among Chinese adults, a positive cross-sectional association between the level of spicy food intake and history of fractures was found in both sexes.

1. Introduction

Bone fractures, as one of the most serious complications of osteoporosis, have received more attention in recent years. Vulnerable groups of fractures are especially concerned with the consequences [1] as aging is one of the major issues across societies. Increased fracture cases may cause disabilities and shorten population's life expectancy [2]. The number of fracture cases is estimated to increase to 6.26 million in 2050 worldwide [3]. It is predicted that in 2040, 316 million individuals worldwide will be at high risk of osteoporotic fracture [4]. Among population of 50 years old or above in China, the prevalence of fractures has increased by 58% in women and 49% in men, from 2002 to 2006 [5]. In Europe, it is estimated that the economic burden of fractures reached €37 billion in 2010 [6]. Identifying risk factors of fractures and developing preventive measures are of great importance to relieve the burden of fractures.

Many studies show a correlation of dietary habits and fractures. Researchers find an increased intake of fruit, vegetables and fish was associated with a lower risk of hip fracture [8–11]. Increased dietary protein intake is found to associate with higher bone mineral density and less osteoporotic hip fracture in certain age groups [7,12]. Despite these evidences, studies addressing the association between spicy food consumption and fractures are still missing.

Abbreviations list: BMD, Bone mineral density; CGRP, Calcitonin gene-related peptide; CHD, Coronary heart disease; MET, Metabolic equivalent tasks; SP, Substance P; TIA, Transient ischemic attack; TRPV1, Transient receptor potential vanilloid 1.

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Chili is one of the most popular and important spices, used as food flavoring [13]. Studies show several positive effects of chili, including antimicrobial, anti-oxidative [14,15], anti-inflammatory, anti-cancer, and anti-obesity through thermogenesis and reducing appetite [15,16]. It is also demonstrated to have a beneficial effect on supporting weight management [17], controlling hypertension [18–20,22]. In a large prospective study of Chinese population, consumption of spicy food has also been found to have inverse associations with both total and certain cause specific mortality, independent of other risk factors of death [21].

As fractures have generated considerable burden on health related quality of life, it is important to explore the potential risk factors for fracture. No observational studies have been conducted to analyze the potential effects of spicy food consumption on fractures. The present study aims to examine whether chili intake is correlated with prevalent fractures by using data from more than half a million Chinese adults.

2. Subjects and methods

2.1. Study design and participants

This study's data was based on the baseline data of a large cohort study, which was originally set up to investigate the main genetic and environmental causes of common chronic diseases in the Chinese populations. 515,681 people attended the baseline survey between June 2004 and July 2008, of whom 261 (0.05%) withdrew before completion, 2208 (0.4%) were found subsequently to have inadvertently attended the survey twice at different time points and 1 had major data errors. The estimated population response rate was ~30% (26–38% in the five rural areas and 16–50% in the five urban areas). 513,211 participants had valid baseline data (i.e. completed questionnaire, physical measurements and consent form). Excluding 320 participants outside 30–79 year-old age range, 512,891 participants were included present analysis.

During August and October of 2008, about 5% randomly chosen surviving participants were resurveyed. The survey sites were selected on the basis of local patterns of disease and exposure to risk factors, quality of death and disease registries, population stability, local commitment and local infrastructures. The population response rate was about 30%.

To collect detailed information, participants were asked to take part in face-to-face interviews. The survey questionnaire included demographic and socioeconomic characteristics, behavior factors, sleep behavior, physical and mental health status. The interviewers used the standard text from the protocol to explain each question and answer option. Logic and error checks were used in the questionnaire to ensure valid and reliable input of answers. A range of physical measurements were taken for each participant by trained staff, using standardized instruments and protocols. Detailed description of the study design can be found elsewhere [23].

The present study included 210,258 men and 302,631 women. All participants provided information on spicy food consumption. All gave informed written consent before taking part. 1300 participants completed the same questionnaire twice at an interval of less than 1.5 years (median 1.4 years) to test the reproducibility of the frequency of spicy food consumption. Spearman's coefficient for the correlation between the two questionnaires was 0.71, indicating that spicy food consumption was reported consistently.

2.2. Assessment of spicy food consumption and fracture history

In the baseline questionnaire, participants were asked, “During the past month, about how often did you eat hot spicy food?” Participants chose from the options of never or almost never, only occasionally, 1 or 2 days a week, 3–5 days a week, and daily or almost every day. 217,104 participant who selected the last three categories were further asked, “At what age did you start to eat spicy food at least once a week?” and “What strength of spicy food do you usually prefer to eat?” with the choices of weak, moderate, and strong. A history of fracture was recorded if the participant self-reported a previous fracture diagnosed by a certified physician.

From the baseline questionnaire, we obtained several covariates including sociodemographic characteristics (i.e. age, sex, education, household income), lifestyle behaviors (i.e. alcohol consumption, tobacco smoking, physical activity), and medical history of chronic diseases. Education background was classified as illiterate and elementary, middle school, high school and above. Household income was classified as <5000 Chinese Yuan, 5000–19,999 Yuan and ≥20,000 Yuan per year. The daily level of physical activity was calculated by multiplying the metabolic equivalent tasks (MET) value for a particular type of physical activity by hours spent on that activity per day and summing the MET hours for all activities. At baseline, trained staff measured body weight and height using standard instruments and protocols with regular calibrations [24]. Several questions were designed to ask the dietary behavior involving vitamin intake, fish oil/cod liver oil intake and mineral intake. Intake during the preceding 12 months was assessed using a frequency questionnaire. Participants were asked, “Have you taken those supplements regularly during the past 12 month?” Choices were dichotomized: “Yes” or “No”. Body mass index was calculated as weight (kg)/(height (m))^2. Participants were asked, “Has a doctor ever told you that you had had the following diseases?” Self-reported chronic disease history included psychiatric disorders, diabetes, stroke or TIA (Transient Ischemic Attack), CHD, hypertension, emphysema or bronchitis, asthma, cirrhosis, chronic hepatitis, peptic ulcer, gallstone or gallbladder disease, kidney disease, rheumatoid arthritis and any types of cancer.

2.3. Statistics

Descriptive statistics were performed to describe the sex-specific distribution of demographic, socioeconomic and lifestyle characteristics among participants with different frequencies of spicy food consumptions. Analyses of the associations between the spicy food eating behaviors (including different frequencies, strengths and duration) and self-reported fractures history were conducted using multivariate logistic regression separately for males and females, and p for trend was reported. The association between spicy food intake and fractures was further examined using multivariate logistic regression models, stratified by age (i.e. <40, 40–49, 50–59, or ≥60), annual household income (i.e. <5000 Yuan, 5000–19,999 Yuan and ≥20,000 Yuan), hometown (i.e. rural, urban), physical activity, and body mass index (i.e. <24.0, 24.0–27.9, or ≥28.0 kg/m^2), and their interactions were tested. The tests for interaction were performed by means of likelihood ratio tests, which involved comparing models with and without cross product terms between the various variables and spicy food consumption as an ordinal variable. In all models, adjustments were commonly made for age, household income, hometown, occupation, education level, alcohol use and smoking history, vitamin intake, fish oil/cod liver oil intake, mineral intake, various chronic diseases, metabolism level and BMI, and all of them were coded as category variables. Adjusted odds ratios (OR) with 95% confidence interval (95% CI) were calculated to assess the strength of cross-sectional associations between consumption of spicy food and fractures.

All the statistical analyses were performed using SAS software (version 9.4, SAS Institute Inc., Cary, NC), and we defined statistical significance level at p <0.05.

2.4. Ethics

Ethical approval for the present study was obtained from 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 (UK). In addition, approvals were obtained from the institutional research boards at the local Center for Disease Control and Prevention in each of the ten survey sites.

3. Results

3.1. Basic demographic, socioeconomic and lifestyle characteristics of the study population

The socioeconomic characteristics and lifestyle of the study population by gender and the frequency of spicy food consumption are summarized in Table 1. 35,449 participants had a history of fracture. 30.32% of males and 29.90% females surveyed were daily spicy food consumers. Mean age of daily spicy food consumers was 51.48 years in males and 49.14 years in females, younger than that of those who never ate spicy food (i.e. 54.91 years in males and 53.49 years in females). The mean BMI of daily spicy food consumers was 22.85 kg/m^2 in males and 23.41 kg/m^2 in females, slightly lower than those who had never eaten spicy food (i.e. 23.41 kg/m^2 in males and 23.89 kg/m^2 in females). On average, no significant difference of physical activity was found between those who ate spicy food every day (mean = 21.49 MET-hours/day) and those who never ate spicy food (mean = 21.46 MET-hours/day). The same trend was also found in female group. Participants with a reported annual income of over 20,000 Yuan reported that they ate non-spicy food (i.e. 49.3% in males and 46.26% in females) more than spicy food daily (i.e. 36.2% in males and 30.81% in females). Most of the daily spicy food consumers were from rural areas (81.63% in males and 81.91% in females); while among non-spicy food consumers, around half (50.81% of males and 54.53% of females) were from urban area. For males, with an increasing frequency of spicy food intake, the proportion of regular smokers increased from 52.64% in non-spicy food consumers to 69.97% in those who ate spicy food every day. Same trend was found in the female group. Fewer people (30.59% in males and 30.08% in females) reported to have a history of chronic disease among those who ate spicy food everyday compared to those who consumed spicy food at a lower frequency. Daily spicy food consumers

Table 1
Basic characteristics of study population by sex and frequency of spicy food intake.[a]

	Male (N = 210,259)					Female (N = 302,632)				
	Never N = 63,154	Occasionally N = 55,240	1–2 d/w N = 14,843	3–5 d/w N = 13,275	Daily N = 63,747	Never N = 105,108	Occasionally N = 72,285	1–2 d/w N = 18,236	3–5 d/w N = 16,522	Daily N = 90,481
Age/year, (SD)	54.91 (11.00)	51.80 (10.84)	49.72 (10.46)	49.61 (10.26)	51.48 (10.60)	53.49 (10.65)	50.73 (10.30)	48.52 (9.90)	48.53 (9.75)	49.14 (10.03)
BMI/(kg/m^2), (SD)	23.41 (3.21)	23.88 (3.25)	23.91 (3.30)	23.94 (3.33)	22.85 (3.16)	23.89 (3.56)	24.15 (3.47)	23.90 (3.35)	24.01 (3.41)	23.41 (3.33)
Physical activity (MET-hours/day), (SD)	21.46 (16.31)	22.29 (15.72)	24.00 (14.39)	23.98 (14.48)	21.49 (14.11)	19.59 (13.39)	19.82 (12.75)	22.69 (12.48)	22.77 (12.64)	20.96 (11.93)
Income last year, %										
<5000 Yuan	9.55	7.46	6.44	7.66	11.50	9.44	8.60	8.26	10.22	12.61
5000–19,999 Yuan	41.01	43.55	40.48	40.93	52.48	44.3	48.11	46.78	46.77	56.58
≥20,000 Yuan	49.43	48.99	53.08	51.40	36.02	46.26	43.30	44.97	43.01	30.81
Hometown, %										
Rural	49.19	44.56	40.35	39.11	81.63	45.47	43.14	42.29	42.4	81.91
Urban	50.81	55.44	59.65	60.89	18.37	54.53	56.86	57.71	57.6	18.09
Highest education, %										
Illiterate and elementary	47.14	33.06	33.15	31.99	49.56	63.49	47.46	47.04	45.57	60.24
Middle school	30.18	35.14	33.89	34.20	31.59	21.84	27.81	26.32	27.54	26.88
High school and above	22.68	31.8	32.96	33.81	18.86	14.67	24.73	26.64	26.89	12.88
Alcohol consumption, %										
Teetotal	26.76	14.73	15.20	13.64	21.47	73.17	52.83	56.63	54.93	64.00
Occasional drinker	32.71	35.42	30.69	29.48	27.31	24.52	43.02	37.52	38.25	29.90
Ex regular drinker	5.02	2.34	2.10	1.94	4.54	0.33	0.30	0.33	0.34	0.72
Monthly drinker	5.07	8.44	7.16	6.98	5.19	0.82	1.71	2.47	2.73	1.36
Weekly	25.81	34.09	40.14	43.62	36.12	0.96	1.80	2.54	3.18	3.26
Reduced intake	4.64	4.97	4.71	4.33	5.37	0.20	0.33	0.50	0.57	0.76
Smoking, %										
Non smoker	18.59	14.76	12.48	11.52	11.05	97.00	95.17	94.37	93.33	92.74
Occasional smoker	11.47	13.32	11.36	10.55	9.32	0.86	1.75	2.50	2.69	2.71
Ex regular smoker	17.30	13.67	11.86	11.46	9.66	0.73	0.84	0.84	1.04	1.05
Regular smoker	52.64	58.25	64.29	66.47	69.97	1.40	2.24	2.29	2.94	3.50
Chronic disease history,[b] %										
No	60.32	66.91	68.61	68.26	69.41	62.88	67.17	68.43	68.01	69.92
Yes	39.68	33.09	31.39	31.74	30.59	37.12	32.83	31.57	31.99	30.08
Dietary supplement										
Regular vitamin intake	1.01	0.87	0.24	0.2	0.66	1.74	1.32	0.37	0.33	1.00
Regular fish oil/cod liver oil intake	0.81	0.81	0.21	0.17	0.70	1.26	1.04	0.22	0.22	0.89
Regular calcium/iron/zinc supplements intake	1.17	1.15	0.31	0.28	2.07	2.52	2.22	0.57	0.52	2.72

[a] BMD: Bone mineral density, the amount of bone mineral in bone tissue. MET: Metabolic equivalent tasks, a physiological measure expressing the energy cost of physical activities and is defined as the ratio of metabolic rate (and therefore the rate of energy consumption) during a specific physical activity to a reference metabolic rate, set by convention to 3.5 ml $O_2 \cdot kg^{-1}$ min^{-1}.

[b] Chronic disease history includes psychiatric disorders, diabetes, stroke or TIA, CHD, hypertension, emphysema or bronchitis, asthma, cirrhosis, chronic hepatitis, peptic ulcer, gallstone or gallbladder disease, kidney disease, rheumatoid arthritis and any types of cancer.

Table 2
Associations between self-reported history of fracture and the patterns of spicy food intake.

	Male		Female		Total	
	OR	95% C.I.	OR	95% C.I.	OR	95% C.I.
Frequency						
Only occasionally	1.07	1.03–1.12	1.03	0.98–1.07	1.04	1.01–1.07
1–2 d/w	1.16	1.09–1.24	1.09	1.01–1.16	1.10	1.05–1.16
3–5 d/w	1.20	1.12–1.28	1.14	1.06–1.23	1.15	1.09–1.20
Daily or almost every day	1.19	1.13–1.26	1.10	1.03–1.17	1.12	1.08–1.17
p for trend	<0.0001		<0.0001		<0.0001	
Strength of spice						
Weak	1.23	1.16–1.29	1.11	1.05–1.18	1.18	1.14–1.23
Moderate	1.25	1.18–1.32	1.11	1.04–1.19	1.24	1.19–1.29
Strong	1.34	1.24–1.44	1.23	1.12–1.34	1.35	1.28–1.44
p for trend	<0.0001		<0.0001		<0.0001	
Years of eating spicy food-to-age ratio						
<50%	1.19	1.13–1.26	1.10	1.03–1.17	1.13	1.09–1.18
50–80%	1.13	1.06–1.20	1.03	0.96–1.11	1.05	1.00–1.10
≥80%	1.23	1.14–1.33	1.12	1.04–1.22	1.14	1.08–1.21
p for trend	<0.0001		0.0024		<0.0001	

Reference group: people who never eat spicy food. All models adjusted for age, household income, hometown, occupation, education level, alcohol use and smoking status, vitamin intake, fish oil/cod liver oil intake, mineral intake, history of chronic diseases, MET and BMI.

reported not taking vitamins regularly (29.66% in males and 28.90% in females), not taking fish oil (29.62% in males and 29.01% in females), higher than that of those who took spicy food 1–2 day per week and 3–5 day per week.

3.2. Bone fracture and spicy food intake

Multivariate logistic regression analyses showed a statistically significant association between spicy food consumption and fractures (Table 2). Among all the participants, the adjusted odds ratios for fractures were 1.04 (95% CI: 1.01–1.07) for those who ate spicy food only occasionally, 1.10 (95% CI: 1.05–1.16) for those who ate spicy food one or two days a week, 1.15 (95% CI: 1.09–1.20) for three to five days a week, and 1.12 (95% CI: 1.08–1.17) for daily consumers, compared to participants who never ate spicy food (p for trend <0.0001). As the frequency of spicy food intake increased, a stronger strength of association was found in both sexes (p for trend <0.0001 in females and males). Compared to participants who never ate spicy food, the adjusted odds ratio for fractures was 1.18 (95% CI: 1.12–1.25) for those who ate strong spicy food, also showing an increasing strength of association as the level exposure increased (p for trend <0.0001). For the number of years of spicy food eating behavior as a percentage of the participant's age at study date, odds ratios were 1.13 (95% CI: 1.09–1.18) for those with a ratio below 50%, 1.05 (95% CI: 1.00–1.10) for those with a ratio between 50% and 80%, and 1.14 (95% CI: 1.08–1.21) for those with a ratio above 80%. All odds ratios were consistently higher in males than those in females in this model, which suggested a higher correlation among males.

3.3. Stratified associations by different socioeconomic and lifestyle factors

Stratified by socioeconomic characteristics and lifestyle, we analyzed the associations between consumption of spicy food and fractures in each stratum (Table 3). Significant associations were found in age groups of 40–49 years old (OR: 1.14, 95% CI: 1.08–1.20), 50–59 years old (OR: 1.09, 95% CI: 1.03–1.14) and of >60 years old (OR: 1.15, 95% CI: 1.08–1.22) (p for interaction = 0.0022), and among those with an annual household income of 5000–19,999 Yuan (OR: 1.10, 95% CI: 1.05–1.16), and more than 19,999 Yuan (OR: 1.11, 95% CI: 1.07–1.15) in both sexes combined (p for interaction = 0.0378). The associations were significant (p for interaction = 0.0033) in both rural (OR: 1.14, 95% CI: 1.09–1.20) and urban areas (OR: 1.09, 95% CI: 1.05–1.12), and the strength of association appeared stronger in rural areas at point estimate level. For physical activity, the odds ratios increased from 1.13 (95% CI: 1.07–1.19) in those with 12.29 MET-hours/day to 1.07 (95% CI: 1.02–1.12) in those with 12.29–25.31 MET-hours/day. The associations between spicy food consumption and fracture was found in most of the BMI categories, and appeared stronger in those in lower BMI category (i.e. <24 kg/m^2). It is noteworthy that, for all significant results, odds ratios were consistently higher in males than in females.

4. Discussion

A positive association between spicy food consumption and self-reported history of fracture was observed in the study population, and it was consistent in both sexes. The strengths of associations were consistently stronger with increasing levels of chili heat, frequency of spicy food consumption and relative duration of spicy food exposure.

We hypothesize that the positive association between spicy food intake and fracture may be facilitated by capsaicin-related physiological pathways, as such a positive association observed in the present study is supported by several previous animal-based or in vivo and in vitro experimental studies. These studies suggested that capsaicin was linked to reduced bone mineral density (BMD), increased bone resorption and decreased bone formation. Ding et al. reported that the skeletal structure of the adult rat was destroyed by high-dose (150 mg/kg) capsaicin treatment [25]. Offley et al. reported a reduction in metaphysical bone mineral density in femur and tibia 4 weeks after capsaicin treatment, resulting in a reduction in ultimate load and stress in the compressing test [26]. Li et al. suggested that capsaicin may cause an impairment in osteogenesis through decreasing expression of IGF-1R mRNA expression which were reported to help regulate development, maintenance and fracture healing [27].

Possible mechanisms underlying the potential effect of spicy food on fracture were suggested in experimental studies. Capsaicin as the major pungent principle in red pepper is a neurotoxic agent, and could activate TRPV1 [28–30]. Capsaicin treatment has been widely utilized to induce sensory denervation in rats to demonstrate neural regulation in bone metabolism. The activation of TRPV1 induces neurotoxic effects leading to a loss of trabecular integrity, reduced bone mass and strength, and increased osteoclast

Table 3
Associations between weekly spicy food intake and self-reported history of fractures, stratified by socioeconomic characteristics and lifestyle factors.

	Male		Female		Total	
	OR	95% C.I.	OR	95% C.I.	OR	95% C.I.
Age/year						
<40	1.07	0.97–1.18	0.98	0.85–1.11	1.01	0.93–1.09
40–49	1.18	1.10–1.27	1.13	1.05–1.23	1.14	1.08–1.20
50–59	1.15	1.07–1.23	1.05	0.98–1.13	1.09	1.03–1.14
≥60	1.16	1.06–1.26	1.12	1.03–1.21	1.15	1.08–1.22
p for interaction	0.3563		<0.0001		0.0022	
Hometown						
Rural	1.18	1.11–1.26	1.16	1.07–1.25	1.14	1.09–1.20
Urban	1.12	1.06–1.17	1.07	1.01–1.12	1.09	1.05–1.12
p for interaction	0.2141		0.0783		0.0033	
Income last year (%)						
<5000 Yuan	1.05	0,90–1.23	1.18	0.99–1.41	1.06	0.95–1.20
5000–19,999 Yuan	1.15	1.08–1.23	1.10	1.02–1.17	1.11	1.06–1.16
≥20,000 Yuan	1.15	1.10–1.21	1.10	1.03–1.16	1.11	1.07–1.15
p for interaction	0.1241		0.0544		0.0378	
Physical activity (MET-hours/day)						
<12.29	1.14	1.06–1.23	1.14	1.06–1.22	1.13	1.07–1.19
12.29–25.31	1.12	1.04–1.20	1.05	0.98–1.13	1.07	1.02–1.12
≥25.31	1.17	1.11–1.25	1.09	1.01–1.18	1.12	1.07–1.17
p for interaction	0.6476		0.0408		0.7221	
BMI (Kg/m^2)						
<24	1.19	1.13–1.26	1.10	1.03–1.17	1.12	1.08–1.17
24–28	1.08	1.02–1.15	1.10	1.03–1.18	1.08	1.03–1.13
>28	1.14	1.01–1.28	1.07	0.95–1.20	1.09	1.00–1.18
p for interaction	0.0611		0.8792		0.0881	

Reference group: people who never ate spicy food. All models adjusted for age, household income, hometown, occupation, education level, alcohol use and smoking status, vitamin intake, dairy intake, mineral intake, history of chronic diseases, MET and BMI.
Chronic diseases include diabetes, COPD, CHD, stroke or TIA, hypertension, emphysema/bronchitis, asthma, cirrhosis/chronic hepatitis, peptic ulcer, gallstone/gallbladder disease, kidney disease, rheumatoid arthritis, psychiatric disorder, neurasthenia and cancer.

number and surface [26]. Researchers postulated that the deleterious effects of capsaicin treatment on trabecular bone may be mediated by reductions in local neurotransmitter content and release. Capsaicin-sensitive afferent neurons contain a variety of transmitter peptides, such as calcitonin gene-related peptide and substance P (SP). Capsaicin treatment in elder rats was shown to destroy the unmyelinated sensory axons, reduce the SP and CGRP content in the sciatic nerve and proximal tibia, and inhibit neurogenic extravasation [28–30]. In bulk experimental studies of capsaicin treatment both in vivo and in vitro, it was reported that unmyelinated and small-diameter myelinated sensory neurons were destroyed and SP vanished in peripheral nerves [25]. Li et al. suggested that capsaicin-induced sensory nerve denervation increased bone resorption but had no influence on bone formation [27], which could potentially reduce bone strength. Despite these pieces of evidence, the underlying mechanisms of the association between spicy food and fracture remain to be elucidated.

Another potential hypothesis may be derived from the culinary culture of spicy food consumption in China. The flavor and properties of spices make them important for culinary uses, namely as flavoring agents, coloring agents and preservatives in processed meat [31]. And hedonic spicy food has been considered to increase palatability of meals and withstand inappetence [32]. Some evidence indicated that spicy food may increase intakes of carbohydrates, meat with heavy salt or oil, sweet food and beverages to relieve the hot stimulation [33–35]. In this regard, excessive fat and salt intake with spicy food may increase the risk of osteoporosis and bone mineral loss. Diet rich in animal protein has been identified as exerting stronger risks for fracture [36]. High salt diet has also been linked to negative effect on bone health [37–39]. It has been observed that high salt intake induces hypercalciuria along with greater calcium excretion [37]. One latest study has indicated that high salt diet (HSD) in male mice impaired both trabecular and cortical bone microarchitecture along with decreasing the mineral density and heterogeneity of bone by modulating Th17-Treg cell balance [40]. Similarly, high-carbohydrate high-fat diet causes imbalance in bone remodeling, leading to deterioration of trabecular bone structure [41,42].

4.1. Strengths and limitations

The present study is the first in literature to analyze the association between spicy food consumption and fracture in a cross-sectional study of 500,000 Chinese people. The positive effects of spices and its bioactive ingredients such as capsaicin and capsorubin on health have been showed in experiments both in vivo or in vitro, as well as in population-based studies [43–49]. It is known that spices could reduce the risk of obesity, cardiovascular disease, type 2 diabetes mellitus, cancers and inflammatory response and ease pain [50–54]. However, there is little epidemiological evidence that suggested spicy food consumption might have an adverse effect in bone health. In contrast to other studies that solely considered frequency, we explored the trend of effect of various frequency, strength and years of spicy food consumption more extensively using a large sample size of 500,000 participants in a high spicy food consumption population.

The present study has several limitations. One of the major limitations is the cross-sectional study design. Although we believe the association of the spicy food consumption with a history of fracture is subject to minimal reverse causality, it still is insufficient to establish a causal relation between the exposure and the outcome. Prospective studies are needed to further proof the existence of such an association. Secondly, the dietary addition of capsaicin enhances satiety and fullness in energy balance [25,55,56]. Without incorporating detailed dietary information, as well as other nutrients contributing to bone mass density, the observed association may still be subject to important dietary confounding factors. However, since self-reported of strength of

spicy was subjective, resulting in inevitable uncertainty of concentration of capsaicin in their diet, the meaning of assessing the total intake of spicy foods would be limited. The lack of information about dietary behaviors limited our ability to perform more extensive analyses, including total nutrient intake, medication use and other specific dietary factors. Thirdly, like any other nutritional surveys, it is difficult to completely eliminate the recall-bias due to self-reported nature of the survey. Furthermore, perception or fondness of taste, olfaction, and somatosensory sensations varies with climate and environment [56]. Possible confounders such as environment, climate, and geographical characteristics, were not included in the present analyses although regions were adjusted in all models.

5. Conclusion

The present study demonstrates that the level of spicy food intake was positively associated with a history of fractures in both sexes. The strengths of associations were consistently stronger with increasing levels of chili heat, frequency of spicy food consumption and relative duration of spicy food exposure. The findings indicated that daily consumption of spicy food might be a risk factor for fractures. Further prospective and experimental studies are needed to explore the underlying mechanisms for the observed associations, as well as other relevant environmental and genetic risk factors.

Conflict of interest

All authors declare: no support from any organization for the submitted work; no financial relationships with any organization that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

Contributors

Chuchu M and Zhe F are joint first authors. Kun T, Ruotong Y designed the study. Ruotong Y conducted the study and analyzed the data. Chuchu M, Zhe F and Ruoyu Y drafted the manuscript. Zhe F contributed to the interpretation of the results, and Kun T contributed to critical revision of the manuscript for important intellectual content. Chuchu M approved the final version of the manuscript. All authors have read and approved the final manuscript.

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