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REVIEW

Tea consumption and risk of fractures: an updated meta-analysis

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Abstract

Summary This meta-analysis included 16 studies, involving seven cohort studies and nine case-control studies, and the results indicated that tea consumption may be associated with a reduced the risk of fractures.

Introduction Regarding relationship of tea consumption with the risk of fractures remains controversial. We performed a meta-analysis to elucidate the association between tea consumption and the risk of fractures.

Methods Relevant articles were identified up to March 2019 by searching PubMed, Web of Science, and Embase databases. The pooled relative risks (RRs) with 95% confidence intervals (CIs) were computed utilizing fixed or random effects model based on heterogeneity.

Results Altogether 16 studies (seven cohort and nine case-control studies) were included in this meta-analysis, involving 772,707 participants with 37,166 fracture cases. The RRs (95% CIs) of fracture for the highest versus lowest category of tea consumption were 0.86 (0.78–0.94). Subgroup analysis indicated significant associations in cohort studies (0.90 (0.86–0.94)) and case-control studies (0.77 (0.69–0.85)).

Conclusions The current meta-analysis indicates that tea consumption may be associated with a reduced the risk of fractures.

Keywords Dose-response relationship · Fracture · Meta-analysis · Tea

Introduction

Fractures are usually defined as impairments to the integrity and continuity of the bone. Common types include traumatic fractures and osteoporotic fractures. Among them, osteoporotic fracture (also known as fragility fracture) is a low-energy or non-violent fracture, referring to the fracture caused by fall no greater than standing height or not severe trauma [1]. Fracture-prone sites are common in the proximal femur (hip), vertebrae (spine), and distal forearm (wrist), among which hip fracture is the most serious [2]. Fracture patients often have long-term bedridden, disability, or even a shock, especially for the elderly [3]. With the aggravation of global population aging, the morbidity and mortality of fracture increase year by year, causing heavy financial burden to individuals and society. Therefore, it is important to explore the risk factors associated with fractures.

Existing studies have demonstrated that fracture is affected by many factors, such as heredity, nutrition, and lifestyle factors [4–7]. Notably, the potential impact of lifestyle factors on fractures cannot be ignored. Tea is one of the substantially consumed soft beverages globally, and its most common types are green tea (unfermented) and black tea (fully fermented). Tea contains numerous chemicals, including tea polyphenols, alkaloids, carbohydrates, amino acids, aromatics, vitamins, and minerals. It is well-known that tea consumption has some potential health benefits, including preventing cardiovascular disease, Parkinson's disease, and certain cancers [8–10]. The effect of tea consumption on fracture may be closely linked to antioxidant components in tea and their effects on osteoblasts and osteoclasts.

Epidemiological studies have been examined on the association between tea consumption and the risk of fractures, but the results were still conflicting [11–26]. Some studies have reported that tea consumption is significantly associated with

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a reduced risk of fractures [15, 17, 21, 23, 25, 26], while other studies showed no significant association [11–16, 18–20, 22, 24]. Existing meta-analysis of tea consumption and fracture risk also yield inconsistent results [27–30]. Studies by Sheng et al. [27] demonstrated that daily consuming 1–4 cups of tea had a protective effect on hip fracture, while others studies manifested that no association between them [28–30]. To our knowledge, existing meta-analysis of the relationship between tea consumption and the risk of fractures were mainly included case-control studies, while few cohort studies were incorporated into the same study. Besides, previous meta-analyses have not explored the relationship between the consumption of different types of tea and the risk of fractures. Meanwhile, the dose-response relationship between tea consumption and the risk of fractures was likewise equally inconclusive. Consequently, we conducted an updated meta-analysis to elucidate the association between tea consumption and the risk of fractures.

Methods

This meta-analysis was undertaken abide by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [31].

Search strategy

Relevant articles were identified up to March 2019 by searching PubMed, Web of Science, and Embase databases. The following search keywords were used: "tea," "green tea," "black tea," "flavonoid," "catechin," "thearubigin," or "theaflavin," and "fracture". The search strategy was as follows: (((((((tea) OR green tea) OR black tea) OR flavonoid) OR catechin) OR thearubigin) OR theaflavin)) AND fracture. Additionally, the reference lists of retrieved articles were further reviewed to ascertain pertinent studies.

Inclusion and exclusion criteria

The studies would be included if it abided by the following criteria: (1) cohort or case-control design, (2) the exposure of interest was tea consumption, (3) the outcome of interest was fracture, (4) adjusted relative risk (RR) or odd ratio (OR) or hazard ratio (HR) with corresponding 95% confidence interval (CI) was provided (all results were expressed in RR for simplicity), and (5) for dose-response analysis, studies must report RR (95% CI) of fractures as well as number of cases and participants (or person-years) for at least three quantitative categories of tea consumption were included. If duplicate data occurred in one study, we would include data covering the largest number of cases.

The exclusion criteria for this study were as follows: (1) cross-sectional design, conference abstract, or animal experiments; (2) the exposure of interest were other beverages rather than tea; (3) the outcome of interest was osteoporosis, bone mineral density, or functional disability rather than fracture; (4) articles on pathological fractures caused by diseases such as bone metastasis were excluded.

The studies ascertained were independently reviewed by two investigators. If any disputes arose, it would be settled by consensus between the two investigators.

Data extraction and quality assessment

The following data were extracted independently from each study by two investigators: author, publication year, location, sex, study design, age range, sample size (cases), follow-up time, tea consumption assessment, fracture ascertaining, the RR and 95% CI for each tea consumption category, and adjusted covariates. For the dose-response analysis, the number of cases and participants (or person-years) in each category was extracted. We convert the amount of tea consumption into cup/day, and one cup of tea amounted to 300 ml. If any disputes arose, it would be settled by consensus between the two investigators.

Furthermore, we adopted the Newcastle-Ottawa Quality Assessment Scale (NOS) [32] to evaluate the quality of the included studies. The NOS consists of three parts including selection, comparability, and outcome or exposure. The quality score ranges from 0 to 9, and the higher the score of the studies included, the higher the methodological quality.

Statistical analysis

The pooled effect was computed as the inverse variance-weighted mean of the logarithm of RR with 95% CI to appraise the strength of the association between tea consumption and the risk of fractures. The forest plot was adopted to depict the results of analyses. The I^2 statistic was adopted to assess the heterogeneity, and I^2 values of 0, 25%, 50%, and 75% represent no, low, moderate, and high heterogeneity, respectively [33]. If I^2 was greater than 50%, the random effect model was employed; if it was less than 50%, the fixed effect model was employed. Subgroup analysis was carried out by study design (cohort or case-control), sex (men, women, both men and women), types of tea (any tea, green tea, black tea), fracture site (hip/femur, wrist/forearm), continent (Asia, North American, Europe, Oceania), quality score (< 7 or ≥ 7), and whether adjusted for covariates of alcohol use (yes or no), smoking (yes or no), body mass index (yes or no), and calcium intake (yes or no). Meanwhile, we also analyzed osteoporotic fractures and postmenopausal women as a specific subgroup. Meta-regression with restricted maximum likelihood estimation was adopted to assess the potentially key covariates that

might exert marked impact on between-study heterogeneity. Influence analysis was conducted by excluding one study at a time to assess whether the results could have been affected significantly by a single study. With $I^2 > 50\%$ as the standard, a sensitivity analysis was conducted on the key studies affecting the essence of between-study heterogeneity. Publication bias was evaluated utilizing the Egger regression asymmetry test and the visual inspection of funnel plot [34].

For the dose-response analysis, two-stage random effects dose-response meta-analysis models were employed. In the first stage, a restricted cubic spline model with three knots at the 25th, 50th, and 75th percentiles of the levels of tea was estimated adopting generalized least square regression, taking into account the interrelation within each set of published RRs. Then the study-specific estimates were combined adopting the restricted maximum likelihood method in a multivariate random effects meta-analysis. The *P* value for nonlinearity was computed through detecting the null hypothesis that the regression coefficient of the second spline is equal to zero.

All the analysis using the statistical software package STATA 12.0 (StataCorp, College Station, Texas, USA). All *P* values were double-sided with $P < 0.05$ deemed statistically significant.

Results

Literature search

We identified 1243 articles from the databases of PubMed ($n = 392$), Web of Science ($n = 352$), and Embase ($n = 499$). Two additional studies were detected through the reference list. After eliminating duplicates ($n = 209$) and reviewing the titles and abstracts ($n = 1008$), 28 relevant articles were reviewed comprehensively. We further excluded a review, a conference abstract, two articles that did not provide the adjusted results directly, and eight articles that did not report RR (95% CI) for tea and fracture. Ultimately, altogether 16 articles [11–26] involving 772,707 participants with 37,166 fracture cases were included in this meta-analysis. The detailed literature screening process was illustrated in Fig. 1.

Study characteristic

All articles included were analytical studies, involving seven cohort studies [11–17] and nine case-control studies [18–26]. These studies were conducted in four continents, six in Asia [16, 17, 22, 24–26], five in North America [11–13, 18, 19], four in Europe [14, 20, 21, 23], and one in Oceania [15]. The average follow-up time of cohort studies included in this meta-analysis was 9.1 years (range from 4.1 to 16.7 years). For black tea and green tea consumption, one article by Huang et al. [26] reported results for men and women, respectively. In these studies, six studies [16, 17, 22, 25, 26] were about the relationship between green tea consumption and fracture risk, and five studies [15, 16, 25, 26] were about the relationship between black tea consumption and fracture risk. The quality of most studies was relatively high (6–9 points) (Supplementary Table 1). Characteristics of included studies were displayed in Table 1.

Quantitative synthesis

Relationship between tea consumption and the risk of fractures

Relationships of included studies between tea consumption and the risk of fractures were presented in Fig. 2. The pooled RR of fracture for the highest versus the lowest consumption of tea was 0.86 (95% CI, 0.78–0.94), with the moderate heterogeneity was discovered ($I^2 = 52.8\%$, $P = 0.007$).

Subgroup analysis

Our subgroup analysis was grouped into 11 main subgroups. Notably, when grouped by study design (Supplementary Fig. 1), a significant association was detected for tea consumption and the risk of fractures in cohort studies (RR, 0.90; 95% CI, 0.85–0.94; $I^2 = 30.1\%$; $P = 0.198$) and in case-control studies (RR, 0.77; 95% CI, 0.69–0.85; $I^2 = 49.6$; $P = 0.044$). When grouped by types of tea (Supplementary Fig. 2), a significant association were discovered that green tea consumption (RR, 0.88; 95% CI, 0.82–0.93; $I^2 = 13.5\%$; $P = 0.328$), black tea consumption (RR, 0.79; 95% CI, 0.63–0.99; $I^2 = 53.9\%$; $P = 0.07$), and any tea consumption (RR, 0.87; 95% CI, 0.79–0.96; $I^2 = 55.4\%$; $P = 0.006$) with the risk of fractures.

Additional subgroup analysis showed a significant inverse association between tea consumption and the risk of fractures in postmenopausal women (RR, 0.89; 95% CI, 0.79–0.99; $I^2 = 0.0\%$; $P = 0.507$). Meanwhile, the result of seven studies [11, 14–16, 22, 25, 26] was combined that met the definition of osteoporotic fracture and found a significant inverse association between tea consumption and the risk of osteoporotic fracture (RR, 0.88; 95% CI, 0.81–0.96; $I^2 = 37.6\%$; $P = 0.142$). The detailed findings of subgroup analysis were presented in Table 2.

Meta-regression

As showed in Fig. 2, moderate heterogeneity ($I^2 = 52.8\%$) was discovered in the analysis of tea consumption and the risk of fractures. So the meta-regression was conducted to explore potential sources of heterogeneity with the covariates of the publication year ($P = 0.786$), continent ($P = 0.342$), sex ($P = 0.495$), study design ($P = 0.121$), evaluation method of tea

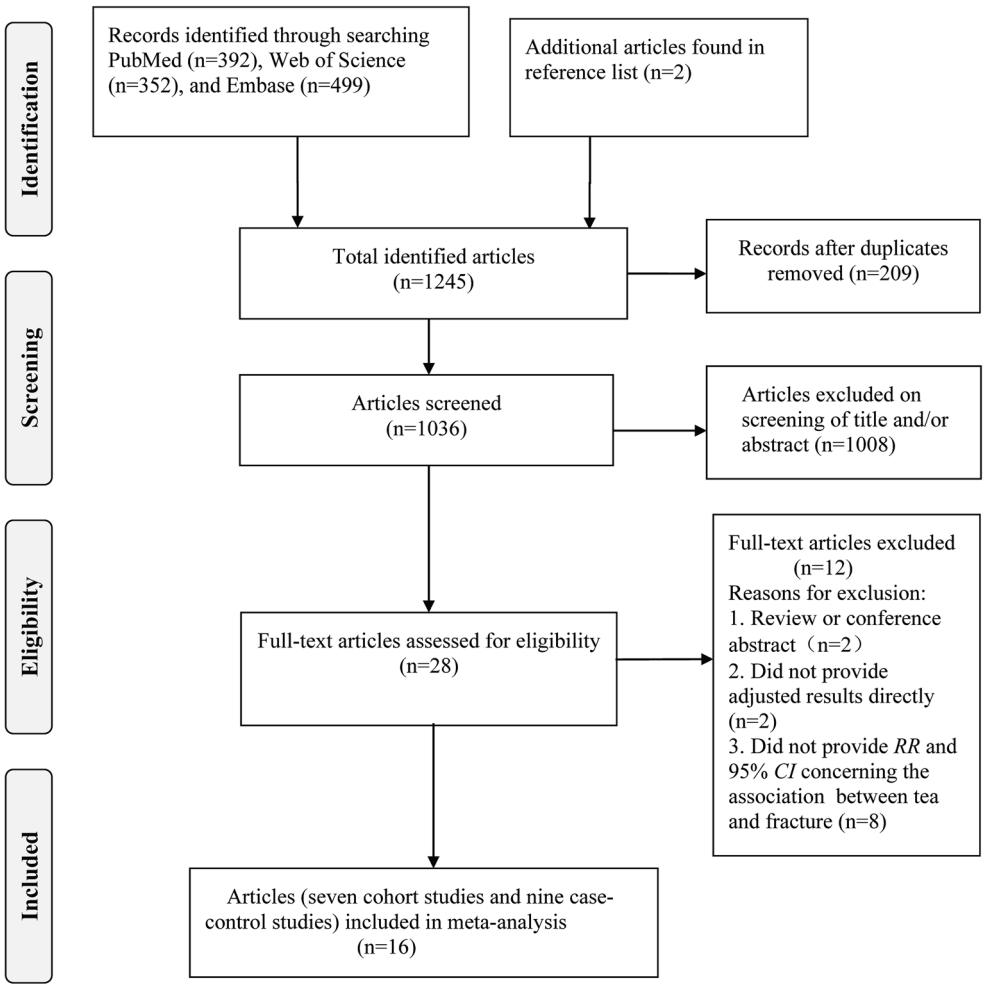

Fig. 1 The flow chart for detailed steps of literature search

consumption ($P = 0.180$), number of adjusted covariates ($P = 0.677$), whether adjusted for smoking ($P = 0.670$), and whether adjusted for alcohol ($P = 0.934$). However, none of these covariates significantly affected the between-study heterogeneity.

Influence analysis and sensitivity analysis

Influence analysis showed that no individual study had a significant impact on tea consumption and the risk of fractures (Supplementary Fig. 3). Sensitivity analysis showed that one study [21] had excessive influence. After further eliminating of these studies, heterogeneity was decreased to 44.4% and the result remained significant (0.88 (0.81–0.96)) (Supplementary Fig. 4).

Dose-response relationship

Four prospective cohort studies [13, 14, 16, 17] involving 24,537 fracture cases were included in dose-response analysis concerning tea consumption and the risk of fractures (Supplementary Table 2). The results showed that the dose-response relationship between tea consumption and the risk of fractures was not statistically significant (0.99 (0.96–1.02)) (Fig. 3).

Publication bias

Egger test illustrated that no publication bias for the analysis between tea consumption and the risk of fractures ($t = -0.73$, $P = 0.477$). Besides, publication bias was also not observed through visual inspection of the funnel plot (Fig. 4).

Discussion

Current meta-analysis manifested that tea consumption might be associated with a reduced the risk of fractures (0.86 (0.78–0.94)). To further explore these associations, subgroup analysis was carried out, and most of the results were consistent with the overall results. Notably, a significant inverse association was observed between tea consumption and the risk of fractures in cohort studies (0.90 (0.85–0.94)) and case-control studies (0.77 (0.69–0.85)).

Table 1 Characteristics of studies included in the meta-analysis on tea consumption and the risk of fractures

Author, year	Location	Study design[b], age range, sex	Follow-up time	Sample size (cases)	Tea consumption assessment[c]	Fracture ascertaining	*RR* (95% *CI*) for highest vs. lowest category[d]	Adjustment for covariates[e]
Hernandez-Avila et al. 1991	USA	Cohort, 34–59 y, women	6 y	84,484 (forearm 588, hip 63)	SQFFQ	Self-reported (follow-up questionnaire and supplementary questionnaire)	≥ 2 cups/day vs. Almost never, Hip 0.71 (0.29–1.73), Forearm 1.01 (0.78–1.29)	Age, Quetelet Index, menopause status, estrogen-replacement therapy, calcium intake, and alcohol intake
Kreiger et al. 1992	Canada	CC, 50–84 y, women	–	383 (hip 102, wrist 54)	FFQ	Radiologically confirmed	≥ 3 cup/day vs. < 3 cups/day, Hip 0.99 (0.54–1.82), Wrist 0.97 (0.60–1.58)	Age, the Quetelet index, ovariectomy, ostrogen replacement, and cigarette smoking
Nieves et al. 1992	USA	CC, 50–103 y, women	–	329 (hip 161)	Frequency questionnaire	Radiologically confirmed	≥ 14 cups/week vs. None, Hip 0.46 (0.21–1.03)	Age, BMI, hospital, smoking, education, and the presence of chronic disease
Tavani et al. 1995	Italy	CC, 18–74 y, women	–	1339 (hip 278)	Structured questionnaire	Medical records (the four largest teaching and general hospitals in Milan)	Drinker vs. Nondrinker, Hip 1.3 (0.9–1.8)	Age, BMI, education, smoking status, total alcohol consumption, calcium intake, menopausal status, and estrogen replacement therapy use
Johnell et al. 1995	Southern Europe[a]	CC, ≥ 50 y, women	–	5618 (hip 2086)	Structured questionnaire	Identified by surveillance (all hospitals, clinics, and nursing home)	Drinker vs. never, Hip 0.71 (0.60–0.84)	Age, BMI, center, recreational physical activity, milk intake, alcohol consumption, coffee intake, smoking, cheese intake, sunlight exposure
Suzuki et al. 1997	Japan	CC, 65–89y, both	–	747 (hip 249)	Frequency questionnaire	Medical records (or log books) and direct information from the attending orthopedic surgeon	≥ 3 cups/day vs. ≤ 2 cups/day, Hip 0.68 (0.37–1.23)	Age, sex, ethnicity, living place, work activity, BMI, sleep disturbance, history of stroke with hemiplegia and diabetes, calcium intake, milk intake, fish eating, sun exposure, physical activity, immobilized or bedridden condition, type of bedding, and ADL for bathing
Kanis et al. 1999	Southern Europe[a]	CC, ≥ 50 y, man	–	1682 (hip 730)	Frequency questionnaire	Identified by surveillance (all hospitals, clinics, and nursing home)	Drinker vs. never, hip 0.72 (0.53–0.98)	Age, BMI, center, recreational physical activity, milk intake, alcohol consumption, coffee intake, smoking, cheese intake, sunlight exposure
Hansen et al. 2000	USA	Cohort, 55–69 y, women	6.5 y	34,703 (total 4378)	SQFFQ	Self-reported (baseline questionnaire)	≥ 6 cups/day vs. < 1 cup/month, Total 0.72 (0.44–1.19)	Age
Chen et al. 2003	USA	Cohort, 50–79 y, women	4.1 y	91,465 (hip 386, forearm 1809, other 6626)	WHIOSQ	Self-reported (follow-up questionnaire) and medical records	≥ 4 cups/day vs. < 1 cup/day, Hip 0.93 (0.44–1.98), Forearm 0.93 (0.66–1.30), Other 1.04 (0.88–1.22)	Age, BMI, ethnicity, hormone replacement therapy use, smoking, years since menopause, fracture history, osteoporosis drug use, walking, soy milk consumption, coffee drinking, and depression
Hallström et al. 2006	Sweden	Cohort, 40–76 y, women	10.3 y	31,527 (osteoporotic 3279)	FFQ	Medical records (local outpatient registers and hospital discharge records, and X-ray records)	≥ 4 cups/day vs. < 1 cup/day, Osteoporotic 0.80 (0.48–1.33)	Age, height, weight, total caloric intake, vitamin D intake, vitamin A intake, calcium intake, phosphorous intake, alcohol intake, education, marital status
Jha et al. 2010	India	CC, NA, both	–	200 (hip 100)	Frequency questionnaire	Radiologically confirmed		Living place, work activity, BMI, sleep disturbance, history of stroke with

Table 1 (continued)

Author, year	Location	Study design[b], age range, sex	Follow-up time	Sample size (cases)	Tea consumption assessment[c]	Fracture ascertaining	*RR* (95% *CI*) for highest vs. lowest category[d]	Adjustment for covariates[e]
							> 1cup/day vs. ≤ 1cup/day, Hip 1.55 (0.72–3.36)	hemiplegia and diabetes, calcium intake, milk intake, fish eating, sun exposure, physical activity, immobilized or bedridden
Xie et al. 2013	China	CC, 52–83 y, both	–	1162 (hip 581)	Frequency questionnaire	Radiologically confirmed	Drinker vs. nondrinker, hip 0.72 (0.54–0.95)	Age, daily energy intake, BMI, education levels, passive smoking, calcium supplement and physical activity
Myers et al. 2015	Australia	Cohort, > 75 y, women	10 y	1188 (osteoporotic 288, Major osteoporotic 212, hip 129)	FFQ	Identified by linkage with the databases (Western Australian hospital morbidity data system)	≥ 3 cups/day vs. ≤ 1 cup/week, Osteoporotic 0.70 (0.50–0.96), Major osteoporotic 0.73 (0.50–1.07), Hip 0.65 (0.40–1.06)	Age, BMI, treatment code, bisphosphonate use at baseline, glucocorticoid use at baseline, smoking, physical activity, protein intake, calcium intake, energy intake, alcohol intake, prevalent fracture, and nontea flavonoid intake
Huang et al. 2016	China	CC, 58–82 y, both	–	870 (hip 435)	Frequency questionnaire	Radiologically confirmed	Drinker vs. nondrinker, hip 0.72 (0.54–0.95)	Age, BMI, education degree, parents' history of fracture, secondhand smoke exposure, calcium supplements, and equivalent energy intake of physical activity
Dai et al. 2018	Singapore	Cohort, 45–74 y, both	16.7 y	63,154 (hip 2502)	SQFFQ	Identified by linkage with the databases (nationwide hospital)	Daily vs. Less than weekly, hip 0.95 (0.85–1.06)	Age, sex, year at recruitment, dialect group, level of education in categories, BMI, smoking status, moderate physical activity, at least weekly use of vitamins/mineral, use of hormone replacement therapy at recruitment, total energy intake, calcium, fruit-vegetable-soy dietary pattern score, caffeinated coffee drinking frequency, and baseline physician-diagnosed history of diabetes and stroke
Shen et al. 2018	China	Cohort, 30–79 y, both	10.1 y	453,625 (total 12,130, hip 1376)	Frequency questionnaire	Identified by linkage with the databases (local health insurance)	Daily vs. never, total 0.88 (0.83–0.93) Hip 0.84 (0.71–1.00)	Sex, level of education, marital status, alcohol consumption, smoking status, physical activity, frequency of red meat intake, fruits and vegetables intake, dairy products intake, BMI, waist-to-hip ratio, prevalent hypertension, and prevalent diabetes

[a] Included 14 centers in six countries comprising Paris and Toulouse in France, Crete in Greece, Rome, Siena, and Parma in Italy, Porto in Portugal, Madrid and Seville in Spain and Istanbul, Ankara and three rural communities (Samssun, Eerzurum, and Diyarbakir) in Turkey

[b] *CC*, case-control study; *NA*, not available

[c] *SQFFQ*, semi-quantitative food frequency questionnaire; *WHIOSQ*, women's health initiative observational study questionnaire; *FFQ*, food frequency questionnaire

[d] *RR*, relative risk; *95% CI*, confidence interval

[e] *BMI*, body mass index; *ADL*, activity of daily living

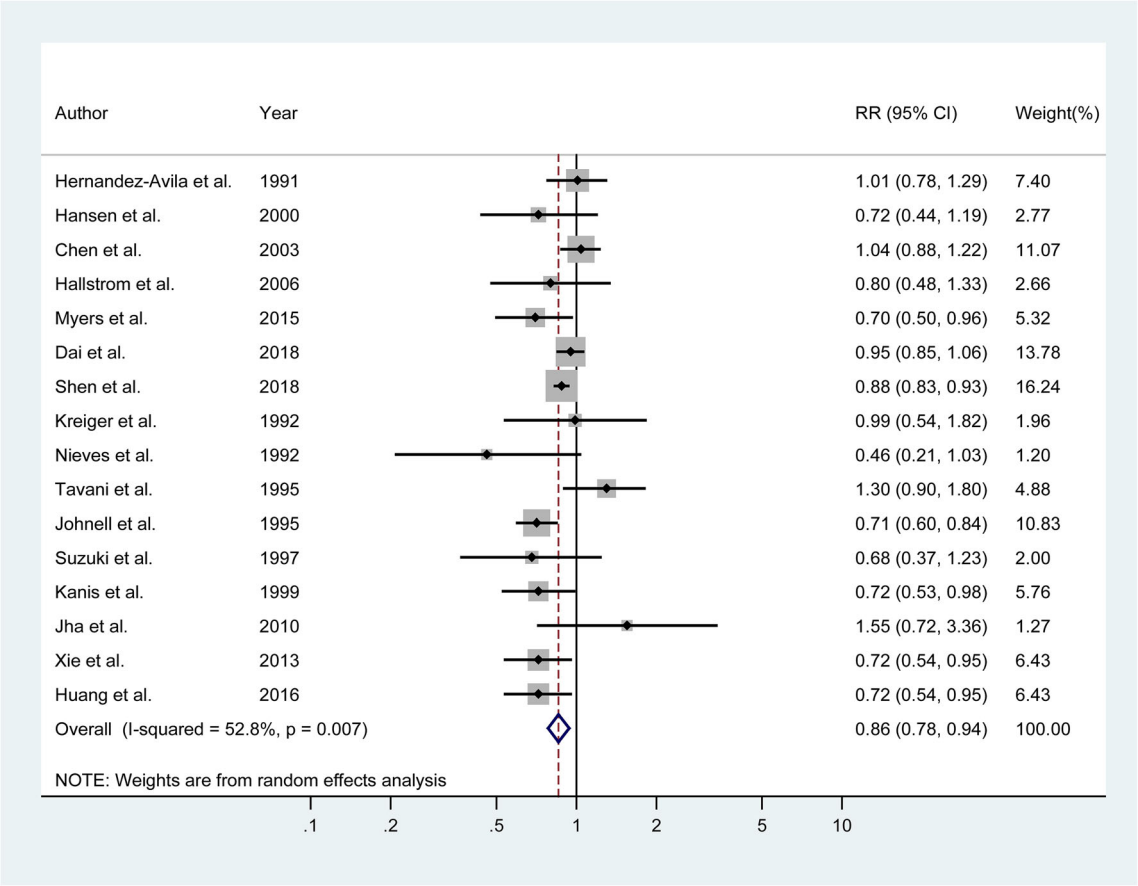

Fig. 2 Forest plot of the pooled relative risks (RRs) with corresponding 95% confidence intervals (CIs) of studies on tea consumption and the risk of fractures. The size of the gray box is positively proportional to the weight assigned to each study, and horizontal lines represent the 95% CIs

There are several possible reasons for the association of tea consumption and the risk of fractures. First, tea polyphenols, as one of the main components of tea, can regulate the bone metabolism of osteoblasts and osteoclasts. Its main bioactive component was catechins, a polyphenol consisting of four monomers: epigallocatechin-3-gallate (EGCG), epigallocatechin (EGC), epicatechin-3-gallate (ECG), and epicatechin (EC). Previous studies revealed that EGCG not only enhance the osteogenic differentiation, but also inhibit osteoclastogenesis by regulating the receptor activator of nuclear factor-κB ligand (RANKL) and osteointegrin [35, 36]. Second, abundant elements such as fluorine, phosphorus, calcium, and manganese, discovered in tea may modulate bone metabolism [37]. Appropriate intake of fluoride was favorable to calcium and phosphorus deposition in bone, which can maintain bone health and prevent dental caries [38]. Manganese was also considered to be an important element in promoting bone growth in tea [39]. Third, tea contains abundant vitamin C and vitamin K. Recent meta-analysis reported that both vitamin C and vitamin K may reduce fracture risk [5, 40].

Between-study heterogeneity frequently occurs in meta-analysis. Random effect was an important cause of heterogeneity, such as racial differences of participants, differences in methodological application, and variability in the adjustment of confounding factors, which may lead to heterogeneity. Our meta-analysis showed moderate heterogeneity between tea consumption and the risk of fractures. To identify the potential sources of heterogeneity, meta-regression analysis was performed. The results of meta-regression analysis indicated that none of the covariates (publication year, continent, sex, study design, evaluation method of tea consumption, number of adjusted covariates, whether adjusted for smoking, and whether adjusted for alcohol) had a significant effect on between-study heterogeneity. Influence analysis was performed to probe the potential sources of the between-study heterogeneity, and the finding manifested that no individual study had an excessive influence on the combined effect on tea consumption and the risk of fractures. Furthermore, sensitivity analysis indicated that one study by Johnell et al. [21] had excessive influence. In this study, a structured questionnaire was adopted to evaluate tea consumption, while other studies mostly used frequency questionnaire, which may lead to high heterogeneity. After further excluding this study, low heterogeneity was observed, and the result was not altered significantly.

Table 2 Subgroup analysis of tea consumption and the risk of fractures

	No. of studies	RR (95% CI)	I^2 (%)	$P_{\text{for heterogeneity}}$	Effect model[e]
All studies	16	0.86 (0.78–0.94)	52.8	0.007	REM
Study design					
Cohort studies	7	0.90 (0.86–0.94)	30.1	0.198	FEM
Case-control studies	9	0.77 (0.69–0.85)	49.6	0.044	FEM
Sex[a]					
Men	4	0.77 (0.56–1.06)	57.8	0.069	REM
Women	12	0.90 (0.79–1.01)	50.7	0.022	REM
Both	6	0.88 (0.84–0.93)	41.4	0.131	FEM
Types of tea[b]					
Any tea	14	0.87 (0.79–0.96)	55.4	0.006	REM
Green tea	6	0.88 (0.82–0.93)	13.5	0.328	FEM
Black tea	5	0.79 (0.63–0.99)	53.9	0.070	REM
Fracture site					
Hip/femur	14	0.84 (0.79–0.90)	47.2	0.026	FEM
Wrist/forearm	3	0.98 (0.81–1.18)	0.0	0.928	FEM
Continent					
Asia	6	0.88 (0.84–0.93)	41.1	0.131	FEM
North America	5	0.98 (0.87–1.12)	27.4	0.239	FEM
Europe	4	0.84 (0.64–1.11)	69.4	0.020	REM
Oceania	1	0.70 (0.51–0.97)	–	–	–
Quality score[c]					
≥ 7	12	0.84 (0.76–0.92)	54.1	0.013	REM
< 7	4	1.10 (0.86–1,40)	34.2	0.207	FEM
Adjustment for alcohol use					
Yes	7	0.85 (0.74–0.97)	61.3	0.017	REM
No	9	0.92 (0.85–0.99)	46.3	0.061	FEM
Adjustment for smoking					
Yes	11	0.85 (0.76–0.94)	63.1	0.003	REM
No	5	0.92 (0.76–1.11)	10.8	0.344	FEM
Adjustment for body mass index					
Yes	12	0.85 (0.76–0.94)	63.0	0.002	REM
No	4	0.93 (0.76–1.12)	0.0	0.614	FEM
Adjustment for calcium intake					
Yes	11	0.84 (0.73–0.95)	58.1	0.008	REM
No	5	0.89 (0.85–0.94)	43.7	0.131	FEM
Specific subgroups					
Osteoporotic fracture[d]	7	0.88 (0.81–0.96)	37.6	0.142	REM
Postmenopausal women	5	0.89 (0.79–0.99)	0.0	0.507	FEM

[a] Three studies were deemed as three results by the sex

[b] Three studies were grouped into three types (any tea, green tea, or black tea) by the types of tea

[c] Evaluated adopting the Newcastle-Ottawa Scale (NOS). The quality score ranges from 0 to 9

[d] Seven of the 16 studies involved fractures that were osteoporotic fracture (occurs after a fall from a standing height or less, without major trauma)

[e] *FEM*, fixed effects model; *REM*, random effects model

Our research has several strengths. First, our meta-analysis involves a large sample size (involving 37,166 fracture cases and 772,707 participants), which can reduce sampling errors and make it more likely to obtain persuasive results. Meanwhile, our investigation was conducted independently by two investigators, which could promote accuracy in investigation and largely avoid systematic errors. Second, all the studies we included were analytical studies (seven cohort

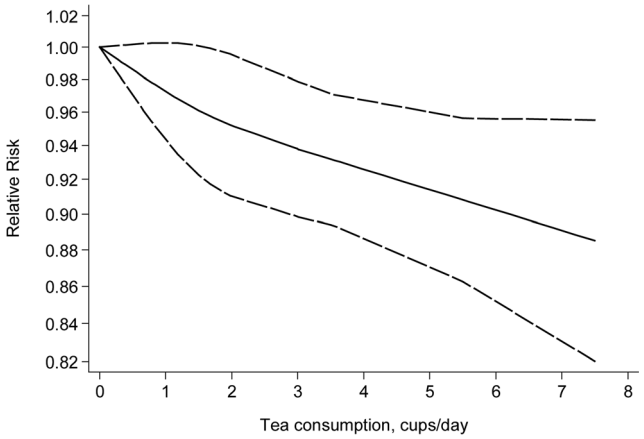

Fig. 3 The dose-response analysis between tea consumption and the risk of fractures. The solid line and the long dash line represent the estimated relative risk (RR) and its 95% confidence interval (CI)

studies and nine case-control studies), and significant negative correlations were found in cohort studies through subgroup analysis, manifesting a possible causality between tea consumption and the risk of fractures. Third, the results of all the studies we extracted adjusted the confounding factors to the greatest extent, which made our results more credible. Forth, after comprehensively subgroup analysis and sensitivity analysis, we observed nearly consistent associations, manifesting that our results were reliable and robust. In particular, subgroup analysis by types of tea was conducted for the first time. Studies have shown that green tea and black tea were not exactly the same in functional components [41]. Green tea (unfermented) was full of vitamin C, catechins and flavonoids, while black tea (fully fermented) was rich in potassium, manganese and theaflavins. The results indicated that both green tea consumption and black tea consumption were associated with reduced fracture risk. Meanwhile, subgroup analysis according to types of fracture concluded that tea consumption might be associated with a reduced risk of hip fractures. This further demonstrates that our results were more reliable.

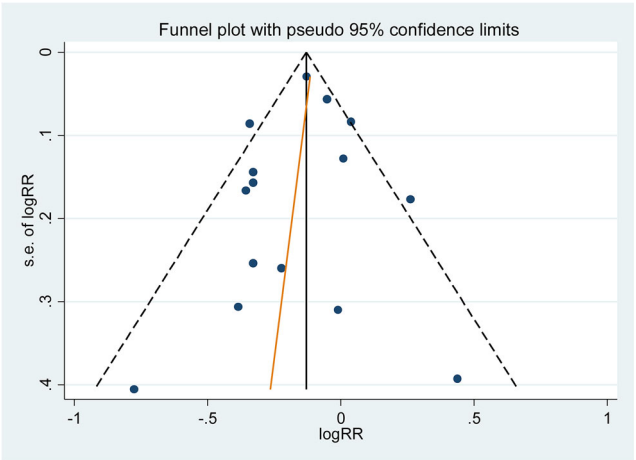

Fig. 4 Funnel plot of the relative risk (RR) of 16 studies on tea consumption and the risk of fractures. Each dot represents a different study

However, our meta-analysis also has a couple of limitations. First, considering that the included studies were cohort study and case-control study, it was hard to avoid the inherent recall bias and information bias. Second, the studies we included involve a variety of methods for assessing exposure factors (tea consumption) and outcome factors (fracture cases), and the differences between these methods might have a bearing on our results. Third, between-study heterogeneity frequently occurs in meta-analysis. We have not fully identified the source of heterogeneity, which might be associated with the diversity of disease effects. Forth, although all the data we extracted were the results after adjusting the confounding factors, the categories and numbers of the confounding factors adjusted in the studies were diverse, and some other unknown factors that were not taken into account might also have an impact on our results. Fifth, although we have subgroup analysis of tea types, the concentration of tea was not known. Considering that different people had different tea consumption habits, this might have a potential impact on the results.

Our article solved some of the limitations of the existing meta-analysis concerning tea consumption and the risk of fractures [27–30]. First, more analytical studies, especially cohort studies [11–17], were included in this meta-analysis through more extensive and in-depth retrieval. Second, some studies [42–45] that did not meet our current inclusion criteria were ruled out for various reasons. Third, the results of the pooled RR and most subgroup analysis all showed that tea consumption was associated with a reduced risk of fractures, which indicated that our results were more reliable.

Summary and conclusion

Tea consumption might be associated with a reduced the risk of fractures, and well-designed prospective studies were also required to verify this conclusion in the future.

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Authorship criteria and contributions Wenzhi Xiang and Xiubo Jiang designed the study, participated in its design and conception, analysis, and interpretation of the data, and involved in drafting the article or revising it critically for important intellectual content. Wenzhi Xiang, Kunfang Gu, and Weijing Wang performed acquisition and interpretation of the data. All authors have seen and approved the final version of the manuscript.

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Compliance with ethical standards

This article does not contain any studies with human participants or animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study.

Conflicts of interest None.

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