Review Article



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Association of Lung Cancer and Tea-Drinking Habits of Different Subgroup Populations: Meta-Analysis of Case-Control Studies and Cohort Studies

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Abstract

Background: We aimed to investigate the association between lung cancer and tea-drinking habits of different subgroup populations.

Methods: Systematic search of the PubMed, Web of Science, China National Knowledge Infrastructure (CNKI) and Sinomed databases from database construction until January 2017 for English and Chinese language articles on association of lung cancer and tea drinking. Meta-analysis was used to calculate the combined odds ratio (OR) value and its 95% confidence interval (95% CI). The Newcastle-Ottawa scale was used to evaluate the quality of the studies and Q-test and I₂ was used for heterogeneity testing.

Results: Forty two papers were included, 30 case-control studies included 14578 lung cancer patients and 180574 controls, 12 cohort studies included 543825 subjects, of which the outcome was 5085 with lung cancer. Tea drinkers were found to have a decreased OR of lung cancer compared with non-tea drinkers (OR 0. 80, 95% CI: 0. 73, 0. 87). Consumption of green, black or unspecified tea has a protective effect compared with not drinking tea at all. Increased intake of green tea to 7. 5 g per day can further reduce the OR of lung cancer (OR 0. 69, 95% CI: 0. 48-0. 98). Tea consumption had a protective effect against lung cancer in non-smokers, Further analysis found that drinking of one or more cups of tea a day has a protective effect on smokers (OR 0. 79, 95% CI: 0. 64–0. 96).

Conclusion: Tea drinking could be a protective factor in lung cancer.

Keyword: Tea; Meta-analysis; Case-control studies; Cohort studies; Lung cancer

Introduction

Currently, lung cancer is one of the malignant cancers in the world with the highest incidence and mortality rates (1). Therefore, the prevention of lung cancer is of utmost importance. Many studies have investigated the risk of lung cancer and tea consumption, but the conclusions were not consistent (2-4). A meta-analysis in 2009 (5) found that drinking green tea has a protective effect on lung cancer statistically, while there was no association between drinking black tea and lung cancer. Either black or green tea consumption have a protective effect on lung cancer statistically. Hence there is a controversy between the results of these two studies (6).

Smoking is a major risk factor for lung cancer (7, 8). In vivo animal experiments have shown that

tea polyphenols can decrease the probability of tumor formation and decrease the size and peak proliferation of tumors (9, 10). When smoking cessation is difficult, whether tea drinking can antagonize the effects of smoking on lung cancer risk is important in the prevention of lung cancer. Intake of green tea can decrease the lung cancer risk in smoking populations (11). However, two previous systematic meta-analyses did not find that tea drinking can decrease the risk of contracting lung cancer in smoking populations.

This study collected all local and overseas published articles up till January 2017 to carry out a meta-analysis to investigate the association between tea intake in different subgroup populations and lung cancer.

Methods

Tea, green tea, black tea, lung cancer, lung neoplasm, lung tumor, and lung carcinoma were used as keywords to search in the PubMed, Web of Science, the China National Knowledge Infrastructure (CNKI) and Sinomed databases. The keywords were used together or individually to search all databases from database construction until January 2017. The literature search was performed independently by two authors. All articles must fulfill the following inclusion criteria: 1) Lung cancer; 2) Case-control studies or cohort studies; 3) Exposure risk factors involves tea drinking, and study contains either OR or relative risk (RR), and its 95% CI, or these values can be computed.

Data extraction and quality assessment: The first author, publication year, study period, region, type of study, type of controls, sample size (number of cases and controls), tea drinking status, adjusted OR or RR and its 95% CI, were extracted from every article. The Newcastle-Ottawa scale (NOS) was used to evaluate the quality. Data extraction and quality assessment were also performed independently by two authors.

Statistical analysis: RevMan 5. 3 software was used for statistical analysis and the OR values and 95% CI comparing either tea drinking or highest tea intake with non-tea drinking were obtained from combining various studies. The amount of tea intake was shown by the weight of tea leaves (in grams). The intake amount in this study was readjusted and one cup of tea was defined as 2.5 g of tea leaves (2).

The Q-test and I_2 was used for heterogeneity testing, both P<0. 1 and $I_2>50\%$ defined as the presence of heterogeneity (12). When heterogeneity presented, subgroup analysis was carried out to eliminate heterogeneity; and if heterogeneity still exists, sensitivity analysis was carried out and each study was omitted individually to see if there were studies with significant effects on heterogeneity. If heterogeneity was still presented, the random effects model was used for statistical analysis. A funnel plot was constructed to investigate publication bias (13), and an asymmetrical funnel plot shows that there is publication bias.

Results

Basic information

The initial search yielded 549 articles. Through screening of titles and abstracts, 413 articles were excluded and 60 articles were selected for data extraction after careful reading of the article. As the data from 13 articles were repeated in subsequent studies, these studies were excluded. Complete data could not be extracted from five studies and these studies were also excluded. Finally, 42 studies were included in the meta-analysis in this study (3-4, 14-53) (Fig. 1). There were 19, 433 lung cancer patients and 718, 854 controls. 30 case-control studies, with 17 population-based case-control studies, one mortality-based casecontrol study and the remainder were hospitalbased case-control studies. Case-control studies included14578 lung cancer patients and 180574 controls. Twelve cohort studies included 543825 subjects, of which the outcome was 5085 with lung cancer. Two studies investigated the association between lung cancer and black and green tea consumption, 12 studies for green tea and seven for black tea. The remaining 21 studies did not specify the type of tea (Table 1).

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Hivonen2001(42)1995-1998FinlandPCC $791/25643$ Tea0. 66[0. 53, 0. 81]7Kei2000(3)1986-1997JapanCohort $69/9483$ Green1. 01[0. 62, 1. 63]6Ki1997(45)1992-1993ChinaHCC $105/105$ Tea0. 50[0. 23, 1. 10]7Fredrik1998(43)1989–1995SwedenPCC $124/235$ Black1. 23[0. 78, 1. 96]8Maria1998(44)1994–1996UruguayHCC $427/428$ Black0. 78[0. 60, 1. 02]7alexandra1996(46)1986-1990NetherlandsCohort $764/120088$ Black0. 58[0. 49, 0. 70]8Zheng1996(47)1986–1993USCohort $312/35057$ Black0. 78[0. 62, 0. 99]7Gosta1996(48)1989–1993SwedenPCC $308/504$ Black0. 71[0. 53, 0. 94]7Xu1996(49)1987-1993ChinaPCC $598/926$ Tea0. 84[0. 68, 1. 03]9Ohno1995(50)1988-1991JapanPCC $303/666$ Tea0. 57[0. 39, 0. 83]9Tewes1990(51)1981-1983ChinaPCC $200/200$ Green&Black0. 98[0. 66, 1. 45]6Mettlin1989(52)1982-1987USHCC $569/569$ Tea0. 71[0. 56, 0. 91]6Kinlen1988(53)1969-1986UKCohort $718/12868$ Tea1. 6711. 31, 2. 1317	Zhong2001(40)	1992-1994	China	PCC	649/675	Green	0. 97[0. 74, 1. 26]	7
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Ohno1995(50) 1988-1991 Japan PCC 333/666 Tea 0. 57[0. 39, 0. 83] 9 Tewes1990(51) 1981-1983 China PCC 200/200 Green&Black 0. 98[0. 66, 1. 45] 6 Mettlin1989(52) 1982-1987 US HCC 569/569 Tea 0. 71[0. 56, 0. 91] 6 Kinlen1988(53) 1969-1986 UK Cohort 718/12868 Tea 1. 6711. 31, 2. 131 7	Xu1996(49)	1987-1993	China	PCC	598/926	Теа	0. 84[0. 68, 1. 03]	9
Tewes1990(51) 1981-1983 China PCC 200/200 Green&Black 0.98[0.66, 1.45] 6 Mettlin1989(52) 1982-1987 US HCC 569/569 Tea 0.71[0.56, 0.91] 6 Kinlen1988(53) 1969-1986 UK Cohort 718/12868 Tea 1.67[1.31, 2.13] 7	Ohno1995(50)	1988-1991	Japan	PCC	333/666	Теа	0. 57[0. 39, 0. 83]	9
Mettlin1989(52) 1982-1987 US HCC 569/569 Tea 0.71[0.56, 0.91] 6 Kinlen1988(53) 1969-1986 UK Cohort 718/12868 Tea 1.67[1.31, 2.13] 7	Tewes1990(51)	1981-1983	China	PCC	200/200	Green&Black	0. 98[0. 66, 1. 45]	6
Kinlen1988(53) 1969-1986 UK Cohort 718/12868 Tea 1.67[1.31, 2.13] 7	Mettlin1989(52)	1982-1987	US	HCC	569/569	Tea	0, 71[0, 56, 0, 91]	6
	Kinlen1988(53)	1969-1986	UK	Cohort	718/12868	Tea	1. 67[1. 31, 2. 13]	7

Table 1: Characteristics of published studies on tea consumption and lung cancer risk

PCC, population-based case-control study; HCC, hospital-based case-control study; US, United States; UK, United Kingdom



Fig. 1: Process followed in the selection of studies

The quality evaluation scores of every article ranged from 6 to 9 points. Among these articles, 36 were high-quality articles (NOS 7-9) and the remaining articles were medium-quality articles (NOS 6) (Table 1).

Association of tea drinking and lung cancer

When compared with non-tea drinking populations, tea drinking was found to have a protective effect against lung cancer (OR 0. 80, 95% CI: 0. 73-0. 87) (Fig. 2). Statistically significant heterogeneity was observed (I₂=80%, P<0. 01) (Fig. 3). Subgroup analyses were done in order to identify sources of heterogeneity. As shown in Table 2, the heterogeneity was not reduced by subgroup analysis of Tea types, Study design, Geographical region, Sex, Smoking status and Study period. When stratified analysis was conducted by study design. It was found to have a decreased OR in the case-control studies (OR 0. 76, 95% CI: 0. 68, 0. 85), but no statistically significant association in cohort studies (OR 0. 88, 95% CI: 0. 74, 1. 05).

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	cases controls		Odds Ratio			Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl	
Romain Pasquet MSc 2016	560	1111	864	1469	3.2%	0.71 [0.61, 0.83]	2016	+	
wang zhe 2015	38	88	37	84	1.4%	0.97 [0.53, 1.76]	2015		
wu wei 2015	196	1174	224	1196	2.9%	0.87 [0.70, 1.07]	2015		
katarzyna 2015	17	92	49	156	1.4%	0.49 [0.26, 0.93]	2015		
mia hashibe 2015	212	1137	20562	94887	3.2%	0.83 [0.71, 0.96]	2015	+	
rup kumar phukan 2014	196	230	395	460	1.9%	0.95 [0.61, 1.49]	2014		
bao liang 2014	7	50	21	50	0.7%	0.22 [0.08, 0.60]	2014		
Yumie Takata2013	131	428	21676	70839	3.0%	1.00 [0.81, 1.23]	2013	+	
xu x 2013	615	1225	626	1234	3.2%	0.98 [0.84, 1.15]	2013	+	
p.gnagnarella 2013	57	178	1649	4158	2.5%	0.72 [0.52, 0.99]	2013		
yumie takata1 2013	241	359	45853	60733	2.9%	0.66 [0.53, 0.83]	2013	-	
zi-yi jin 2013	386	1424	1186	4543	3.2%	1.05 [0.92, 1.20]	2013	+	
zhang h 2012	454	900	62666	133811	3.2%	1.16 [1.01, 1.32]	2012	-	
i-hsin lin 2012	25	170	114	340	1.8%	0.34 [0.21, 0.55]	2012		
jiang hui 2011	55	100	57	100	1.5%	0.92 [0.53, 1.61]	2011		
b ganesh 2011	395	408	1372	1383	1.0%	0.24 [0.11, 0.55]	2009		
lu wang 2009	127	201	25931	38207	2.6%	0.81 [0.61, 1.08]	2009		
yan cui 2008	342	558	629	837	2.9%	0.52 [0.42, 0.66]	2008		
zhang ke 2008	368	505	369	529	2.7%	1.16 [0.89, 1.53]	2008	+-	
wang jingyuan 2008	95	363	135	363	2.5%	0.60 [0.44, 0.82]	2008		
g li 2008	236	302	30254	41138	2.7%	1.29 [0.98, 1.69]	2008		
han rengiang 2008	83	523	482	1924	2.8%	0.56 [0.44, 0.73]	2008		
tao wenhu 2007	36	47	77	.94	0.9%	0.72 [0.31, 1.70]	2007		
shinichi kuriyama 2006	173	222	12305	16247	2.5%	1.13 [0.82, 1.56]	2006	+-	
ia 2005	573	993	582	986	3.1%	0.95 (0.79, 1.13)	2005	-+	
matthew r.bonner 2005	95	122	98	121	1.4%	0.83 [0.44, 1.54]	2005		
hu j 2002	122	161	414	483	2.0%	0.52 [0.34, 0.81]	2002		
nagano i2001	328	395	30582	35930	2.7%	0.86 [0.66, 1.12]	2001		
hirvonen t 2001	95	791	4421	25643	2.9%	0.66 (0.53, 0.81)	2001	-	
li jie zhong 2001	130	649	139	675	2.7%	0.97 [0.74, 1.26]	2001	+	
kei nakachi 2000	41	69	5565	8483	1.8%	0.77 [0.47, 1.24]	2000		
maria mendilaharsu 1998	207	427	234	428	2.7%	0.78 [0.60, 1.02]	1998		
fredrik nybera 1998	84	124	148	235	1.9%	1.23 (0.78, 1.96)	1998		
ving-chin ko 1997	11	105	20	105	1.0%	0.50 (0.23, 1.10)	1997		
xu z 1996	235	598	404	926	3.0%	0.84 [0.68, 1.03]	1996		
wei zheng 1996	112	312	14742	35162	2.9%	0.78 [0.61, 0.98]	1996		
r.alexandra glodbohm 1996	610	764	104675	120088	3.1%	0.58 (0.49, 0.70)	1996	-	
gosta axelsson 1996	117	308	234	504	2.6%	0.71 [0.53, 0.94]	1996		
ohno v 1995	274	333	593	666	2.2%	0.57 (0.39, 0.83)	1995		
tewes fi 1990	105	200	106	200	2.1%	0.98 [0.66, 1.45]	1990		
mettlin c1989	315	569	361	569	2.8%	0.71 [0.56, 0.91]	1989		
l.j.kinlen 1988	643	718	10769	12868	2.8%	1.67 [1.31, 2.13]	1988		
T-4-1/05% CD		40.422		74005 *	400.0%	0.0010.72.0.07		▲	
Total (95% CI)		19433		/ 18854	100.0%	0.80 [0.75, 0.87]		•	
i otai events	9142		401620						
Heterogeneity: I auf = 0.07; Cl	nr= 202.7	7, dt = 4	1 (P < 0.0	0001); l*:	= 80%			0.01 0.1 1 10 100	
rest for overall effect: Z = 4.79	(P < 0.00)	JU1)						Favours [experimental] Favours [control]	





Fig. 3: Funnel plot of studies on tea consumption and lung cancer

Study	Number (n)	OR (95%CI)	Case-control	Heterogeneity test		
			or cohort(n)	TO (0 ()		
A 11 / 1'	42	0 00[0 72 0 07]	10422/710054	<u>12(%)</u>	P-value(%)	
All studies	4Z 25	0.80[0.73, 0.87]	19455//18854	80	< 0.01	
2.5g/day	23 10	0.79[0.08, 0.91]	10932/404100	82 97	<0.01	
Conort	10	0. 89[0. 71, 1. 11]	4888/394604	8/	<0.01	
	15	0.71[0.58, 0.87]	6044/9562	79	< 0.01	
7.5g/day	16	0.82[0.6/, 1.01]	/652/2//3/3	86	< 0.01	
Cohort	6	0.87[0.60, 1.28]	24/0/234/54	93	< 0.01	
CC Tea types	10	0. 91[0. 70, 1. 18]	4904/54490	80	<0.01	
Green tea	14	0 75[0 61 0 92]	5750/111640	84	<0.01	
Cohort	4	1 02[0 81 1 28]	988/101798	51	0.1	
CC	10	0.79[0.73, 0.86]	4762/9842	86	< 0.01	
$2.5\sigma/day$	0	0.73[0.54, 0.98]	1959/104387	76	<0.01	
Cohort	4	1 00[0, 87, 1, 15]	1511/103722	49	0.1	
CC	5	0 41[0 21 0 80]	971/2589	73	<0.01	
$7.5\sigma/day$	7	0.41[0.21, 0.00] 0.69[0.48, 0.98]	1667/103926	84	<0.01	
Cohort	4	0.05[0.40, 0.90] 0.86[0.74, 0.98]	988/101798	90	<0.01	
CC	3	0.60[0.74, 0.90]	679/2128	50	0.00	
Black too	9	0.01[0.44, 0.05] 0.80[0.70, 0.01]	4707/150000	65	< 0.01	
Cohort	2	0.30[0.70, 0.91] 0.78[0.72, 0.84]	1076/155250	72	<0.01 0.05	
Conort	2	0.78[0.72, 0.84] 0.82[0.76, 0.90]	2721 / 4650	15	0.00	
$2 = \frac{1}{2} \int day$	7	0.02[0.70, 0.90]	J/21/4039 4020/150072	43	0.09	
2. 5g/ day	2	0.00[0.00, 1.14] 0.76[0.44, 1.20]	4039/156672	07	<0.01	
Conort	2 E	0.70[0.44, 1.29] 0.04[0.72, 1.22]	10/0/155250	90 70	<0.01	
	5 F	0.94[0.72, 1.23]	2905/3022 2905/1571/9	79	<0.01	
7.5g/day	5	0.75[0.50, 1.02]	2805/15/108	18	< 0.01	
Conort	2	0.81[0.49, 1.30]	10///155250	0/	0.08	
	3 21	0.08[0.40, 1.16]	1/28/1918	73	0.02	
Tea unknown	21	0. 84[0. 73, 0. 96]	862//316//0	/8	< 0.01	
Cohort	4	0.77[0.70, 0.86]	2056/254560	0	0.39	
	1/	0. 89[0. 83, 0. 95]	/526/119181	/6	< 0.01	
2.5g/day	9	0.75[0.59, 0.96]	4934/14090/	84	< 0.01	
Cohort	4	0.86[0.56, 1.32]	2824/13/556	92	< 0.01	
	6	0. 67[0. 58, 0. 78]	2110/3351	20	0.29	
/. 5g/day	5	1. 13[0. 81, 1. 57]	4258/2/690	83	<0.01	
Cohort	1	1. 67[1. 31, 2. 13]	718/12868	-	-	
	4	1. 01[0. 71, 1. 43]	2462/3411	79	<0.01	
Study design	10	0.0050 54.4.051				
Cohort	12	0. 88[0. 74, 1. 05]	5085/538740	84	<0.01	
CC	30	0. 76[0. 68, 0. 85]	14578/180574	78	<0.01	
Geographical region						
Western population	15	0. 81[0. 70, 0. 94]	7325/329216	79	<0.01	
Cohort	6	0. 93[0. 74, 1. 16]	3310/299387	83	<0.01	
CC	9	0. 73[0. 61, 0. 88]	4015/29829	73	<0.01	
Asian population	25	0. 80[0. 70, 0. 92]	10630/321441	80	<0.01	
Cohort	5	0. 94[0. 91, 0. 98]	1416/172637	91	<0.01	
CC	20	0. 96[0. 94, 0. 99]	9214/148804	75	<0.01	
Sex						
Male	11	0. 82[0. 64, 1. 05]	5183/240914	90	<0.01	
Cohort	4	1.00[0.61, 1.61]	1980/150566	94	<0.01	
CC	7	0. 73[0. 55, 0. 98]	3203/90348	87	<0.01	
Female	14	0. 80[0. 67, 0. 95]	4447/304808	64	<0.01	
Cohort	5	0. 93[0. 82, 1. 06]	1105/228461	19	0. 29	

Table 2: Subgroup analyses of tea intake and lung cancer risk

CC	8	0. 90[0. 82, 0. 97]	3073/76121	28	0. 21	
Smoking status						
Smoking	8	0.80[0.63, 1.01]	3663/32347	79	<0.01	
2. 5g/day	7	0. 79[0. 64, 0. 96]	3164/32002	63	0.01	
Cohort	2	0.67[0.56, 0.81]	969/29801	0	0.65	
CC	5	0.85[0.63, 1.15]	2694/2546	80	<0.01	
No-smoking	8	0.67[0.51,0.89]	2973/74512	81	<0.01	
Cohort	1	0. 66[0. 53, 0. 83]	359/60733	-	-	
CC	7	0.63[0.46, 0.85]	2545/3673	77	<0.01	
Study period						
Before 2000	22	0.80[0.70,0.91]	9660/326269	77	<0.01	
Cohort	7	0. 91[0. 67, 1. 23]	2761/291876	89	<0.01	
CC	15	0.76[0.67,0.85]	6899/34393	57	<0.01	
After 2000	15	0.75[0.64, 0.89]	7422/147484	81	<0.01	
Cohorts	2	0. 87[0. 63, 1. 20]	606/74997	66	<0.01	
CC	13	0. 74[0. 61, 0. 91]	6457/11754	83	<0.01	

CC, case-control study

All subgroup analysis by study design Type of tea

Green, black or unspecified tea were correlated with protection against lung cancer in the casecontrol studies. Black tea and tea un-know also showed protective effect in cohort studies (Table 2).

There were no statistical significances in consumption of more than one cup/day black tea and lung cancer. Increasing daily intake of green tea to 7. 5 g increased the protective effect against lung cancer both in case-control studies and Cohort studies (Table 2).

Geographical region

There were obvious differences in the protective effect of tea drinking on lung cancer of Western and Asian countries in different study designs (Table 2).

Gender

Both females and males, tea drinking had a protective effect against lung cancer the case-control studies (Table 2). But no statistically significant association was found in cohort studies.

Study period

In both time periods of studies conducted before 2000 and after 2000, tea drinking showed a protective effect against lung cancer in the casecontrol studies. But no statistically significant association in cohort studies (Table 2).

Smoking status

Tea consumption has a protective effect against lung cancer in non-smoking populations. When daily tea intake was greater than 2.5 g, there was a protective effect of tea drinking on lung cancer in smoking populations (Fig. 4). All studies showed heterogeneity but no publication bias (I2=63%, P=0.01).





Discussion

This study showed that tea drinking had some protective effect against lung cancer. Increasing amounts of green tea intake showing a further decrease in lung cancer OR. Black tea also showed a protective effect of against lung cancer, but it didn't further decrease the OR of lung cancer by increasing the amount. This can be attributed to the differences in the production of the two tea (49). The main active component in green tea, EGCG was present in higher amounts in green tea than black tea. This could explain why increasing black tea consumption didn't increase its protective effect against lung cancer.

In smoking populations, when increased tea consumption to 2. 5 g/day, it showed a protective effect against lung cancer, which was consistent with previous studies (9). The preventive effect on lung cancer by tea could be due to the presence of polyphenols in tea. Evidence has shown that EGCG can prevent the formation of mutated cells and that EGCG can increase the activity of phase II enzymesin vivo animal studies (54-57). Phase II enzymes are involved in the detoxification of carcinogens that will be subsequently excreted (58). EGCG could induce apoptosis in cells that were damaged by carcinogens in cigarette smoke (59-61). However, smoking is considered as chronic exposure and long-term smoking has a much greater effect on lung cancer risk than just cumulative effects of daily smoking (62). Hence, long-term intake of high EGCG doses is required to reduce the damage caused by tobacco carcinogens. The types of tea involved in this study are complex, and there was no adjustment for amount of smoking, period of smoking, period of tea drinking, etc. Hence, It need for welldesigned studies with larger sample sizes and better control of various confounding factors, and the inclusion of intervention and mechanistic studies, in order to more accurately verify the association of lung cancer and different amounts of different tea in smoking populations.

It showed heterogeneity in this study. Subgroup analysis of sex, smoking status, type of tea, intake amounts and other adjustment factors could not reduce the heterogeneity. The study by Kinlen et al. (53) is the source of heterogeneity when study type, region, sex and study period were used as subgroups. This study had a NOS score of 7, with large number of cases and low sensitivity, and removing it from inclusion did not cause any obvious differences in results. Therefore, the random effects model was used for data analysis in this study.

In addition, The combination of results of studies with different designs (case-control and cohort) lead to biased results, the subgroup analysis by study design of tea types (green tea, black tea and tea un-know), geographical region, sex, smoking status, study period and the amount of tea also have shown different. However, cohort study reveals a causal relationship, and case-control cannot, cohort studies are considered preferable to case-control studies in the hierarchy of scientific evidence, and Cohort studies results should play as the standard. Our results showed that significant association existed in case-control studies, but not in cohort studies. The results may be related to the difference of study design types and sample size. Participants in case-control studies were greatly less than participants included in cohort studies.

The results of this meta-analysis were limited by some factors. Firstly, some articles did not specify the type of tea. Secondly, the data from included studies were raw primary data and most studies were retrospective case-control studies that could have possible bias and confounding factors. Lastly, this study included a small number of countries such as China, Japan and the USA, etc., and the representation by these countries requires further verification. Despite these limitations, our study collected all studies published to date on the association of tea drinking and lung cancer for a meta-analysis, and results showed that tea drinking could have protective effect against lung cancer. Increasing the amount of green tea intake to 7.5 g a day showed an increased protective effect of green tea against lung cancer. Regular intake of one cup of tea or more could antagonize the effects of smoking on lung cancer in smokers. However, larger sample sizes or prospective cohort studies are required for verification of these results and for further mechanistic studies.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interests

The authors declare that there is no conflict of interests.

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