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ORIGINAL RESEARCH

Association between cooking oil fume exposure and lung cancer among Chinese nonsmoking women: a meta-analysis

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Abstract: Lung cancer has been the main cause of cancer death around the world. Cigarette smoking has been identified as a risk factor for lung cancer in males. However, the etiological factors in nonsmoking women remain elusive. A meta-analysis was conducted to evaluate the relationship between cooking oil fume exposure and lung cancer among Chinese nonsmoking women. Thirteen articles containing three population-based case–control and ten hospital-based case–control studies were included in this meta-analysis. These studies with a total of 3,596 lung cancer women and 6,082 healthy controls were analyzed by RevMan 5.3. Fixed effects model or random effects model was used to obtain pooled estimates of risk ratio. The risk ratios with a 95% CI were 1.74 (95% CI =1.57–1.94) and 2.11 (95% CI =1.54–2.89), respectively. Cooking oil fume exposure as well as not using a kitchen ventilator when cooking was significantly associated with lung cancer among nonsmoking women (Z=10.07, P<0.00001; Z=4.65, P<0.00001). Cooking oil fume exposure, especially lacking a fume extractor, may increase the risk of lung cancer among Chinese nonsmoking women.

Keywords: cooking oil fume exposure, lung cancer, meta-analysis, nonsmoking women

Introduction

Lung cancer accounts for ~17% of cancer-related deaths around the world, and cigarette smoking is regarded as the principal risk factor for lung cancer in males.[1] As it is well known, other risk factors also increase the risk of lung cancer in female nonsmokers. A study demonstrated that 15% of male patients and 53% of female patients with lung cancer in five continents were not due to smoking.[2] A number of epidemiological studies suggested that in lifetime never smokers, lung cancer morbidity in women was significantly higher than that in men.[3] Prominent epidemiological, clinical, and pathological differences in various types of lung cancers have been discovered between lifetime never smokers and heavy smokers.[4] In recent years, indoor PM2.5,[5] housing characteristics,[6] home passive smoking exposure,[7] indoor air pollution,[8] cooking oil fume exposures,[9] and previous respiratory disease have been demonstrated as the causes of lung cancer.[10] On the other hand, numerous studies have showed that daily intake of fruits and vegetables is associated with low risk of several cancers, especially of the digestive tract.[11] However, the various risk factors and complicated epidemiological feature of lung cancer in nonsmokers are not well understood.

Exposure to environmental risk factors is worthy of attention in the development of lung cancer. Lung cancer susceptibilities of population differ in the same environment due to genetic susceptibility.[12] MicroRNAs play an important role in some

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biological processes, such as differentiation, apoptosis, proliferation, and progression of multiple types of diseases, including lung cancer.[13] Exposure to polycyclic aromatic hydrocarbons, a harmful compound in cooking oil fumes, will lead to oxidative DNA damage and lipid peroxidation.[14] Cooking oil fume exposure increased oxidative stress and endoplasmic reticulum stress, which induced cytotoxicity and apoptosis in primary fetal alveolar epithelial cells (AEC) II cells.[15] Several studies have demonstrated that mutagens and carcinogens are released by fumes from heated cooking oils, using the Ames assay or SOS chromotest.[16] Biology experiments in human lung adenocarcinoma cells found that various mutagenic compounds were generated by cooking oil fume that lead to DNA damage and oxidative damage to cells.[17] Moreover, epidemiological investigation in Chinese nonsmoking women showed that exposure to cooking oil fume might increase the risk of lung cancer.[18] Cooking oil fume exposure was significantly associated with risk of lung cancer, particularly when there is a lack of a fume extractor or ventilator.[19] A previous study has shown that household stove improvement reduces the risk of lung cancer in Xuanwei, People's Republic of China.[20] The Chinese-style cooking is thought to be the main cause increasing the risk of lung cancer among nonsmoking women.

Although several epidemiological studies have proved the association between cooking oil fume exposure and lung cancer, due to limitations, such as relatively small sample size and regional differences, the results are still inconclusive. Here, we, for the first time, carried out a meta-analysis of the published studies reporting the association of cooking oil fume exposure with lung cancer in Chinese nonsmoking women. We also investigated the relationship of lacking a ventilator in kitchen with risk of lung cancer in female nonsmokers.

Materials and methods

Search strategy and selection criteria

We reviewed all the available publications that reported the association of cooking oil fume exposure with lung cancer in Chinese nonsmoking women. The electronic databases, including PubMed, Embase, Web of Science, MEDLINE, and CNKI, were searched for all articles published before June 14, 2015, using the keywords "lung cancer" or "lung neoplasm" or "lung carcinoma" or "lung tumor" or "cancer" and "cooking oil fume." All studies included in this meta-analysis must meet the following criteria: 1) original study; 2) all cases were confirmed by X-ray computed tomography or histopathology; 3) the size of the samples and the number of patients with lung cancer with or without cooking oil fume exposure were available; 4) when the same population exists in more than one publication, we included the studies with a larger sample size; and 5) the meta-analysis was confined to English-language and Chinese-language articles. Letters to the editor, abstract, reviews, and articles published in books were excluded. All included studies were assessed by two reviewers. The Ethics Committee of Guizhou Provincial People's Hospital did not require ethics approval and patient informed consent for meta-analysis study.

Data extraction

Information of included studies was extracted by two co-authors independently using the same selection criteria, and uncertainties were analyzed by all coauthors to achieve consensus. The following data were obtained: first author, publishing year, study type, study location, study period, use of kitchen ventilator, and smoking history.

Statistical analysis

The meta-analysis of these dichotomous outcomes was conducted using Excel (Microsoft Corporation, Redmond, WA, USA) and ReviMan (computer program) Version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014, Copenhagen, Denmark). Odds ratio (OR) with 95% CI was used to evaluate the association between cooking oil fume exposure and lung cancer in Chinese nonsmoking women. We assessed between-study heterogeneity by I^2 statistics. $I^2>50\%$ or P-value of <0.05 was considered significantly heterogeneous. Random effects model (DerSimonian–Laird) was used to estimate the pooled ORs when significant heterogeneity existed among the included studies. The pooled effect size of studies and the significant P-value of overall ORs were determined using a Z-test. A Z-score, a standard score, indicates how many SDs are from the mean. A Z-score is calculated from the following formula: $Z=(X-\mu)/\sigma$, where Z is the Z-score, X is the value of the element, μ is the mean of the population, and σ is the SD. A funnel plot was obtained to test the publication bias.

Results

Study selection

According to the strict criteria for inclusion, 236 potentially relevant studies were identified by screening titles and abstracts, of which 194 articles were excluded for the following reasons: animal or cell experiments, no original information, letters, reviews, or abstracts. After reading the full text, four articles were excluded for overlapping information. Twenty-five

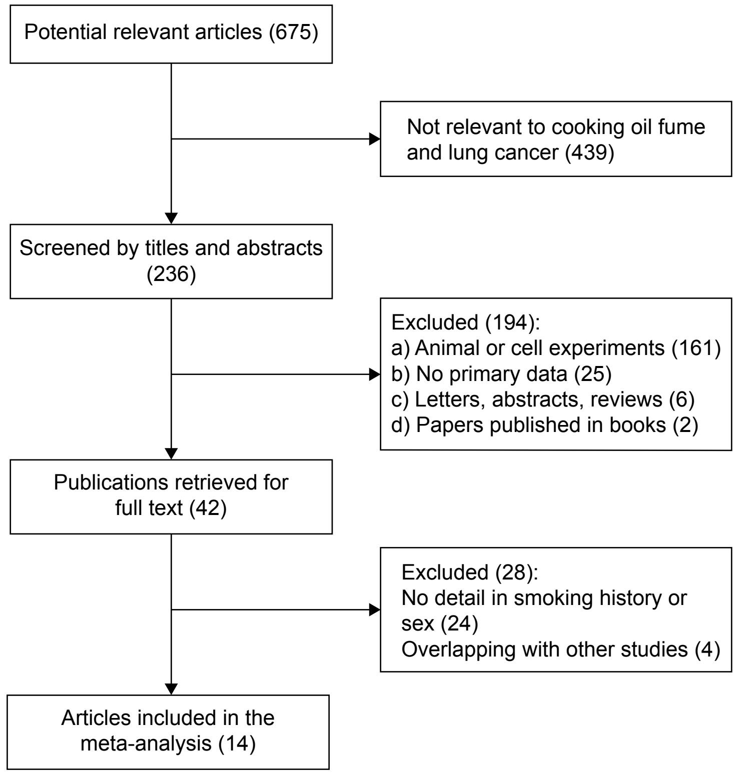

Figure 1 Flowchart of study identification.

articles were abandoned for lack of smoking history or sex information. Finally, 14 articles met the selection criteria and were included in this meta-analysis, as shown in Figure 1.

Study characteristics

The main characteristics of 14 case–control studies published between 1996 and 2014 are presented in Tables 1 and 2. Ten were hospital-based case–control studies, and the remaining four were population-based case–control studies. There were totally 3,596 lung cancer women and 6,082 healthy controls in the meta-analysis study sample sizes ranged from 187 to 1,603 with a mean of 745. All of them were lifetime nonsmokers.

Results of meta-analysis

As shown in Figure 2A, the pooled estimate of the OR was acquired using the fixed effects model on account of heterogeneity across studies (P=0.16; I^2=31%). The combined results of ten studies (2,641 cases and 4,076 controls) showed the association between cooking oil fume exposure and lung cancer in nonsmoking women (OR =1.74; 95% CI =1.57–1.94; ten studies). Cooking oil fume exposure significantly increases the risk of lung cancer among Chinese nonsmoking women.

The meta-analysis of four studies (955 cases and 2,006 controls) demonstrated that cooking oil fume exposure with no

Table 1 Main characteristics of ten studies included in the meta-analysis of lung cancer associated with cooking oil fume exposure among nonsmoking women

Study (year)	Study location	Study period	Study design	Cases (N)	Controls (N)	Language
Ko[27] (1997)	Greater Kaohsiung	1992–1993	Hospital-based case–control	310	306	English
Li et al[21] (2008)	Liaoning	2002–2006	Hospital-based case–control	225	475	English
Liu[28] (2000)	Shanghai	1995–1997	Population-based case–control	94	93	Chinese
Liu[29] (2001)	Shanghai	1992–1993	Population-based case–control	498	595	Chinese
Metayer[30] (2002)	Gansu	1994–1998	Population-based case–control	227	449	Chinese
Su[31] (2014)	Liaoning	2004–2009	Hospital-based case–control	363	370	Chinese
Wang[32] (1996)	Shenyang	1991–1994	Hospital-based case–control	166	166	Chinese
Yin et al[26] (2014)	Shenyang	2004–2010	Hospital-based case–control	306	318	English
Zhong[33] (1999)	Shanghai	1992–1994	Hospital-based case–control	504	601	English
Zhu[34] (2010)	Changsha	2009	Hospital-based case–control	160	160	Chinese

Abbreviation: N, number.

Table 2 Main characteristics of four studies included in the meta-analysis of lung cancer associated with use of a kitchen ventilator when cooking among nonsmoking women

Study (year)	Study location	Study period	Study design	Cases (N)	Controls (N)	Language
Ko (1997)	Greater Kaohsiung	1992–1993	Hospital-based case–control	310	306	English
Ko[35] (2000)	Greater Kaohsiung	1993–1996	Hospital-based case–control	339	1,264	English
Mu et al[8] (2013)	Taiyuan	2005–2007	Hospital-based case–control	153	216	English
Yu[36] (2006)	Hong Kong	2002–2004	Hospital-based case–control	251	1,069	English

Abbreviation: N, number.

ventilator in kitchen increased the risk of lung cancer among Chinese nonsmoking women (OR =2.11; 95% CI =1.54–2.89; four studies) (Figure 2B). The pooled ORs for the risk of lung cancer were calculated with the random effects model because statistically significant heterogeneity was observed (P=0.08; I^2=55%). More clinical studies should be carried out taking into account age, habit of cooking, passive smoking, histological grades, and the types of lung cancer.

Publication bias and sensitivity analysis

The publication bias of the studies included in this meta-analysis was assessed by funnel plots. The funnel plot was mainly symmetrical, suggesting that no obvious publication bias existed in this study (Figure 3). On the other hand, sensitivity analysis was performed to assess whether individual study affected the final summary results. The sensitivity analysis showed that none of the studies remarkably affected the pooled ORs and CIs, and deletion of any one study had no significant effect on the final results (data not shown).

Discussion

Cooking oil fume contains >200 kinds of harmful gases. Exposure to cooking oil fumes is related to the high mortality rate of lung cancer among Chinese women.[21] Cooking oil fumes are mainly composed of two types of chemical compounds, including polycyclic aromatic hydrocarbons and aldehydes.[16] Exposure to 2,4-decadienal has been proved to aggravate the genotoxicity of cooking oil fumes and to promote cell proliferation and cytokine levels in a human bronchial epithelial cell line.[22] A study showed that DNA adducts were generated in human lung adenocarcinoma CL-3 cells when they were exposed to cooking oil fumes.[23]

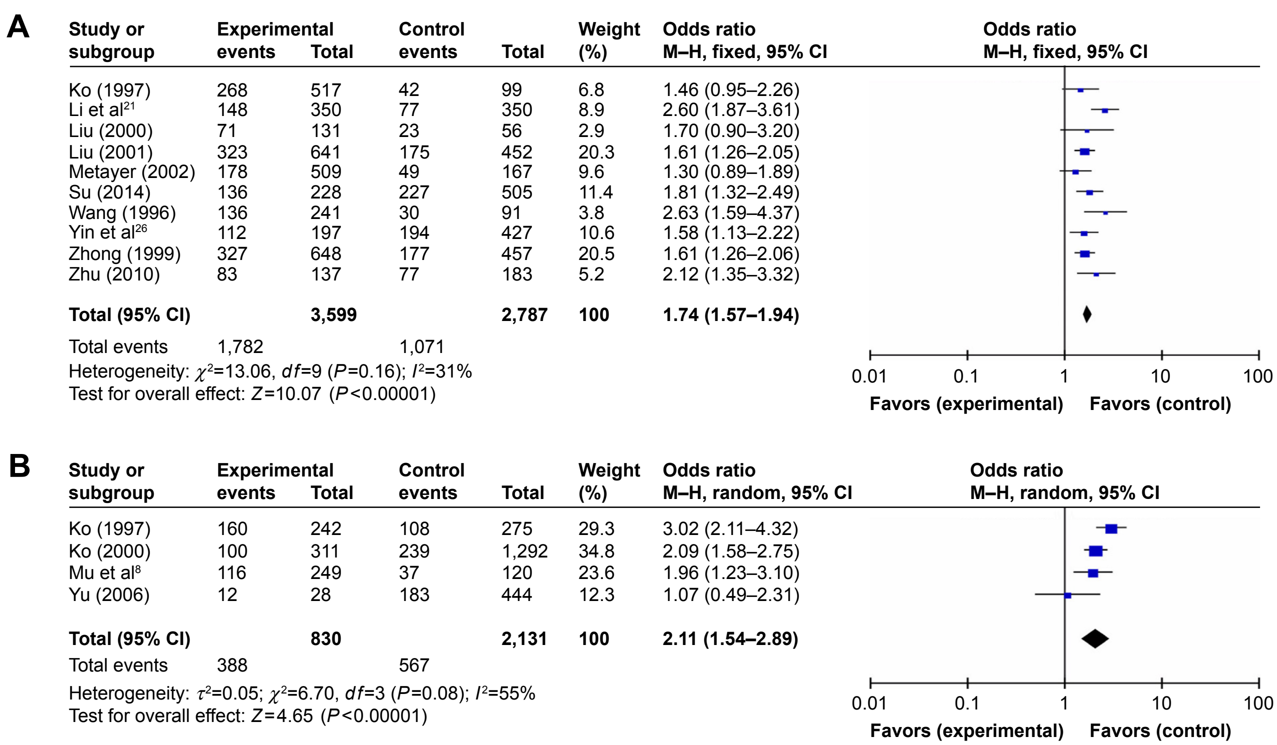

Figure 2 The forest plot of OR for lung cancer with studies included in this meta-analysis.

Notes: (**A**) Forest plots of meta-analysis for association between cooking oil fume exposure and lung cancer among Chinese nonsmoking women. (**B**) Correlation of lacking a kitchen ventilator with risk of lung cancer among Chinese nonsmoking women exposed to cooking oil fume. The total RR and 95% CI are summarized with fixed effects model or random effects model.

Abbreviations: CI, confidence interval; *df*, degrees of freedom; RR, risk ratio; OR, odds ratio.

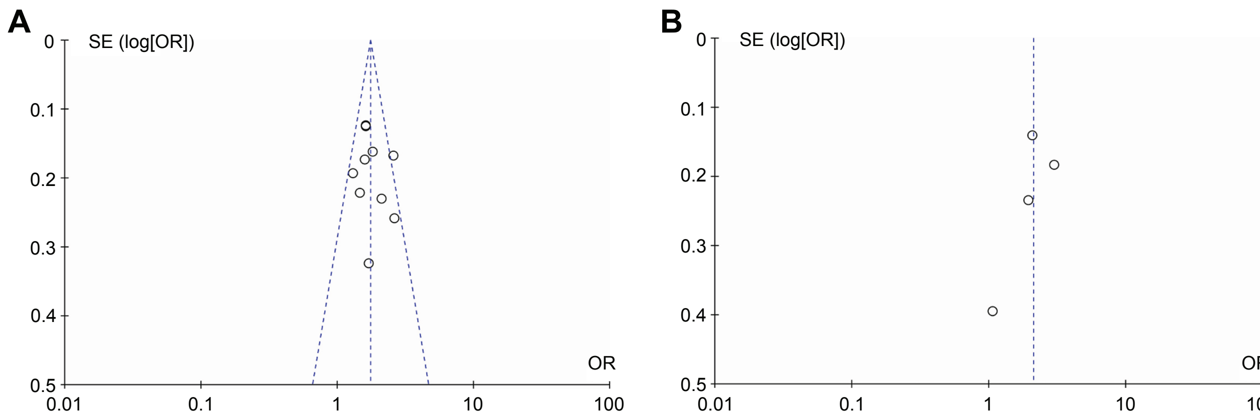

Figure 3 Funnel plots for the meta-analysis suggest that there was no obvious publication bias.
Notes: (**A**) Funnel plots for association between cooking oil fume exposure and lung cancer among Chinese nonsmoking women. (**B**) Funnel plots for correlation of lacking a kitchen ventilator with risk of lung cancer among Chinese nonsmoking women exposed to cooking oil fume.
Abbreviations: SE, standard error; OR, odds ratio.

3-(4,5-dimethyl-2-thiazolyl)- 2,5-diphenyl-2-H-tetrazolium bromide (MTT) cell proliferation assay showed that A549, a lung adenocarcinoma cell line, with cooking oil fume exposure for 48 hours exhibited significantly increased cell viability compared with control group. Nuclear factor kappa B facilitates the expression of inhibitor of apoptosis 2 (IAP2), an inhibitor of apoptosis proteins, to fully inhibit the tumor necrosis factor-induced apoptosis under cooking oil fumes and 2,4-decadienal condition.[24] To date, quite a number of biochemistry studies in vivo have revealed the mechanism by which cooking oil fumes improve lung adenocarcinoma cell survival.

In the past few years, although a large number of studies on nosetiology of lung cancer are performed, the results are inconclusive. Cigarette smoking is thought to be an impact factor of lung cancer, but the epidemiologic characteristics of lung cancer in women who smoke rarely or never smoke remain complicated.[25] Genetic and environmental factors, especially occupational exposure, may also increase the risk of lung cancer. Indoor particulate matter level and various indoor poisonous air accelerate the incidence rate of lung cancer among lifetime never smokers in Taiyuan, People's Republic of China.[8] Yin et al[26] found that the cooking oil fume exposure was associated with high risks of lung cancer among nonsmoking females in the People's Republic of China, and telomerase reverse transcriptase (TERT) polymorphism (rs2736100) might be a genetic susceptibility factor. Although numerous studies have investigated the association between cooking oil fume and risk of lung cancer in nonsmoking women, the results remain uncertain at present.

To our knowledge, we for the first time conducted a meta-analysis to summarize the association between oil fuel smoke and lung cancer in Chinese nonsmoking women. The results showed that cooking oil fume exposure significantly increases the risk of lung cancer in nonsmoking female population. However, some limitations do exist in this meta-analysis. First, although we did our best to obtain all the publications, some studies may not have been included in this analysis due to lack of detailed data; thus, publication bias may exist in this meta-analysis. Second, other factors in the studies may increase between-study heterogeneity. The heterogeneity may be from regional differences, indoor PM2.5, coal type, outdoor air quality, housing characteristics, second-hand smoking, and previous lung disease. Third, most of the study locations were in the People's Republic of China, which may increase the heterogeneity and result in publication bias. Therefore, further high-quality studies in rural or urban regions of different countries with a high incidence of lung cancer still should be conducted in future to elucidate the causes of lung cancer.

Conclusion

In summary, this meta-analysis sheds light on the relationship between cooking oil fume exposure and lung cancer in Chinese nonsmoking female population. Our results show that long-term cooking oil fume exposure significantly increases the risk of lung cancer among Chinese nonsmoking women. The use of a kitchen smoke exhaust ventilator when cooking may reduce the risk of lung cancer among nonsmoking women. Therefore, some improvable strategies in cooking habits, gas filtration, and kitchen ventilation should be used to attenuate the harmful effects of cooking oil fume on human health. A meta-analysis including more high-quality epidemiological studies and passive smoking stratified analysis is necessary in the future.

Disclosure

The authors report no conflicts of interest in this work.

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