Relationship between Air Pollution and Lung Cancer in Fujian Province: A Case-control study

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Abstract

Background: Outdoor air pollutants, especially particulate matters, are defined as a type of carcinogen by the International Agency for Research on Cancer. Studies have shown that air pollution is associated with lung cancer morbidity or mortality. This study is aimed at exploring the relationship between air pollutants and primary lung cancer in Fujian Province, China.

Methods: We conducted a hospital-based, retrospective, case-control epidemiological study on three different populations to assess the occurrence of lung cancer caused by exposure to various levels of air pollution.

Results: The total study population comprised 885 lung cancer patients and 1,220 healthy controls. The following parameters were identified as risk factors for lung cancer among the total population: smoking; exposure to cooking oil fumes; passive smoking; medical history of lung disease; family history of lung cancer; and exposure to PM₁₀, PM_{2.5}, and O₃. Fruit intake and physical exercise were protective against lung cancer. For smokers, medical history of lung disease, family history of lung cancer, and exposure to PM₁₀ and PM_{2.5} were risk factors for lung cancer, while fruit intake and physical exercise were protective factors. Among non-smokers, exposure to cooking oil fumes; medical history of lung disease; family history of lung cancer; and exposure to PM₁₀, PM_{2.5}, and O₃ were factors increasing the risk of lung cancer, while fruit intake, physical exercise, and tea drinking were protective.

Conclusions: Long-term exposure to PM₁₀, PM_{2.5}, and O₃ was found to be significantly associated with increased risk of lung cancer, with the risk being greater for non-smokers and persons exposed to cooking oil fumes.

Background

As per GLOBOCAN 2018, approximately 18.1 million new cancer cases are diagnosed worldwide each year. Lung cancer ranks first among the causes of new cancer cases, with about 2.09 million cases diagnosed annually, accounting for 11.6% of new cases of malignant tumors. The incidence of lung cancer in East Asia, particularly in China, is far higher than that worldwide (more than 40/100 000)¹. Lung cancer was the leading cause of cancer incidence and mortality in China for many years². According to the 2017 Malignant Tumors report from Fujian Province, lung cancer ranked first among all types of cancers in males (62.61/100 000) and second in females (24.8/100 000). Clearly, lung cancer has become a serious threat to public health and places a heavy disease burden in Fujian Province and China as a whole.

Smoking is a known and confirmed risk factor for lung cancer. The increase in the number of female smokers in developed countries is one of the reasons for the increase in the incidence of lung cancer among women and decrease in the comparative incidence among men³. However, some studies have found that about 15% of men and 53% of women with lung cancer do not smoke. Moreover, about 25% of lung cancer cases worldwide cannot be attributed to tobacco usage⁴. This has led to an increased interest in the exploration of the causes of lung cancer other than smoking, particularly air pollution⁵, diet⁶, infection^{7,8}, cooking fumes⁹, medical history of respiratory diseases¹⁰, and occupational exposure¹¹.

For nearly 50 years, research has been underway to confirm the relationship between outdoor air pollution and lung cancer¹². The International Agency for Research on Cancer (IARC) defines outdoor air pollutants, especially particulate matter, as a type of carcinogen. This classification is primarily based on evidence that long-term persistence of high average concentrations of PM_{2.5} in outdoor air is associated with lung cancer morbidity or mortality¹³. However, the IARC report is a qualitative assessment of hazard identification, and it does not provide the relative risk or odds ratio (RR or OR) of lung cancer associated with outdoor air pollution. The current research results still leave several key points unclear. First, the population groups that are most vulnerable to air pollution are yet to be identified^{14–17}. Second, few studies have focused on the dose-response relationship between long-term exposure to outdoor air pollution and lung cancer^{16,18,19}. In particular, very few studies from China have investigated the risk of lung cancer in relation to air pollution; among these studies, case-control studies and cohort studies are very few, and most of the existing studies focus on lung cancer mortality.

Given the limitations of epidemiological research methods, cohort studies on the causal relationship between outdoor air pollution and lung cancer would require a long time to yield conclusive results. In this study, we sought to conduct a hospital-based, case-control study to investigate the relationship between air pollutants and lung cancer in Fujian Province, with special focus on the exposure levels of different population groups to air pollutants. We expect that the results of this study would provide a scientific basis for targeted improvement of the atmospheric environment for protection of public health.

Materials And Methods

Study subjects

Between January 2010 and December 2015, we recruited from three sources: Department of Thoracic Surgery and Respiratory Medicine of the First Affiliated Hospital of Fujian Medical University, Union Hospital Affiliated to Fujian Medical University, and Fuzhou General Hospital of Nanjing Military Region. Patients were included if they had been newly diagnosed with primary lung cancer, as confirmed by fiberoptic bronchoscopy or surgical histopathology, and had resided in Fujian province of China for more than 10 years.

The population-based approach was applied to recruit the control group, which comprised healthy community dwellers randomly selected from the resident records of Fujian province. The control group was frequency-matched to the cases by ethnicity, gender, and age. Every control subject was of ages ± 2 years as compared to the matching cases. All the selected control individuals successfully met the inclusion criteria and completed the study, without any drop-out during the study.

In total, the case group comprised 885 patients with lung cancer, while the control group comprised 1,220 healthy individuals. All participants provided written, informed consent before undergoing the examination. The study protocol was approved by the Ethics Committee of Fujian Medical University.

Questionnaire and variables

All participants were surveyed using a standardized questionnaire, which was administered during a scheduled phone interview conducted via a study team member. The 18-page questionnaire had questions pertaining to the patients' demographic characteristics information, tumor characteristics, and data regarding the subject's living environment, dietary habits, smoking history, alcohol consumption, intensity of physical activity, occupational exposure to air pollutants, and exposure to domestic pollutants. The questionnaire also included items regarding medical history, family history, and lifestyle-related parameters. Data regarding reproductive health were collected for female participants.

Body mass index (BMI) was determined as the ratio of body weight (kg) and height[m]². A positive smoking history was defined as a history of having smoked more than 100 cigarettes during his/her lifetime. Passive smoking history was defined by non-smoking history of inhaling cigarette smoke generated by others or exposure to exhaled smoke more than 15 minutes per day. A history of alcohol consumption was defined as drinking at least one alcoholic beverage per week for more than six months, irrespective of the type of alcoholic drink. Drinking tea was defined as consuming at least one cup of any kind of tea per week for more than six months. A family history of cancer was defined as the occurrence of a malignant tumor in first-degree or second-degree relatives. Occupational physical activity was rated as low, moderate, or high intensity, as defined by the Reference Standard of Labor Intensity recommended by the Chinese Nutrition Society in 2000. To check for exposure to cooking oil fumes, participants were enquired about whether their degree of exposure to fumes in the kitchen was none (no exposure), light, moderate, or heavy²⁰.

Overview of the study area

Fujian Province is located on the southeast coast of China. The land area is 124 000 square kilometers in total. From north to south, the province measures about 530 kilometers and occupies about 480 kilometers from east to west. Fujian is located at a latitude of 23°30' and 28°22' north and at longitude of 115°50' and 120°40' east. The terrain is higher in the northwest and lower in the southeast. About 90% of the total land area of the province is covered by mountains and hills. In addition, the coastal landform pattern is dominated by a tortuous coastline that includes several bays and peninsulas. The climate in Fujian Province is subtropical monsoon climate, which makes the area warm and humid. The annual average temperature is 15°C–22°C, which increases from the northwest to the southeast. The annual average precipitation is 800–1,900 mm, with the precipitation being greatest between May and June every year, with several typhoons occurring at the turn of summer and autumn.

Air pollution data collection

For this study, we aimed to obtain a reasonable estimate of each subject's exposure to atmospheric pollutants by using a longer average annual concentration. The levels of sulfur dioxide (SO₂), nitrogen dioxide (NO₂) and suspended particulates smaller than 10 µm in aerodynamic diameter (PM₁₀) in Fujian Province were obtained from the complete monitoring data of national control points, which has been maintained since 2005. Since 2013, China has implemented new monitoring standards, which include the current maximum of eight hours average for ozone (O₃). Accordingly, the maximum value of continuous 8-hour ozone concentration in a day is taken as the standard for evaluating the ozone pollution level of the same day and the six indicators of air quality are monitored: SO₂, NO₂, PM₁₀, carbon monoxide (CO), and suspended particulates smaller than 2.5µm in aerodynamic diameter (PM_{2.5}). The ambient air quality data collected in this study was collected for the period between January 1, 2005 and December 31, 2015.

The daily average concentration values and monthly average values of SO₂, NO₂, PM₁₀, CO, O₃, and PM_{2.5} were collected for 39 monitoring points (national control points) in Fujian Province; the data were collected from the Fujian Provincial Environmental Monitoring Center Station (Figure 1). The strategic value of the location of each monitoring point has been demonstrated previously, and the points have been shown to be geographically representative. The air pollution monitoring data for SO₂, NO₂, PM₁₀, CO, O₃, and PM_{2.5} were evaluated according to the Chinese Ambient Air Quality Standard (GB3095-2012).

Since it would be impractical to measure the individual exposure level to concentrations of atmospheric pollutants by having each subject wear a monitoring device, we used an individual atmospheric pollutant exposure estimation method, according to the approach proposed by Dadvand et al²¹. Basically, we constructed an algorithm to predict atmospheric pollutant exposure for each location within Fujian province by integrating air pollution monitoring data and spatial coordinates of 39 monitoring points. By using the spatial prediction function of ArcGIS 10.3, the spatial distribution map of air pollution indexes in Fujian Province was generated by applying inverse distance to a power (IDW) interpolation in areas that lacked derived data. The annual average level of cumulative concentration served as the matched measurement data for each index. Further, the levels of SO₂, NO₂, and PM₁₀ were the annual average values from 2005 to the time that subjects enrolled. In addition, the concentrations of O₃, CO, and PM_{2.5} were measured from 2013 to the time of enrollment of the subjects. According to the detailed home address (specific to the district, street, and house number), the spatial coordinates (latitude and longitude) of each subject was accurately determined by GPSspgGeo coding software and Tencent map software, which can be further mapped to the predicting model and used to generate the estimating pollution data for each subject.

Statistical analysis

The Chi-square test was used to compare the general characteristics of cases and controls. Stratified analysis for different populations was performed using a *t* test for the exposure levels of air pollution indexes. Unconditional logistic regression modeling and identification of possible confounding factors were performed by calculating odds ratios (ORs) and 95% confidence intervals (CIs) for air pollution indexes and lung cancer risk. All analysis was performed using the SPSS 25.0 software package (IBM Corporation, Armonk, New York, USA) and ArcGIS 10.3 (ESRI Inc, USA). All p-values were based on a two-sided test with an α of 0.05.

Results

Demographic characteristics of the study subjects

The current study comprised 2,105 subjects, including 885 cases and 1,220 controls. Subjects included 1,354 males and 751 females, with ages between 23 and 90 years of age and average age of 58.94 ± 10.73 years. The case and control groups did not show any significant difference in the distribution of gender, age, ethnicity, and marital status ($P > 0.05$). However, significant intergroup differences were noted in the educational level, occupation, and BMI ($P < 0.05$).

Among the smokers, no significant difference was noted between the case group and the control group in terms of the distribution of gender, ethnicity, and marital status ($P > 0.05$). However, statistically significant intergroup differences were noted in the distribution of education, occupation, and BMI ($P < 0.05$). Among the non-smokers, the case group and control groups did not differ significantly in the distribution of age, ethnicity, and marital status ($P > 0.05$), but showed significant differences in gender, education level, and occupational exposure ($P < 0.05$).

Among the 885 cases included, 551 (62.3%) were of adenocarcinoma, 208 (23.5%) were of squamous cell carcinoma, and 126 (14.2%) were of other pathological types of cancers. Among the 519 smokers, 253 (48.7%) had adenocarcinoma, 177 (34.1%) had squamous cell carcinoma, and 89 (17.4%) had tumors of other pathological types. Of 366 non-smoking lung cancer patients, 298 (81.4%) had adenocarcinoma, 31 (8.5%) had squamous cell carcinoma, and 37 (10.1%) had lesions of other pathological types (Table 1).

The risk factors of lung cancer

In this study, we explored the potential factors for lung cancer in the three groups: general population, smokers, and non-smokers (Table 2). Of the total population, after adjusting for BMI, education, and occupation, we found that subjects with a family history of lung cancer or medical history of lung disease, drinking alcohol, smoking, passive smoking, or exposure to cooking oil fumes were susceptible to lung cancer. We found that the risk of lung cancer was low for subjects who performed physical exercise and had a regular intake of fruit (more than 3 times per week). Among the smokers, after adjustment for age, BMI, education, and occupation, the risk factors for lung cancer were family history of lung cancer, medical history of lung disease, and exposure to cooking oil fumes, while the protective factors were physical exercise and fruit intake. Similarly, for non-smokers, the risk factors for lung cancer were family history of lung cancer, history of lung diseases, passive smoking, and exposure to cooking oil fumes, after adjustment for gender, education, and occupation, whereas the protective factors were drinking tea, physical exercise, and fruit intake.

Univariate analysis of levels of exposure to atmospheric pollutants in different populations

The annual average of SO_2 , NO_2 , and PM_{10} concentrations for the period between 2005 and 2015 and those of CO , $\text{PM}_{2.5}$, and O_3 for the period 2013–2015 are shown in Figure 2. Notably, the distribution of different pollutants differed from one another. Thus, we noted that NO_2 , $\text{PM}_{2.5}$, and O_3 had similar distribution patterns, with the pollutants being highly aggregated in cities along east coast; this may be associated with the dense population and severe traffic pollution. The remaining three common pollutants showed completely different distribution patterns, with CO mainly concentrating in northeast area, SO_2 aggregating in the mid–west region, and PM_{10} mainly affecting the southwest. The discrepancy in the distribution patterns may be attributed to the complex effect of factory contamination and factors such as climatic and geographic conditions.

Univariate analysis was performed to levels of exposure to evaluate the impact of atmospheric pollutants on different populations. The values for concentrations of atmospheric pollutants were classified into four levels based on ± 1 standard deviation (Table 3). For the total population, after adjustment for education, occupation, BMI, family history of lung cancer, and medical history of lung disease, alcohol consumption, smoking, passive smoking, exposure to cooking oil fumes, physical exercise, and fruit intake, the results showed that the risk of developing lung cancer with exposure to NO_2 concentrations of $0.019\text{--}0.029$ (mg/m^3) was 1.356 times greater than at concentrations of less than 0.019 (mg/m^3) (95% CI: 1.028–1.788). As compared to exposure to PM_{10} concentrations of less than 0.051 (mg/m^3), exposure to concentrations of $0.051\text{--}0.057$ (mg/m^3) increased the risk of developing lung cancer by 2.450 times greater (95% CI: 1.728–3.474), while exposure to concentration of $0.057\text{--}0.064$ (mg/m^3) and increased the risk by 1.637 times (95% CI: 1.178–2.276).

Exposure to $\text{PM}_{2.5}$ is also a risk factor for lung cancer. For exposure to concentrations of $0.020\text{--}0.027$ (mg/m^3), the OR was 33.658 (95% CI: 15.450–73.325), and for exposure to concentrations of $0.027\text{--}0.035$ (mg/m^3), the OR was 5.059 (95% CI: 2.390–10.712). Furthermore, exposure to O_3 is also a risk factor for lung cancer. For exposure to O_3 concentrations of $0.047\text{--}0.065$ (mg/m^3), the OR was 125.056 (95% CI: 29.902–523.012); 17.746 (95% CI: 4.322–72.862), for O_3 concentrations of $0.065\text{--}0.083$ (mg/m^3); and 50.896 (95% CI: 11.069–234.032) for concentrations of more than 0.083 (mg/m^3).

Next, we compared the results for smokers, after adjusting for age, education, occupation, BMI, family history of lung cancer, and medical history of lung disease, exposure to cooking oil fumes, physical exercise, and fruit intake. Further, for non-smokers, the results were compared after adjusting for gender, education, occupation, family history of lung cancer, medical history of lung disease, passive smoking, exposure to cooking oil fumes, drinking tea, physical exercise, and fruit intake. The analysis indicated that for both groups, exposure to PM_{10} and $\text{PM}_{2.5}$ was a risk factors for lung cancer. Moreover, exposure to $\text{PM}_{2.5}$ had a greater impact on non-smokers than on smokers, as shown by the following results for both groups: OR was 61.431 (95% CI: 18.041–209.181) and 24.545 (95% CI: 8.12–74.265) (in non-smokers and smokers, respectively, for exposure to $\text{PM}_{2.5}$ concentrations of $0.020\text{--}0.027$ (mg/m^3)) and OR was 11.814 (95% CI: 3.622–38.540) and 2.630 (95% CI: 0.910–7.595) (for non-smokers and smokers, respectively, for exposure to $\text{PM}_{2.5}$ concentrations of $0.027\text{--}0.035$ (mg/m^3)). Since none of the participants were exposed to O_3 concentrations of less than 0.047 mg/m^3 in the control group, the effect of O_3 exposure on the smokers could not be assessed. Among the non-smokers, exposure to O_3 was identified as a risk factor for lung cancer. However, SO_2 and lung cancer did not show any associated, both in the general population and in the group of smokers or non-smokers. Similarly, none of the participants in the control group were exposed to a low concentration of CO , and therefore, the association of CO with lung cancer could not be evaluated (Table 3).

We also analyzed the relationship between air pollution and lung cancer stratified by passive smoking and exposure to cooking oil fumes, and the results were consistent with those of smoking. The detailed results are shown in Additional Table 1 to 3 (for passive smoking) and Additional Table 4 to 6 (for cooking oil fume exposure).

Multivariate analysis of levels of exposure to atmospheric pollutants in different populations

All the variables that were found to have a significant impact on the development of lung cancer in the previous analysis were further subjected to multi-factor unconditional logistic regression analysis using the backward stepwise method. We used $P \leq 0.05$ as the inclusion criterion and $P \geq 0.10$ as the exclusion criterion. The results of the analyses indicated that the following factors increased the risk of lung cancer among the general population: smoking; exposure to cooking oil fumes; passive smoking; medical history of lung disease; family history of lung cancer; and exposure to O_3 , PM_{10} , and $PM_{2.5}$. On the other hand, fruit intake and physical exercise were found to be protective factors against risk of lung cancer (Table 4). For smokers, medical history of lung disease; family history of lung cancer; and exposure to PM_{10} and $PM_{2.5}$ were factors that increased the risk of lung cancer, whereas fruit intake and physical exercise were factors that reduce the risk of lung cancer (Table 5). Similarly, among the non-smokers, cooking oil fumes; medical history of lung disease; family history of lung cancer; exposure to PM_{10} , $PM_{2.5}$, and O_3 may increase the risk of lung cancer, while fruit intake, physical exercise, and drinking tea were found to protect against the risk of lung cancer (Table 6).

The results of the analysis in different populations are shown in Additional Table 7-9 for passive smoking and in Additional Table 10-12 for exposure to cooking oil fumes.

Discussion

This hospital-based case-control study was designed to evaluate the relationship between atmospheric concentrations of air pollutants and the occurrence of lung cancer in Fujian Province. We found that the overall risk factors for lung cancer were smoking; exposure to cooking oil fumes; passive smoking; medical history of lung disease; family history of lung cancer; and exposure to PM_{10} , $PM_{2.5}$, and O_3 . Fruit intake and physical exercise were identified as protective factors. Our results on the risk factors are consistent with those of several previous reports. We found that long-term exposure to PM_{10} , $PM_{2.5}$, and O_3 was significantly associated with an increased risk of lung cancer, and the risk appears to be greater in non-smokers than in smokers or the general population. Further, this difference appears to be even greater for people exposed to cooking oil fumes than among those without such an exposure.

In the recent past, extensive research has been conducted in China on the short-term health effects of air pollution^{22,23}. However, studies exploring the long-term effects of air pollution on health, particularly those employing more reliable methods such as cohort studies, have been scarce. Most of the studies conducted thus far are related to mortality²⁴⁻²⁷. In recent years, China has been making continuous improvement in air pollution monitoring system. However, China is a vast country. Therefore, further investigation is necessary to evaluate the exposure characteristics, dose-risk models, and long-term health risks of single or multiple pollutants in different regions.

At present, there is a strong research focus on the relationship between air pollution and lung cancer. Studies^{28,29} have reported that long-term exposure to $PM_{2.5}$, NO_2 , NO_x , and SO_2 is significantly associated with an increased risk of lung cancer. Such associations have been shown to hold true for both smokers and non-smokers as well as men and women, with the impact being the same for all groups. For non-smokers, exposure to outdoor $PM_{2.5}$ is greater for patients with lung cancer and exhibits a linear dose-response relationship³⁰. The results of the ACS CPS-II study³¹ and the European Air Pollution Impact Cohort Study (ESCAPE)^{5,32} have also demonstrated a positive correlation between exposure to outdoor $PM_{2.5}$ and the occurrence of lung cancer. Our results had a wide 95% CI range, which might be attributed to the small sample size in our study, but our results also suggested that PM_{10} and $PM_{2.5}$ were risk factors for lung cancer. Similar to our study, the study by Yang et al.²⁸ also revealed that the association of $PM_{2.5}$ with lung cancer ($RR = 1.18$) was more pronounced in non-smokers than in the general population ($RR = 1.07$). However, because of the limited number of studies included ($n = 3$) and a wide overlap between the general population and people who never were smokers, the controversy still remains regarding whether there is a connection between lung cancer and air pollution. Currently, there is still no report on the effect of exposure to cooking oil fumes on individuals.

Gerard Hoek et al.³³ investigated the risk of lung cancer in the general population associated with exposure to ambient air pollution. They used the population attributable risk fraction (PAF) indicator, which describes the fraction of lung cancer incidence in the general population that can be prevented by eliminating $PM_{2.5}$ exposure. The proportion of the population with lung cancer was found to be between 28.6% and 86.7% when $RR = 1.5$ and the concentration of $PM_{2.5}$ was reduced by 10–60 $\mu g/m^3$. The RR value of ambient air pollution was found to be much smaller than that for active smoking; however, air pollution affects the entire population. Thus, a reduction in the concentration of $PM_{2.5}$ will result in a substantial reduction in the incidence of lung cancer in the overall population.

Study results on the association between long-term exposure to O_3 and lung cancer have been contradictory, with some studies showing a positive^{34,35}, negative^{36,37}, or invalid association³⁸. In our study, the OR value of O_3 was 17.746–125.056 ($P < 0.05$). Since the resulting 95% CI was wide, this could suggest that O_3 may be a risk factor for lung cancer. Recently, N. Rocks et al.³⁹ measured the migration of tumor cells using the Boyden chamber test. They also established a mouse model- and employed an automated tumor recognition software with supervised classification to quantify the spread of lung tumor cells. Their results showed that exposure to O_3 enhanced lung cancer cell proliferation and migration. This was strong evidence for the causative relationship between O_3 exposure and lung cancer.

In our study, we examined only the relationship between lung cancer and air pollution, but not the specific underlying biological mechanisms. Currently, two main explanations have been proposed to explain this relationship. First, exposure to atmospheric pollution can cause oxidative stress, and which may cause

macrophages to release reactive oxygen species (ROS) that can damage DNA, protein, and lipid cells. Additionally, ROS production may be triggered by metals present on the surface of particulate matter through the Fenton reaction or anthraquinones in the redox cycle. Second, exposure to air pollutants may directly or indirectly induce inflammatory effects, which may lead to the generation of chemokines and cytokines, thereby inducing angiogenesis and transforming epithelial cells into malignant and invasive cells, which ultimately invade distal organs^{40,41}

The current study has a few limitations. First, the study was conducted with a hospital case–control design and, therefore, it has flaws that are inherent in the method itself. To overcome this, various control measures, such as selecting cases from multiple hospitals and choosing objective indicators, were employed in this study. However, most of the controls were from Fuzhou, and the difference in the regional distribution of cases and controls may have influenced the results. Second, although the locations of the atmospheric sampling points were established scientifically and were reasonable, the air quality in Fujian Province that was analyzed in this study may not completely reflect the air quality of the entire Fujian Province because of the limited number of sampling points. Third, the levels of SO₂, NO₂, and PM₁₀ were measured since 2005, while those of O₃, CO, and PM_{2.5} were obtained since 2013. The difference in the data collection period for the two set of parameters may have influenced the results. Fourth, the concentrations of the air pollutants measured in the indices of this study were not obtained by individual portable monitoring; therefore, there is a possibility of an estimate bias that resulted in a wider CI. Future research that is based on a greater sample size and forward-looking research design is necessary to provide in-depth insight into these points and strengthen environmental and public health monitoring.

Conclusion

This hospital-based case–control study revealed a few factors that influence the onset of lung cancer, including smoking, passive smoking, exposure to cooking oil fumes, family history of lung cancer, and medical history of lung disease. Increasing fruit intake, physical exercise, and drinking tea were found to be protective against lung cancer. More importantly, long-term exposure to PM₁₀, PM_{2.5}, and O₃ is significantly associated with increased risk of lung cancer, and the risk appears to be greater in non-smokers than in smokers or the general population; moreover, this difference appears to be greater in people exposed to cooking oil fumes than those without.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Fujian Medical University (Fuzhou, China) and all participants signed informed consent forms.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CGM, HF and WJS conceived of the study, and carried out the experiments, participated in the drafted the manuscript. SJ, LZQ, and LJB collected samples. XJF, BL, ZKC and CL participated in the design of the study and helped to review the manuscript. CGM, HF and YHM performed the statistical analysis. All authors read and approved the final manuscript.

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Tables

Table 1 Comparison of demographic characteristics between two groups in different populations

Variables	Total				Smoker				Non-smoker			
	Cases n(%)	Control n(%)		P	Cases n(%)	Control n(%)		P	Cases n(%)	Control n(%)		
Age (years.)	59.34±9.94	58.64±11.26	-1.473	0.141	60.82±9.27	58.90±10.19	-3.030	0.003	57.24±10.47	58.50±11.81	1.746	0.08
Gender			1.379	0.240				0.004	0.948		67.678	<0.0
Male	582(65.8)	772(65.8)			512(98.7)	423(98.6)				70(19.1)	349(44.1)	
Female	303(34.2)	303(34.2)			7(1.3)	6(1.4)				296(80.9)	442(55.9)	
Nationality			0.026	0.873				2.807	0.094		0.670	0.41
Han	863(97.5)	1191(97.6)			505(97.3)	424(98.8)				358(97.8)	767(97.0)	
Others	22(2.5)	29(2.4)			14(2.7)	5(1.2)				8(2.2)	24(3.0)	
Marital status			1.547	0.214				1.025	0.311		0.001	0.97
Married	824(93.1)	1118(91.6)			492(94.8)	400(93.2)				332(90.7)	718(90.8)	
Single	61(6.9)	102(8.4)			27(5.2)	29(6.8)				34(9.3)	73(9.2)	
Educational status			169.749	<0.001				46.084	<0.001		116.641	<0.0
Primary school and below	477(53.9)	360(29.5)			255(49.1)	133(31.0)				222(60.7)	227(28.7)	
Middle school	320(36.2)	505(41.4)			221(42.6)	208(48.5)				99(27.0)	297(37.5)	
College and higher	88(9.9)	355(29.1)			43(8.3)	88(20.5)				45(12.3)	267(33.8)	
Occupation			114.919	<0.001				23.277	<0.001		102.522	<0.0
Agriculture, forestry, animal husbandry and fishery personnel	263(29.7)	180(14.8)			157(30.3)	76(17.7)				106(29.0)	104(13.1)	
Production of transport workers	219(24.7)	268(22.0)			134(25.8)	113(26.3)				85(23.2)	155(19.6)	
Enterprises and institutions personnel	241(27.2)	573(47.0)			159(30.6)	175(40.8)				82(22.4)	398(50.3)	
Business service staff	74(8.4)	116(9.5)			45(8.7)	47(11.0)				29(7.9)	69(8.7)	
Other and unemployed	88(9.9)	83(6.8)			24(4.6)	18(4.2)				64(17.5)	65(8.2)	
BMI			22.331	<0.001				29.042	<0.001		1.926	0.38
18.5-24	547(61.8)	682(55.9)			333(64.2)	231(53.8)				214(58.5)	451(57.0)	
<18.5	68(7.7)	57(4.7)			42(8.1)	14(3.3)				26(7.1)	43(5.4)	
≥24	270(30.5)	481(39.4)			144(27.7)	184(42.9)				126(34.4)	297(37.5)	
Pathological type												
Adenocarcinoma	551(62.3)				253(48.7)					298(81.4)		
Squamous cell carcinoma	208(23.5)				177(34.1)					31(8.5)		
Others	126(14.2)				89(17.1)					37(10.1)		

Table 2 Analysis of risk factors of lung cancer in different populations^a

Variables	Total		Smoker		Non-smoker	
	case/control	aOR (95%CI) ^b	case/control	aOR (95%CI) ^c	case/control	aOR (95%CI) ^d
Family history of lung cancer						
	825/1185	1	490/421	1	335/764	1
	60/35	3.193(2.029-5.025)	29/8	3.601(1.584-8.187)	31/27	3.448(1.901-6.253)
Personal history of lung disease						
	761/1135	1	431/381	1	330/754	1
	124/85	2.547(1.874-3.462)	88/48	1.647(1.105-2.457)	36/37	3.486(2.042-5.951)
Drinking alcohol						
	608/942	1	276/244	1	332/698	1
	277/278	1.568(1.277-1.925)	243/185	1.208(0.924-1.5580)	34/93	1.415(0.879-2.278)
Drinking tea						
	464/596	1	179/147	1	285/449	1
	421/624	1.088(0.905-1.309)	340/282	1.166(0.878-1.548)	81/342	0.588(0.432-0.799)
Drinking						
	366/791	1	-	-	-	-
	519/429	2.489(2.065-3.000)	-	-	-	-
Passive smoking						
	288/598	1	-	-	157/466	1
	597/622	1.933(1.601-2.332)	-	-	209/325	1.632(1.247-2.135)
Detecting smell after renovation						
	789/1080	1	464/369	1	325/711	1
	96/140	1.007(0.754-1.345)	55/60	0.797(0.530-1.198)	41/80	1.153(0.750-1.772)
Cooking oil fume exposure						
	148/324	1	87/110	1	61/214	1
	737/896	1.615(1.287-2.026)	432/319	1.487(1.070-2.067)	305/577	1.521(1.086-2.130)
Physical activity						
	683/683	1	403/259	1	280/424	1
	202/537	0.428(0.350-0.524)	116/170	0.475(0.354-0.638)	86/367	0.437(0.325-0.588)
Caffeine intake						
	mes/week 357/751	1	208/219	1	149/532	1
	mes/week 528/469	2.034(1.690-2.447)	311/210	1.447(1.106-1.893)	217/259	2.574(1.953-3.392)

a Each variable was run independently

b Adjusted for educational status, occupation, BMI

c Adjusted for age, educational status, occupation, BMI

d Adjusted for gender, educational status, occupation

Table 3 Comparison of air pollutant exposure in two groups in different populations^a

Variables (mg/m ³)	Total		Smoker		Non-smoker	
	case/control	aOR (95%CI) ^b	case/control	aOR (95%CI) ^c	case/control	aOR (95%CI) ^d
SO₂						
<0.011	6/12	1	1/6	1	5/6	1
0.011-0.017	617/840	1.466(0.499-4.309)	361/285	5.674(0.640-50.333)	256/555	0.637(0.150-2.704)
0.017-0.023	170/246	1.186(0.397-3.541)	101/90	4.953(0.550-44.602)	69/156	0.503(0.115-2.191)
>0.023	78/106	1.347(0.438-4.141)	46/42	5.288(0.572-48.855)	32/64	0.601(0.131-2.751)
Continuous		<0.001(<0.001-3.315)		-		-
NO₂						
<0.019	310/229	1	127/108	1	102/202	1
0.019-0.029	236/250	1.356(1.028-1.788)	156/88	1.447(0.975-2.147)	97/148	1.241(0.831-1.853)
0.029-0.038	257/443	0.862(0.666-1.115)	143/146	0.804(0.555-1.165)	114/297	0.893(0.617-1.293)
>0.038	139/215	0.889(0.653-1.209)	90/81	0.854(0.559-1.304)	49/134	0.961(0.605-1.529)
Continuous		<0.001(<0.001-1.000)		<0.001(<0.001-0.977)		-
PM₁₀						
<0.051	79/166	1	49/64	1	30/102	1
0.051-0.057	316/287	2.450(1.728-3.474)	181/97	2.571(1.591-4.153)	135/190	2.366(1.395-4.014)
0.057-0.064	438/667	1.637(1.178-2.276)	259/231	1.517(0.974-2.363)	179/436	1.795(1.083-2.975)
>0.064	36/83	0.975(0.575-1.653)	22/31	1.042(0.513-2.116)	14/52	0.946(0.415-2.158)
Continuous		-		-		-
PM_{2.5}						
<0.020	8/132	1	5/19	1	3/113	1
0.020-0.027	397/101	33.658(15.450-73.325)	260/41	24.545(8.112-74.265)	137/60	61.431(18.041-209.181)
0.027-0.035	497/987	5.059(2.390-10.712)	253/369	2.630(0.910-7.595)	226/618	11.814(3.622-38.540)
>0.035	0/0	-	0/0	-	0/0	-
Continuous		0.001(<0.001-877.108)		-		-
CO						
<0.491	0/128	1	0/18	1	0/110	1
0.491-0.681	342/74	-	221/36	-	121/38	-
0.681-0.871	542/1018	-	297/375	-	245/643	-
>0.871	0/0	-	0/0	-	0/0	-
Continuous		0.839(0.481-1.466)		0.042(0.006-0.311)		2.882(1.306-6.360)
O₃						
<0.047	2/129	1	0/18	1	2/111	1
0.047-0.065	367/86	125.056(29.902-523.012)	243/38	-	124/48	95.041(21.772-414.879)
0.065-0.083	479/984	17.746(4.322-72.862)	255/368	-	224/616	17.068(4.084-71.342)
>0.083	36/21	50.896(11.069-234.032)	5/20	-	16/16	37.313(7.301-190.700)
Continuous		-		<0.001(<0.001-0.001)		-

a Each variable was run independently

b Adjusted for educational status, occupation, BMI, family history of lung cancer, medical history of lung disease, drinking alcohol, smoking, passive smoking, exposure to cooking oil fumes, physical exercise, and fruit consumption

c Adjusted for age, educational status, occupation, BMI, family history of lung cancer, and medical history of lung disease, exposure to cooking oil fumes, physical exercise, and fruit intake

d Adjusted for gender, educational status, occupation, family history of lung cancer, medical history of lung disease, passive smoking, exposure to cooking oil fumes, drinking tea, physical exercise, and fruit intake

Table 4 Multivariate logistic regression analysis of lung cancer in total population

Variables	β	S.E	Wald χ^2	P	OR [¶]	95%CI [¶]
Family history of lung cancer	1.399	0.290	23.222	<0.001	4.051	2.293-7.155
Personal history of lung disease	0.878	0.182	23.305	<0.001	2.405	1.684-3.435
Smoking	0.502	0.115	19.099	<0.001	1.653	1.319-2.070
Physical activity	-0.894	0.122	53.364	<0.001	0.409	0.322-0.520
Cooking oil fume exposure	0.396	0.137	8.330	0.004	1.486	1.136-1.945
Passive smoking	0.239	0.117	4.171	0.041	1.270	1.01-1.598
Fruit intake	0.523	0.112	21.913	<0.001	1.686	1.355-2.099
O ₃ (mg/m ³)			25.979	<0.001		
0.047-0.065	3.701	0.884	17.516	<0.001	40.493	7.155-229.155
0.065-0.083	2.749	0.942	8.525	0.004	15.635	2.469-99.007
>0.083	3.083	0.943	10.687	0.001	21.818	3.437-138.515
PM _{2.5} (mg/m ³)			19.510	<0.001		
0.020-0.027	1.575	0.612	6.628	0.010	4.829	1.456-16.015
0.027-0.035	0.398	0.684	0.339	0.560	1.489	0.39-5.688
PM ₁₀ (mg/m ³)			34.179	<0.001		
0.051-0.057	1.064	0.218	23.827	<0.001	2.898	1.891-4.444
0.057-0.064	1.252	0.273	21.111	<0.001	3.499	2.051-5.969
>0.064	0.193	0.300	0.415	0.519	1.213	0.674-2.185
Constant	-4.018	0.785	26.194	<0.001	0.018	

¶Unconditional logistic regression with the backward stepwise method

Table 5 Multivariate logistic regression analysis of lung cancer in smokers

Variables	β	S.E	Wald χ^2	P	OR [¶]	95%CI [¶]
Family history of lung cancer	1.599	0.504	10.063	0.002	4.947	1.842-13.285
Personal history of lung disease	0.585	0.234	6.270	0.012	1.796	1.136-2.84
Physical activity	-0.890	0.178	24.998	<0.001	0.411	0.29-0.582
Fruit intake	0.280	0.161	3.026	0.082	1.323	0.965-1.813
PM _{2.5} (mg/m ³)			137.807	<0.001		
0.020-0.027	3.399	0.580	34.317	<0.001	29.947	9.603-93.392
0.027-0.035	1.016	0.554	3.370	0.066	2.763	0.934-8.175
PM ₁₀ (mg/m ³)			24.844	<0.001		
0.051-0.057	1.285	0.280	21.030	<0.001	3.614	2.087-6.258
0.057-0.064	0.781	0.260	9.018	0.003	2.184	1.312-3.636
>0.064	0.200	0.412	0.235	0.628	1.221	0.545-2.738
Constant	-2.321	0.832	7.782	0.005	0.098	

¶Unconditional logistic regression with the backward stepwise method

Table 6 Multivariate logistic regression analysis of lung cancer in non-smokers

Variables	β	S.E	Wald χ^2	P	OR [¶]	95%CI [¶]
Family history of lung cancer	1.357	0.364	13.878	<0.001	3.885	1.902-7.933
Personal history of lung disease	1.239	0.313	15.667	<0.001	3.451	1.869-6.373
Physical activity	-0.841	0.176	22.935	<0.001	0.431	0.306-0.608
Cooking oil fume exposure	0.506	0.201	6.331	0.012	1.658	1.118-2.458
Fruit intake	0.749	0.161	21.705	<0.001	2.115	1.544-2.899
Drinking tea	-0.512	0.183	7.849	0.005	0.599	0.419-0.857
PM _{2.5} (mg/m ³)			10.692	0.005		
0.020-0.027	2.499	0.891	7.869	0.005	12.173	2.123-69.788
0.027-0.035	1.681	1.002	2.813	0.093	5.372	0.753-38.311
PM ₁₀ (mg/m ³)			14.721	0.002		
0.051-0.057	0.874	0.287	9.262	0.002	2.397	1.365-4.208
0.057-0.064	0.814	0.272	8.976	0.003	2.258	1.325-3.847
>0.064	-0.038	0.438	0.008	0.931	0.963	0.408-2.27
O ₃ (mg/m ³)			12.585	0.006		
0.047-0.065	2.619	1.032	6.443	0.011	13.721	1.816-103.662
0.065-0.083	1.493	1.135	1.731	0.188	4.450	0.481-41.15
>0.083	1.697	1.123	2.283	0.131	5.458	0.604-49.339
Constant	-6.482	0.929	48.680	<0.001	0.002	

¶Unconditional logistic regression with the backward stepwise method

Figures

Figure 1

Map of the monitoring sites in Fujian Province, China Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 2

Annual average of SO₂, NO₂ and PM₁₀ concentrations in 2005-2015 and CO, PM_{2.5}, and O₃ concentrations in 2013-2015 Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

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