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Original Article

Association between psychological factors and lung cancer in a Chinese population: a meta-analysis

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Abstract: This meta-analysis is to investigate the association between psychological factors and lung cancer pathogenesis in a Chinese population. PubMed, EMbase, MEDLINE, Cochrane Library, CNKI, VIP, and WanFangData (from January 2000 to January 2015) were searched for the case-control studies concerning psychological factors and lung cancer in Chinese population. Meta-analysis was performed with the RevMan 5.2 software. Totally 16 studies were included for meta-analysis, with 9500 subjects. Our results from meta-analysis for psychological depression and lung cancer showed that the combined OR value was 1.94 [1.69, 2.23], and the overall effect test indicated Z = 9.39 and $P < 0.00001$, suggesting statistical significance. Moreover, for the meta-analysis of psychological trauma and lung cancer, the combined OR value was 2.36 [1.96, 2.85], and the overall effect test indicated Z = 8.91 and $P < 0.00001$ (statistically significant). Furthermore, meta-analysis of poor interpersonal relations and lung cancer in this population showed that, the combined OR value was 2.32 [1.91, 2.81], and the overall effect test indicated Z = 8.44 and $P < 0.00001$, with statistical significance. In addition, for life stress and lung cancer, the combined OR value was 2.23 [1.88, 2.65], and the overall effect test indicated Z = 9.07 and $P < 0.00001$, suggesting statistical significance. Psychological depression, psychological trauma, poor interpersonal relations, and life stress are associated with increased risk of lung cancer in the studies Chinese population. Psychological factors should be taken into consideration for the prevention and treatment of lung cancer in clinic.

Keywords: Lung cancer, psychological factors, Chinese population, meta-analysis

Introduction

Lung cancer is one of the most common malignant tumors, which is also one of the greatest threats to the survival and health of humanity [1]. Over the past half century, the incidence and mortality of lung cancer have been significantly increasing throughout the world. There are approximately 1.3 million new lung cancer case reports each year, with an increasing rate of 3% [2]. In China, the lung cancer incidence and mortality continues to go up in recent years [3, 4]. Therefore, the risk factors for lung cancer have always been the focus in related epidemiological investigation.

Nowadays, due to the overwhelming social pressure and deteriorating mental health of modern people, the influence of psychological status on the incidence of malignant tumors (including lung cancer), has been attracting increasing attention [5-7]. Psychological status may affect the immune system and endocrine function, thus influencing the body's susceptibility to tumors [8]. It has been shown that, the heavy living and working pressure and increasingly prominent psychological problems of modern people may be important causes for the elevated incidence and mortality of lung cancer [9, 10]. Moreover, the surprisingly elevated incidences of lung cancer in females, youths, and non-smokers have challenged the determination of conventional risk factors for the disease [11]. Therefore, it is of great importance to investigate the role of psychological factors in the pathogenesis and development of lung cancer.

In this meta-analysis, case-control studies concerning the relationship between psychological

Table 1. Characteristics of studies in the meta-analysis

	Year	Gender (male/female)	Patients (n)	Controls (n)	Location
Liu *et al.* [13]	2000	Male, female	350	350	Shanghai, China
Li *et al.* [14]	2000	Male, female	350	350	Beijing, China
Shi *et al.* [15]	2001	Male, female	33	132	Beijing, China
Sun *et al.* [16]	2002	Male, female	218	618	Harbin, Heilongjiang, China
Gu *et al.* [17]	2003	Male, female	170	170	Jiangyan, Taizhou, Jiangsu, China
Lv *et al.* [18]	2003	Male, female	445	445	Guangzhou, Guangdong, China
Yao *et al.* [19]	2003	Male, female	209	209	Wuhan, Hubei, China
Han *et al.* [20]	2005	Male, female	248	243	Xi'an, Shaanxi, China
Fang *et al.* [21]	2006	Female	157	314	Multiple centers
Shi *et al.* [22]	2007	Male, female	173	173	Cixi, Zhejiang, China
Zhang *et al.* [23]	2008	Male, female	505	529	Changzhou, Jiangsu, China
Gu *et al.* [24]	2010	Male, female	251	273	Dafeng, Yancheng, Jiangsu, China
Cui *et al.* [25]	2010	Male, female	106	106	Qingdao, Shandong, China
Song *et al.* [26]	2011	Male, female	404	808	Sichuan, China
Zheng *et al.* [27]	2011	Male, female	306	306	Multiple centers
Pan *et al.* [28]	2014	Female	169	380	Zhejiang, China

factors and lung cancer in Chinese population from 2000 to 2015 have been analyzed. The effects of psychological factors on lung cancer pathogenesis and development have been investigated from the perspective of evidence-based medicine.

Materials and methods

Literature searching

PubMed, EMbase, MEDLINE, Cochrane Library, CNKI, VIP, and WanFangData (all from January 2000 to January 2015) were searched for publications concerning the relationship between psychological factors and lung cancer in Chinese population.

Inclusion criteria

The inclusion criteria for this meta-analysis were as follows: (1) independent case-control studies; (2) studies informing years for investigation or publication; (3) studies with clearly defined sample size; (4) studies providing raw data, as well as the OR and 95% CI, or SE, values; (5) studies in which the psychological factors (exposure factors) in Chinese population were defined as: psychological depression, psychological trauma, poor interpersonal relations, and life stress; (6) studies with definite diagnostic criteria; (7) studies concerning human lung cancer cases; and (8) studies providing the sources for cancer patients and controls.

Quality assessment

Quality assessment was performed according to the criteria from Lichtenstein *et al.* [12]. The duplicate studies, studies of poor quality, and studies with incomplete information were excluded from this meta-analysis.

Statistical analysis

Meta-analysis was performed with the RevMan 5.2 software (Cochrane IMS, Oxford, UK). The χ^2 test and *P*-value analysis were performed to investigate the heterogeneity across studies, and the I^2 values were used to assess the heterogeneity. The fixed-effect model was used for meta-analysis if $P > 0.1$ and $I^2 < 50\%$; on the contrary, the random-effect model was applied. If the analyzed studies were more than 10, the funnel plot was obtained by the RevMan 5.2 software to evaluate the publication bias.

Results

Literature search results

The primary search yielded 110 potentially eligible studies, all published in Chinese. After eliminating the duplicates and non-case-control studies, totally 32 articles met the inclusion

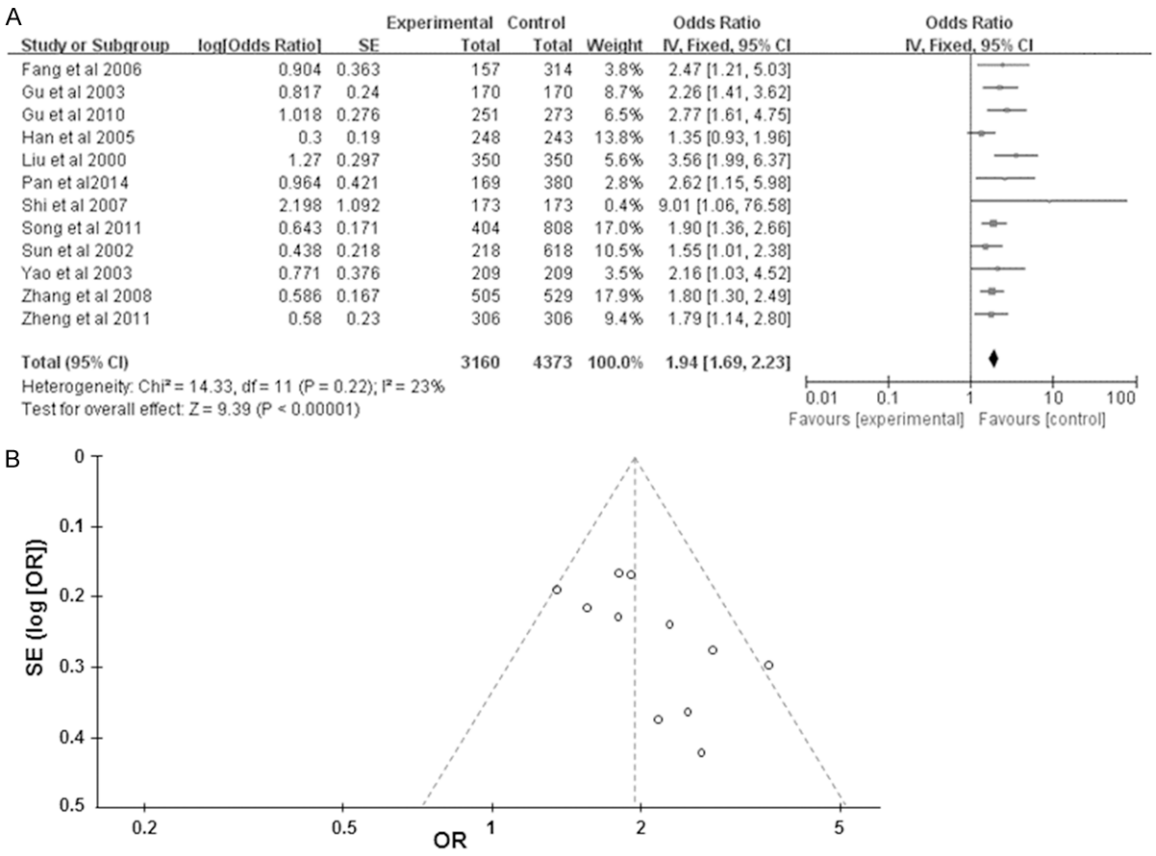

Figure 1. Meta-analysis of psychological depression and lung cancer (A), as well as the funnel plot analysis (B).

criteria. Full-text reading finally confirmed 16 studies for this meta-analysis [13-28], concerning totally 9500 subjects. In these 16 studies, these were 2 multi-center studies [21, 27], 3 studies in which the cases were collected from a certain province in China [20, 26, 28], and 11 studies in which the cases were collected from a certain city [13-19, 22-26]. Moreover, there were 2 studies in which only female cases were included and analyzed [21, 28], while all other 14 studies were concerning both male and female cases. Characteristics of these 16 studies were shown in **Table 1**.

Meta-analysis of psychological depression and lung cancer in Chinese population

Out of these studies, there were 12 concerning the relationship between psychological depression and lung cancer [13, 16, 17, 19-24, 26-28]. The fixed-effect model was used for the meta-analysis according to that $I^2 < 50\%$. The combined OR value was 1.94 [1.69, 2.23], and the overall effect test indicated Z = 9.39 and $P < 0.00001$ (**Figure 1A**), suggesting statistical significance. These results demonstrate that, psychological depression is clearly associated with the pathogenesis of lung cancer in this Chinese population. Because the studies concerning the association between psychological depression and lung cancer were more than 10, the publication bias was evaluated. As shown in **Figure 1B**, the funnel plot appeared symmetric, indicating a small publication bias.

Meta-analysis of psychological trauma and lung cancer in Chinese population

In these 16 studies, there were 8 concerning the relationship between psychological trauma and lung cancer [14-18, 20, 23, 28]. The fixed-effects model was used for the meta-analysis based on that $I^2 < 50\%$. The combined OR value was 2.36 [1.96, 2.85], and the overall effect test indicated Z = 8.91 and $P < 0.00001$ (**Figure 2**), suggesting statistical significance. These results demonstrate that, psychological trauma is clearly associated with the pathogenesis of lung cancer in this Chinese population.

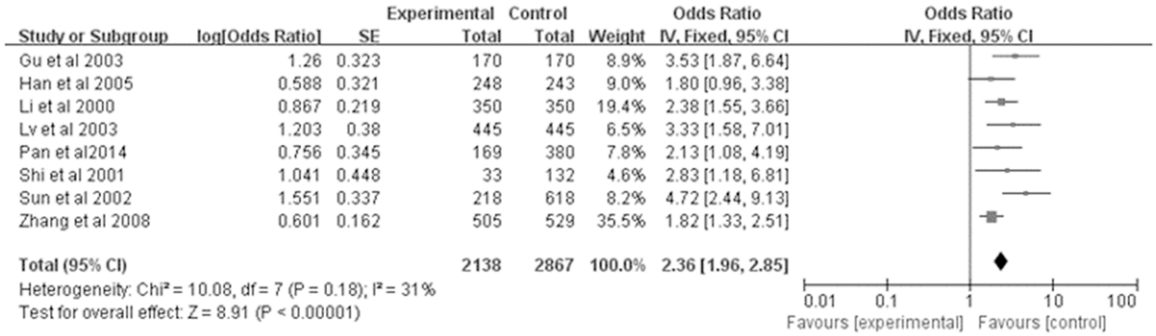

Figure 2. Meta-analysis of psychological trauma and lung cancer.

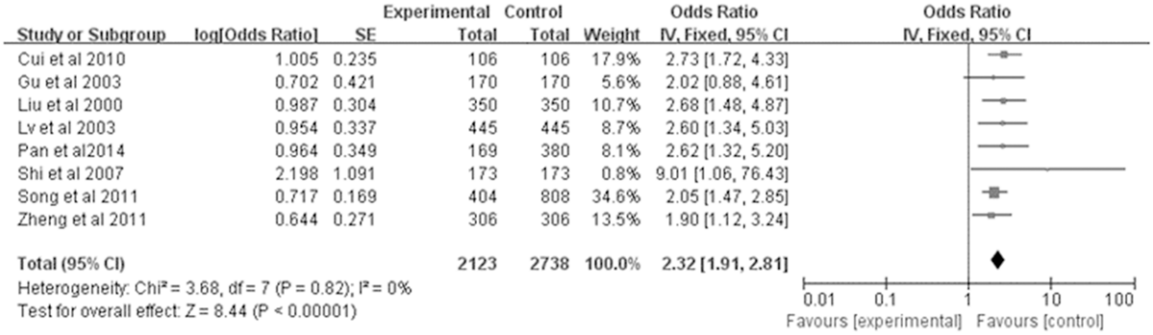

Figure 3. Meta-analysis of poor interpersonal relations and lung cancer.

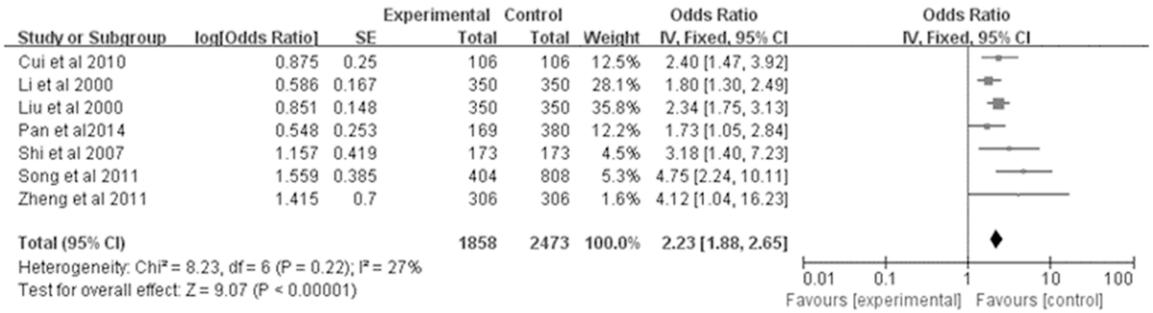

Figure 4. Meta-analysis of life stress and lung cancer.

Meta-analysis of poor interpersonal relations and lung cancer in Chinese population

Out of these 16 studies, 8 concerned the relationship between poor interpersonal relations and lung cancer [13, 17, 18, 22, 25-28]. The fixed-effects model was used for the meta-analysis according to that $I^2 < 50\%$. The combined OR value was 2.32 [1.91, 2.81], and the overall effect test indicated Z = 8.44 and $P < 0.00001$ (**Figure 3**), suggesting statistical significance. These results demonstrate that, the factor of poor interpersonal relations is clearly associated with the pathogenesis of lung cancer in this Chinese population.

Meta-analysis of life stress and lung cancer in Chinese population

In these 16 studies, these were 7 concerning the relationship between life stress and lung cancer [13, 14, 22, 25-28]. The fixed-effects model was used for the meta-analysis based on that $I^2 < 50\%$. The combined OR value was

2.23 [1.88, 2.65], and the overall effect test indicated Z = 9.07 and $P < 0.00001$ (**Figure 4**), suggesting statistical significance. These results demonstrate that, life stress is clearly associated with the pathogenesis of lung cancer in this Chinese population.

Discussion

Roles of psychological factors in the pathogenesis of malignant tumors have been attracting more and more attention in recent years [6]. Recognition of psychological factors associated with the tumor occurrence and development might be of great importance for the disease prevention and treatment [7]. However, no general consensus has been reached on this issue. Several recent studies even suggest that, no such conclusive evidence could be obtained for the effects of psychological factors on the development of tumors [9, 29].

A previous study has shown that, psychological factors are moderately associated with lung cancer, with the population attributable risk of 9.66% [30]. Accordingly, lung cancer cases caused by psychological factors might account for nearly 10% in all the disease cases. In recent years, numerous epidemiological studies have been focusing on the relationship between the psychological factors and lung cancer in Chinese population. In this study, a comprehensive meta-analysis was performed based on the related studies over the past 15 years, and totally 9500 subjects were involved in the combined analysis, concerning psychological depression, psychological trauma, poor interpersonal relations, and life stress. Our results indicated clear association between the psychological factors and lung cancer in this Chinese population. The combined OR values for the relationship between lung cancer and psychological depression, psychological trauma, poor interpersonal relations, as well as life stress were 1.94, 2.36, 2.32, and 2.23, respectively. According to the criteria from Wynder *et al.* [31], there was moderate association between these psychological factors and lung cancer in the studied Chinese population, i.e., psychological factors would increase the risk for lung cancer. Moreover, Song *et al.* [26] have shown that, in the modern society, work stress and sleep quality is closely linked with the human health. The chronic mental alterations might not cause obvious emotional disorders (such as long-term depression or anxiety), but they could significantly increase the risk of lung cancer in these population. Some researchers believe that, long-term mental depression might increase the risk of lung cancer by more than 2 folds, with a significant interaction with smoking [29, 32, 33]. Along with the rapid development of economy and society in China, the increasing competition and challenges people are facing would more and more intensive. The increasing exposure of adverse psychological factors would inevitably become the main risk factor for lung cancer.

There are several hypotheses about the mechanisms through which psychological factors are linked with the tumor pathogenesis [8, 10]. Mental status may affect the immune system and endocrine function, thus influencing the body's susceptibility to tumors. It has been shown that, adverse psychological events such as pressure and stress could induce alterations in the cerebral cortex and hypothalamus, which may directly or indirectly impair the immune system and cause tumor progression [34]. Behavior immunological studies have also shown that, unpleasant or hostile emotions could elevate the secretion of adrenocortical hormone, cortisol, and catecholamine, cause the immune system dysfunction, thus getting involved in the occurrence and development of malignant tumors [35]. Based on these findings, close attention should be paid to the supervision of the population psychological status in the prevention and treatment of lung cancer in modern society.

In conclusion, our results from the meta-analysis showed that, psychological factors (i.e., psychological depression, psychological trauma, poor interpersonal relations, and life stress) were significantly associated with increased risk of lung cancer in the studied Chinese population. According to these findings, psychological factors should be taken into consideration for the prevention and treatment of lung cancer in clinic.

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Disclosure of conflict of interest

None.

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