

# Meta Analysis of the Relationship between Smoking, Drinking and Esophageal Cancer in China

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**Keywords:** Meta analysis; esophageal cancer; smoking; drinking.

**Abstract:** Objective: This paper uses a systematic comprehensive evaluation to analyze and explore the relationship between smoking and drinking and the risk of esophageal cancer in China in recent years. And it provides a scientific theoretical basis for the prevention of esophageal cancer. Methods: This paper is based on the retrieval of three major domestic databases: CNKI database, Wanfang databases and knowledge service platform, and Chinese biomedical literature database. And it obtained all the literature of case-control studies on smoking and drinking and the risk of esophageal cancer published in China from January 2010 to January 2019. It selects the obtained articles through the inclusion and exclusion criteria, and uses the article quality evaluation tool to systematically evaluate and screen them. And this paper also uses Stata12.0 software to analyze the selected articles, such as sensitivity analysis, heterogeneity test, and publication bias and so on. And it also uses the fixed effect model to calculate the combined OR and 95%CI. Results: After a series of screening, a total of 12 articles were included. And the results of Meta analysis showed that there was no statistical heterogeneity among the studies. The calculation using the fixed effect model showed that the smoking OR value was 1.98 (95%CI=1.64~2.33), the drinking OR value was 2.13 (95%CI=1.78~2.48), and the combined OR value of smoking and drinking was 2.06 (95%CI=1.81~2.30). Conclusion: Smoking and drinking can significantly increase the risk of esophageal cancer. Compared with smoking, drinking is a greater risk factor for esophageal cancer.

## 1. Introduction

Esophageal cancer (EC) is a common malignant disease originating from esophageal mucosa. At the same time, as a high-burden disease, it makes patients and their families face great economic and social challenges. The incidence of esophageal cancer is relatively high in the United States and Asian countries such as China and Japan [1,2]. The disease often occurs in the middle-aged and elderly, and our country is in an aging society. Therefore, this study is of great significance to clarify the risk factors of the disease; prevent the occurrence and development of the disease; maintain the quality of life of every family; lighten the family burden and improve the risk resistance of the family [3]. Epidemiological studies have shown that smoking, drinking, obesity, overweight and betel nut chewing increase the risk of EC. Among them, smoking, drinking and their interaction with diet are the biggest factors leading to EC [2,4,5]. Among the two factors of smoking and drinking, which factor has a greater risk of esophageal cancer is controversial. On the one hand, some scholars believe that smoking is the biggest risk factor for esophageal cancer [6]. Another scholar thinks that drinking alcohol is more likely to induce the occurrence of esophageal cancer [7]. In the face of this problem, this study follows the principle of evidence-based medicine, and uses the method of Meta analysis to systematically evaluate and analyze the current domestic articles. And this method is used to determine the risk of esophageal cancer increased by smoking and drinking, and provide a decision-making basis for the prevention of the disease.

## **2. Materials and methods**

### **2.1. The Strategy of Article Retrieval**

By searching the three major Chinese databases including CBM, CNKI and China Wanfang database, we obtained some articles on the relationship between smoking, alcohol consumption and esophageal cancer. The key is "esophageal cancer OR esophageal malignant tumor OR esophageal cancer OR esophageal malignant tumor" AND "smoking, drinking"; The time for publication of the articles is limited to January 1, 2010 to January 1, 2019; the articles are limited to Chinese; In order to eliminate the bias caused by ethnic, religious, regional, and other differences, the object of the study is the Chinese.

### **2.2. Inclusion criteria and exclusion criteria of articles**

Inclusion criteria of articles :(1) The subjects were adults aged 18 or above. (2) The patients in the study group were esophageal cancer patients and the control group were non-esophageal cancer patients. (3) The definite diagnosis of esophageal cancer was made in this paper. (4) Smoking and drinking are among the risk exposure factors. (5) The OR value and 95%CI of smoking and drinking provided in the articles.

Exclusion criteria :(1) The research object of this paper is animals. (2) The patient was not diagnosed according to esophagoscopy or pathological examination. (3) Literature not grouped according to esophageal cancer patients and non-tumor patients. (4) Review articles.

### **2.3. Quality evaluation and information extraction of articles**

According to the JadadAR[8] quality score method, the quality of each article was evaluated in the following aspects: (1) the original article must be a case-control experiment; (2) whether the design of the study was reasonable; (3) whether the demographic data included in the case group and the control group in each experiment were comparable; (4) whether the measurement methods of exposure factors and results in the case group and the control group were comparable. We Carried on the literature information extraction to the high-quality articles after the evaluation. Each article is independently extracted and evaluated by two evaluators. When we disagree, we solve it through discussion. There are 6 items to extract the information of the article, namely, the first author, the year of publication, the study area, the control source, the OR value of smoking and the 95% confidence interval (CI), the drinking OR value and the 95% confidence interval (CI). We eliminate the articles that can not be used, such as poor quality, insufficient reporting information and statistical indicators that do not meet the requirements.

### **2.4. Statistical methods**

We used Stata12.0 software for Meta analysis and tested the heterogeneity of the included studies. If the research results are heterogeneous, we use the corrected random effect model to calculate the OR value and 95%CI; if the research results are not heterogeneity, we use the fixed effect model to calculate the combined OR value and its CI. if there is no heterogeneity of the research results, we use the fixed effect model to calculate the combined OR value and 95% CI. And we have drawn the analytical forest map of Meta. We also use Begg and Egger methods to objectively evaluate publication bias.

## **3. Results**

### **3.1. The screening results of the article**

We finally determined the retrieval form through repeated retrieval. The search formula retrieved 56, 95, and 146 documents in CBM, CNKI, and China Wanfang databases, respectively. A total of 297 articles were retrieved. According to the screening criteria of literature inclusion and exclusion, 12 articles were finally obtained. Among them, 100 duplicate articles were excluded; 8 review articles were excluded; 145 articles with irrelevant contents were excluded; 29 articles with no full

text or unreported OR values or 95% CI were excluded; non-case-control studies and non-cross-sectional studies were excluded 3 articles; a total of 285 articles were excluded.

### **3.2. Meta analysis of the relationship between smoking, drinking and esophageal cancer**

We conducted a heterogeneity test on the extracted 12 article information, and the result was  $I^2=21.3\%$ ,  $P=0.173$ . This shows that there is no heterogeneity among the various studies, so we adopted a fixed-effect model for article merging. The combined results show that the risk of esophageal cancer will increase after exposure to smoking, its OR value is 1.98, 95% CI = 1.64 ~ 2.33; after exposure to alcohol, the risk of esophageal cancer increases, and its OR value is 2.13, 95% CI = 1.78 ~ 2.48; after co-exposure to smoking and drinking, the risk of esophageal cancer will increase, with an OR value of 2.06, 95% CI = 1.81 ~ 2.30.

### **3.3. Publish a biased evaluation**

We evaluated the possible publication bias in 12 articles by funnel chart, Begg rank correlation method and Egger regression method. The results show that the funnel chart shows an asymmetrical figure, and the  $P > |z|$  index in Begg rank correlation method is 0.012, which indicates that there is an obvious bias in this study. Coef 2.236562 in the Egger test table is the intercept of regression analysis, and 0.8645476 and 3.608576 are 95% confidence intervals of this intercept. The slope is 0.358649, of which 95% confidence zones are -0.0119392 and 0.7292372. The  $P > |t|$  index of Egger regression method is 0.003, which indicates that there is obvious bias in this study. The results of the three test methods show that the literature included in this study has obvious publication bias, but the bias is small.

### **3.4. Sensitivity analysis**

In order to ensure the stability of the conclusion, we conducted a sensitivity analysis of the relationship between smoking, alcohol consumption and the risk of esophageal cancer. The results of sensitivity analysis between smoking and drinking and the risk of esophageal cancer showed that the results were within the upper and lower limits of the confidence interval. It shows that there are no articles in these 12 articles that have a negative impact on the results of the study.

## **4. Discussion**

Through a meta-analysis of the information extracted from 12 strictly screened articles, the analysis results indicate that the risk of esophageal cancer increases after exposure to smoking, with an OR value of 1.98, 95% CI=1.64~2.33; the risk of esophageal cancer After exposure to alcohol, the OR value was 2.13, 95% CI = 1.78 to 2.48; the risk of esophageal cancer increased after co-exposure to smoking and alcohol, the OR value was 2.06, 95% CI =1.81~2.30. Through the analysis of publication bias of funnel chart, Begg rank correlation method and Egger regression method, we can see that there are some publication biases among 12 articles, but their values are small. The results show that publication bias has little effect on the results of this Meta analysis, and articles with positive results may be easier to publish than articles with negative results. But not necessarily without negative results. And this difference, namely publication bias, may eventually affect the results of Meta analysis. And sensitivity analysis showed that there was no literature that had a negative impact on the results of the study in the 12 articles included. In short, based on the results of this Meta analysis, smoking and drinking can significantly increase the risk of esophageal cancer, and drinking is a higher risk factor for esophageal cancer than smoking.

Drinking is a major risk factor for esophageal cancer. There is not only a dose-response relationship between alcohol consumption and esophageal cancer, but also a genetic polymorphism in the population [4,9,10]. Studies have shown that there is a dose-response relationship between alcohol consumption and the occurrence of esophageal cancer, and the risk of esophageal cancer increases linearly with the increase of drinking times [11].The gene polymorphism in the population also has a certain influence on the process of esophageal cancer induced by drinking. Acetaldehyde

dehydrogenase plays an important role in predicting the multiple occurrence and development of esophageal cancer [12]. In addition, it is amazing that gender factors are controversial in the analysis of the relationship between alcohol consumption and esophageal cancer. An epidemiological study conducted in China shows that alcohol consumption is associated with the risk of esophageal cancer in Chinese men, but not with Chinese women [13]. However, there is still literature that heavy drinking can also induce the occurrence of esophageal cancer in women [14]. It can be used as a research point that needs to be paid attention to in the next step in the epidemiological study of alcohol consumption and esophageal cancer.

There are still some shortcomings in this study: (1) the data of this paper are all from the published literature of domestic major databases, and the unpublished relevant data cannot be obtained, which may cause some errors; (2) because the literature is restricted by objective factors, it may affect the conclusions of this study to a certain extent. (3) the 12 articles included in this analysis are all case-control studies, so the effects of selective bias and information bias on the conclusions can not be completely excluded. However, sensitivity analysis shows that the existence of publication bias and heterogeneity in this Meta analysis has little impact on the results, so the conclusion of this paper is reliable.

To sum up, the incidence of esophageal cancer is still at a very high level. This study confirmed that smoking and drinking are the main risk factors for esophageal cancer in China, among which drinking is more closely related to esophageal cancer. The results of this study have a certain reference value for the epidemiological study of esophageal cancer, which is helpful to grasp the pathogenesis of esophageal cancer. The significance of prevention of esophageal cancer is far greater than that of treatment. Therefore, Chinese residents should develop good living habits; carry out physical exercise properly, strengthen health education and advocate a healthy lifestyle; so as to reduce the risk of cancer.

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