

Research Progress on Pathogenesis of Lung Cancer and Prevention Discussion

Xiaofan Wang*

Tianjin Wutong High School, Tianjin, China

*Corresponding author: cychao@cauc.edu.cn

Abstract. Lung cancer is one of the most common malignant tumors, it has brought a great threat to human health. In recent years, the mortality and incidence of lung cancer have ranked first among cancers, the characteristics of lung cancer, such as being difficultly diagnosed in the earlier stage; rapidly developing condition, difficult treatment, and high rate of morbidity, which has taken harm to people's normal living quality, Lung cancer is related to internal factor-human body, and external factor-environment and human factors. In this paper, smoking, diet and nutrition, regional distribution, indoor and outdoor air pollution, gender, occupational exposure, lung-related medical history, genetics, gene mutation and other factors related to the occurrence of lung cancer are reviewed in the latest domestic research. The prevention actions to be done by individuals like changing lifestyle, sufficient physical exercises, emotional control, physical examination in certain periods, and sleeping improvement are reviewed; The prevention actions to be done by the government like improving environment, carbon emission control, and air pollution improvement are discussed. Both individuals and society should pay attention to these preventative actions, and make sure these actions are followed up and reached, so the serious impact from lung cancer can be greatly reduced. People's normal living quality can be greatly improved.

Keywords: Lung cancer, risk factors, prevention measures.

1. Introduction

Recently, it has been reported that Lung cancer as common malignant tumors is becoming more and more prevalent now than in the past, and its morbidity and mortality have risen to the top of the common diseases found in society till now. Lung cancer is categorized into two types: small cell lung cancer and non-small cell lung cancer, the mobility rate of small cell lung cancer is much higher than non-small cell lung cancer; without any positive intervention or treatment, the average survival period of patients who got small cell lung cancer is just around 2 to 4 months. In China, It is predicted that by 2025, there will be more than one million patients diagnosed with lung cancer, and China will become the world's largest country with lung cancer [1-2]. Lung cancer has a serious impact to human health, it will cause great damage to the patients' physical and mental health, and even more, their normal life is severely disrupted. With the acceleration of modernization, people's material living standards continue to improve, and their lifestyles gradually become diversified and personalized. However, the number of persons who have lung cancer is increasing [3]. The factors of population aging, air pollution, urbanization, etc. may cause an increasing incidence rate of lung cancer. Ranking the worst prognosis of malignant tumors in the same period, lung cancer is becoming the main reason that causes people to die [4]. Epidemiological investigations and studies have shown that the occurrence and development of lung cancer are the combined consequence of the interaction of genetics, environment and individual [5-7]. In this paper, the environmental factors and individual factors of lung cancer are reviewed, and the research progress of the prevention of lung cancer is discussed. Lung cancer is related to environmental pollution, air quality, working environment and occupational exposure. Individual underlying diseases, especially chronic lung diseases, affect the patients' immunity. For individuals, smoking is the biggest risk factor that causes lung cancer, diet nutrition and poor lifestyle are intimately connected to lung cancer occurrence. In addition, among the gender factors, the proportion of men and females with the disease is changing subtly, this change is related to the smoking cessation of men, and female's physiological mechanisms, passive smoking and the housework distribution between men and females. Lung cancer may be a disease with a

combination of internal and external factors. Under the action of precipitating factors, malignant transformation of human cells and irreversible gene change are triggered. Gene mutation weakens the anticancer function of the human body, and both personal and environmental factors are the causes of gene change. The prevention of lung cancer includes positive changes in personal life and eating habits, maintaining emotional stability, taking appropriate physical exercise, and creating a healthy living environment. The purpose of this paper is to study the internal and external causes of lung cancer, to provide the instructive guidance for the preventing action of lung cancer, and to explore the effective action guidelines of preventing action of lung cancer. This article is divided into three parts: the classification of lung cancer, the lung cancer risk factors, and prevention measures to be taken.

2. The classification of lung cancer

According to histological differences, people classified lung cancer into two categories: small-cell lung cancer (SCLC), and non-small cell lung cancer (NSCLC) [2]. Inside them, NSCLC makes up roughly 85% of lung cancers and can be subdivided into 3 types: large cell carcinomas, adenocarcinomas and squamous cell carcinomas. Among these types, Adenocarcinoma is an extremely common lung cancer, It often starts in peripheral lung tissue; the second is squamous cell carcinoma, most of which originated in the tracheal area, with common cavities and apoptosis in tumors. The incidence of large cell carcinoma is relatively low, is a kind of undifferentiated cancer, the cell is larger, so it is also called large cell undifferentiated cancer. SCLC, also known as "oat cell carcinoma," makes up about 15 percent of lung cancers. Histopathologically, SCLC is characterized by small cell size, little cytoplasm, micro granular nuclear chromatin, insignificant or absent nucleolus, and nuclear division and Nuclear atypia are common and so on. SCLC is the most lethal subtype of lung cancer due to its rapid growth, high degree of malignancy, strong invasiveness and easy-to-develop tolerance to radiotherapy and chemotherapy, etc. Without treatment, the average survival of patients with SCLC is only 2 to 4 months.

3. Risk factors for lung cancer

3.1. Lifestyle

3.1.1 Smoking

WHO reports that smoking is the key reason that causes lung cancer. If we compare them with non-smokers, smokers are 22 times more likely to the risk of getting lung cancer [3]. Even with changes in cumulative annual smoking, smokers who inhaled cigarette smoke were nearly twice as likely to develop lung cancer, the result is based on the comparison between those persons who did inhale cigarette smoke and persons who did not inhale cigarette smoke.

3.1.2 Nutrition and diet

Postprandial blood glucose and insulin response are considered to be the main factors in carcinogenesis. The risk of lung cancer is closely related to Glycemic index and glycemic load [3]. Therefore, having diabetes and/or elevated HBA1c is connected to an increasing risk of getting lung cancer. Additionally, people's regular consumption of pickled food will cause a high risk of getting lung cancer, the reason might be that nitrite in pickled food reacts with amino acids and low amines, forming nitrosamines and nitrosamines carcinogens.

3.2. Regional distribution and change

According to the regional study on new cases of lung cancer all over the world from 1990 to 2020, lung cancer incidence is related to the socioeconomic level of a region, and the incidence of lung cancer is higher in the regions with a high socio-demographic index (SDI)[4].

3.3. Air Pollution

Air pollution usually refers to the phenomenon of some harmful substances that enter the air in large quantities due to human life and production activities or some natural processes, reach a certain concentration and accumulate enough time, and cause harm to the survival of human beings or other organisms.

3.3.1 Indoor factors

Indoor air pollutants in the house include VOCs from building materials, formaldehyde which is released from furniture, nitrogen oxides from gas installations, and gases from coal and other solid fuels used for cooking or heating in unventilated rooms, etc. For non-smokers, passive smoking can result in lung cancer. The lung cancer risk resulting from environmental tobacco pollution should not be underestimated. Non-smokers who are exposed to secondhand smoke at home or in the workplace have a 30% greater risk of getting lung cancer [5]. The relationship between third-hand smoke exposure and lung cancer is a relatively new research direction related to environmental tobacco pollution in recent years [3]. People who take frequent public transport or often go to saunas, bars and Internet cafes are more likely to be exposed to third-hand smoke, as are those who have experienced adverse events such as divorce or bereavement, have low education levels and have smokers in their homes. Third-hand smoke contains a variety of toxic substances such as PM_{2.5}, acrolein, furan, acrylonitrile and 1, 3-butadiene, which can pose a variety of hazards to the human body.

3.3.2 Outdoor factors

According to PM_{2.5} in air pollution based on cohort studies Meta-analysis of the association with lung cancer suggests that every 10 μ g /m³ increase in air pollution exposure to PM_{2.5} may elevate lung cancer risk[6]. At present, the more clear carcinogens in the air are: Fine particulate matter (PM), silicon dioxide (SiO₂), nitrogen oxides (NO_x) and polycyclic aromatic hydrocarbons (PAHs), the pollutants that affect AQI include sulfur dioxide, nitrogen dioxide, nitric oxide, ozone, PM_{2.5} and PM₁₀. Among them, the increase in PM will increase the possibility of getting lung cancer. This may be related to the long-term exposure of the body to a polluted environment, which causes nuclear factor-kappa B (NF- κ B) inflammatory response, resulting in cellular oxidative damage [7].

3.4. Gender Factors

Wang proposed that although the new cases of lung cancer reported continues to increase, the overall world-standard incidence remains stable. Between 1990 and 2019, the difference in incidence between males and females is narrowing, with the incidence of lung cancer increasing by 22.3% in females and decreasing by 12.5% in males [4]. Tobacco control is a key action for the decline in lung cancer rates among males. Exposure to cooking fumes, the effects of second-hand and third-hand smoke, and the effect of female estrogen may all contribute to the increased lung cancer incidence rate among females.

3.5. Occupational Exposure

In the occupational environment, people with long-term occupational exposure risks, such as exposure to uranium, radium and other radioactive substances, and/or exposure to asbestos, radon, arsenic and their compounds, will significantly increase the likelihood of lung cancer [4].

3.6. Respiratory diseases

A variety of respiratory diseases are connected to the occurrence and development of lung cancer. For example, chronic obstructive pulmonary disease (COPD), in particular, has been considered as one of the main risk factors. In addition, COPD plays a mediating role between smoking, passive smoking, biomass burning, and lung cancer.

3.7. Genetic Factors

Genetic sensitivity is related to the phenomenon of family clusters of cancer in non-smoking lung cancer patients, for individuals who have a lung cancer family history or any other cancer (especially if the mother got lung cancer) the risk of lung cancer may be much higher, genetic sensitivity may be closely connected to lung cancer [3].

3.8. Genes

3.8.1 Gene mutation

3.8.1.1 Mutation of P53 gene

P₅₃ is the most common genetic change known in hu cancer. The normal wild-type P₅₃ is a tumor suppressor gene, and the nucleophosphorin encoded by P₅₃ can bind to the large T antigen of the SV40 virus into an oligomeric complex, which is a protein that maintains the malignant transformation of cultured cells. Normal P₅₃ negatively regulates cell growth and division, while mutated P₅₃ can stimulate cell division and contribute to cell growth and proliferation [8].

3.8.1.2 K-ras gene mutation

The K-ras gene, also known as K-RAS-Z, is one of three 103 genes (K-ras, N-ras, H-ras) that encode proteins consisting of 188 or 189 amino acids. ras proteins normally bind to guanine nucleotides to form guanosine 2 or 3 phosphate. Guanosine triphosphate is active and plays an important role in signal transduction, thereby regulating cell proliferation. Ras protein mutations associated with carcinogenesis are amino acids at positions 12, 13, or 61 [9-10]. Lung cancer caused by smoking, non-smoking and radon has different forms of K-ras mutation.

3.8.2 VEGF

Angiogenesis is an essential condition for tumor growth and metastasis, it is associated to the occurrence, development and metastasis of tumors. VEGF is the strongest known pro-angiogenic factor, which can stimulate the proliferation of tumor neovascularization endothelial cells, promote the increase of microvascular permeability, and induce blood vessel formation. VEGF gene has single nucleotide polymorphisms, and some SNPS of it may increase the expression of the VEGF gene, which is related to the susceptibility of certain tumors. Wang Tao conducted a controlled study on 300 lung cancer patients, and the conclusion showed that the VEGF-2578A allele could significantly increase the risk of getting lung cancer, and it was related to the pathological types of lung cancer [11].

3.8.3 Other genes

Other genes, such as CYP2C19 slow metabolism genotype, glutathione S-transferase M1, GSTM1 gene deletion, abnormal expression of p16 and FHIT genes, decreased expression of RGS16 gene, low or high level of serum MBL, etc., may have adverse effects on the body, and cause different degrees of impact on the occurrence of lung cancer [12-16]. Anxiety and depression are significantly related to the lung cancer incidence rate, indicating that they are partly responsible for the formation of lung cancer [17].

4. Prevention of lung cancer

4.1. Lifestyle

4.1.1 Reasonable diet

It is advisable to increase the intake of foods such as fruits, vegetables, fish, nuts, soybeans and other foods that have protective effects on lung parenchyma. A diet rich in vitamins and trace elements including B vitamins, vitamin D, vitamin E, vitamin C and zinc also has great help in the prevention of lung cancer. In addition, eating more garlic foods can reduce the risk of lung cancer,

because garlic foods can reduce the synthesis of carcinogens such as nitrosamines, and garlic foods are rich in trace elements such as selenium and germanium, which is conducive to inhibiting the growth of cancer cells.

4.1.2 Reduce tobacco exposure

Smoking cessation can not only reduce the harm of nicotine to individuals but also reduce the impact of exposure to second-hand smoke and third-hand smoke in the surrounding population. Reducing exposure to second-hand smoke is of great significance for the prevention and treatment of lung cancer in smokers and non-smokers.

4.1.3 Sleep factors

Sufficient sleep can restore the normal physiological function of tired nerve cells while making the mental and physical recovery, therefore, sleep is necessary to health, it plays an essential role of the body recovery, integration and consolidation of memory, it is an indispensable part of health. Sleep not only has the function of maintaining individual survival but also promotes growth and development. Adequate sleep also inhibits the development of lung cancer.

4.1.4 Physical activity

Physical activity includes occupational physical activity, traffic-related activities on the way to and from work, physical exercise activities in leisure time and housework in daily life, climbing stairs, going out shopping, etc. Physical activity reduces the risk of lung cancer. Increased levels of physical activity can increase lung ventilation and perfusion, reduce the concentration, deposition and duration of action of lung carcinogens, and may also improve immune surveillance by enhancing the body's immune function.

4.2. Improving the Environment

Change cooking methods, use healthy and green materials for decoration, strengthen indoor air quality testing (especially radon concentration), and maintain indoor ventilation to improve indoor air quality. In addition, protective measures should also be taken against occupational exposure, therefore the risk of getting lung cancer can be reduced. Advocate low-carbon green travel, implement garbage sorting, control and manage industrial waste gas and waste emissions, and reduce PM2.5 emissions.

4.3. Health Monitoring

Maintain emotional stability, keep smiling, avoid and reduce anxiety and depression, and reduce the impact of negative emotions on the body. Disease lies in prevention, and prevention is better than cure. Therefore, regular physical examination and timely standardized treatment of patients with respiratory diseases can promote the improvement of lung diseases to a certain extent, thus reducing the formation of lung cancer.

5. Conclusion

To sum up, lung cancer is a serious threat to human health. With the progress and development of modern society, timely updating and exploring the related risk factors of lung cancer is of great significance for the prevention and control of the occurrence and development of lung cancer. Smoking and environmental tobacco exposure (such as second-hand smoke, third-hand smoke, etc.) are relatively clear risk factors for lung cancer. Diet and nutrition, indoor and outdoor air pollution, occupational exposure, lung-related medical history, genetics, etc. are all correlated with the occurrence of lung cancer, although to different degrees. But its exact pathogenesis remains to be further explored. Gender factors and the occurrence of female lung cancer have an increasing trend. Preventing diseases is more important than treating them. In addition to personal smoking cessation, improving eating habits, reducing tobacco exposure, improving sleep and mood, increasing

appropriate scientific physical exercise, and conducting frequent physical checking, advocating low-carbon green travel for human beings, implementing garbage classification, controlling and managing industrial waste gas and waste emissions, and reducing PM_{2.5} emissions. All of these have obvious effects on the prevention of lung cancer. The lung cancer incidence rate is the result of the joint effort of multiple factors, and it is still necessary to conduct more in-depth joint research and exploration in combination with multiple disciplines such as immunology, genetics, genomics, molecular science and epidemiology, so as to provide more accurate and clear scientific guidance and opinions for the prevention of lung cancer.

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