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Review

Lung Cancer Risk factors - A Review Article

Cagnur Elpen Kodaz

Family Medicine, Cifteler State Hospital, Eskisehir, Türkiye

Abstract

Lung cancer is the most frequent cancer type with high mortality and morbidity rate worldwide. Studies have shown that smoking, environmental factors including occupational exposure, radon exposure, air pollution, radiation, onesity, diet and hereditary susceptibiliy are related to developing risk of LC. By raising public awareness, the incidence of LC can be diminished by preventing modifiable etiological causes of LC, such as effective and practical public health policies and legal regulations restricting tobacco use, studies and regulations to reduce air pollution, and anti-smoking education for all age groups.

Keywords: Lung cancer, risk factors, review

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Lung Cancer (LC) is the most important reason of cancer-related deaths worldwide, as it is often asymptomatic at the onset of disease and generally discovered at advanced stages.[1] LC is mainly divided into two large groups according to histological subtype as follows; small-cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). NSCLC comprises of 85% of all LC cases. Histological subtypes of NSCLC include squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. Among these subtypes, adenocarcinoma is the predominant subtype.[2] LC screening via Low-dose Computed Tomography (LDCT) has been found to effective in decreasing mortality, hence the application of this practice is gradually increasing.[1] One of the most important reasons of poor survival rate for LC is due in large part to the delayed diagnosis and advanced stage at the time of diagnosis. Providing an effective early diagnosis, itemized pathogenesis, and appropriate treatment and drug selection at the appropriate stage will be helpful in the optimal treatment of LC. Therefore, diagnosis of LC cancer at the earliest stage is highly vital, particularly in high-risk groups where the identification of new biomarkers are urgently needed.[3]

Epidemiology

Today, Lung Cancer (LC) is the most frequently diagnosed cancer, comprising of 11.6% of all diagnoses related to cancer diseases and also the prominent reason of deaths associated with cancers in both genders in all over the world, with mortality rate of 18.4 among all cancer types.[4] In USA, the estimated number of new LC cases in 2022 is 236,740, with 130,180 expected deaths from the same disease.[5] Although the risk of LC increases with age, it is relatively rare before the 5th decade.[6] Historically, incidence rates of LC according to the gender have been found to be greater in men than in women; however, this difference has decreased lately, with a shift towards an increase in the incidence rate in women.[7] In the last few decades, the incidence of adenocarcinoma subtype has increased more rapidly compared to squamous cell subtype in both genders, particularly in women. According to World Health Organization (WHO), lung adenocarcinoma has become the most frequent histologic subtype since 2004. This shift towards an increase in lung adenocarcinoma may be related to the change of historic pattern of tobacco use. Gender diversity in LC mor-

Address for correspondence: Cagnur Elpen, MD. Family Medicine, Cifteler State Hospital, Eskisehir, Türkiye
Phone: +90 507 236 22 13 **E-mail:** cagnur_elpen@hotmail.com

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tality model demonstrates the historical differences in the amount of tobacco smoking in the past 50 years between men and women.[8]

Risk factors

Tobacco

Smoking has widely been known as the most important cause of LC worldwide and its increasing prevalence has been shown to be a result of widespread smoking addiction. Every year, smoking leads to approximately 80% of new LC cases in men and 50% in women worldwide.[8] Many evidences, such as dose-response relation and biological causation, heavily endorse the presence of a causal relationship between smoking and LC risk.[9] Since the 1950s, tobacco was shown to be harmful on lung tissue in many epidemiological studies, hence its carcinogenic properties became known by public health thereafter.[10] The extreme risk in permanent smokers is 20 to 50 times greater than in never-smokers and smoking duration in smokers is one of the most important predictor of LC risk.[11] Thus, in order to decrease the LC risk, some effective measures should be taken, such as anti-smoking campaigns which may help teenagers or any person at any age quit smoking.[12] A study showed that filtered cigarettes could reduce the tar absorption while augmenting nitrosamine intake, proposing that as an crucial factor leading to a pathological shift from squamous cell carcinoma to adenocarcinoma.[13]

Asbestos

Asbestos, one of the most well-known occupational reasons of LC, is a kind of strength and fire-retardant natural fibrous mineral which is widely used for commercial purposes such as in construction after the late 1800s. It consists of 2 main fiber types as follows; serpentine and amphibole. In addition to being a cause of LC, inhaling asbestos fibers can also lead to other important pulmonary diseases, including interstitial lung disease known as asbestosis and pleural disease which commonly presents with pleural effusion. Even though amphibole is more fibrogenic compared to chrysotile, both can result in interstitial lung disease.[14]

Radon

Radon-an inert, tasteless and colorless radioactive gas-is generated from radium and emits alpha particle which has a high energy, resulting in a damage in cell DNA of the respiratory epithelium. It constitutes about %50 of the radiation in the environment to which living things are exposed during their lifetime. After smoking, radon is known the second most frequent reason of LC, leading to approximately 20,000 radon-associated deaths each year in the US.[15, 16] Smoking and radon have synergistic effects in increasing LC risk.[17]

Domestic biomass fuels

About half of the population in the world, particularly in southern Asia, utilize unprocessed biomass fuels such as wood, coal and crop residues for cooking and heating in their homes. Many carcinogenic compounds including polycyclic aromatic hydrocarbons and benzene are found in households as a result of indoor emissions.[18] Some studies showed an elevated LC risk related to biomass fuels. Moreover, a pooled analysis of coal users in Asia demonstrated 4.93-fold increased risk of LC (95% CI: 3.73–6.52), as compared with nonsolid-fuel users.[19]

Air Pollution

Air pollution, as a result of long-term release of smoke due to automobiles and factories is a well-known remarkable risk factor for LC.[20] Ecologic studies revealed that more than half of the LC cases occur in urban areas. This is more likely due to the increased air pollution caused by large amount of smoke from industrial sources and vehicles in urban areas, as compared with rural areas. Some case-control and cohort studies showed significant relation between LC and air pollution.[21, 22]

Diet and Nutrition

It is well-known fact that there are mutagenic substances in human diet as well as antimutagenic ingredient. In Western countries, processed foods that have great amount of fat and sodium are consumed, hence promoting a unhealthy body condition, being responsible for one-third of cancer-related deaths in this population.[23] Diet has been thought to be a cause in about 30% of all cancer types.[24] Fruit and vegetable consumption has been linked to a decrease in the risk of developing LC in current smokers. Likewise, cruciferous vegetables have been found to be inversely associated with LC risk.[25, 26] Some specific micronutrients such as retinol and beta-carotene have long been suggested to have anticarcinogenic activity.[27] The effects of vitamin intake and serum vitamin levels on LC risk have been evaluated in many studies. Calcium intake in female nonsmokers and current smokers was shown to decrease LC risk.[28]

Radiation

Studies evaluating the effects of high-dose radiation on populations who are exposed to ionizing radiation showed LC as one of the commonest cancer type associated with ionizing radiation. According to rate of energy transfer, there are two types of radiation associated with LC as follows; Low linear energy transfer (LET) radiation (e.g., x-rays) and high-LET radiation (e.g., neutrons). Even in an equivalent dose, high-LET radiation may cause grater tissue damage than low-LET radiation because High-LET radiation generates ionization with higher density.[17]

Genetic factors

Many studies reveal more than %80 of LC cases is caused by smoking or other environmental factors. On the other hand, less than 20% of LC cases are thought to be associated with genetic predisposition.[29] Studies are limited regarding the genetic factors causing increased predisposition to LC. After adjusting for cigarette smoking, there is an increased LC risk in first-degree relatives of LC patients.[30]

Conclusion

Despite new advances in medicine, LC is still the most common tumor type that has a high mortality and morbidity rate worldwide. Many studies have shown that smoking, environmental factors including radon exposure, air pollution, ionizing radiation, diet, and to some extent, hereditary predisposition are associated with an increased LC incidence. In the light of these findings, by raising public awareness, the incidence of LC can be reduced by at least preventing modifiable etiological causes of LC. Effective and practical public health policies should be performed, such as legal regulations that restrict tobacco use, studies and regulations to reduce air pollution, and anti-smoking education for all age groups.

Disclosures

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Conflict of Interest: None declared.

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