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Modifiable risk factors for the prevention of lung cancer

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

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Summary

Background

Lung cancer is the most frequent malignant disease worldwide. In 2002, the number of new lung cancer cases was estimated at 1.3 million, which makes over 12.4% of all new cases of neoplasm registered all round the globe. It is also the leading cause of death from cancer.

Aim

The objective of this paper was to provide a review of some modifiable risk factors for lung cancer.

Materials/Methods

Data sources were MEDLINE from January 1950 to November 2006, title in the field. Search terms included: lung cancer, tobacco smoke, social class, diet, alcohol consumption and physical activity terms. Book chapters, monographs, relevant news reports, and Web material were also reviewed to find articles.

Results

The results of the literature review suggest that smoking is a major, unquestionable factor of lung cancer risk. Exposure to environmental tobacco smoke (ETS) and social class could also play a role in the occurrence of the disease. Diet, alcohol consumption and physical activity level are other important but less extended determinants of lung cancer.

Conclusions

Effective prevention programmes against some of the lifestyle-related factors for lung cancer, especially against smoking, must be developed to minimize potential health risks and prevent the future cost of health.

Key words

lung cancer • risk factors • prevention

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BACKGROUND

Lung cancer has been the most common cancer in the world since 1985. With a total number of 1.3 million new cases and 1.1 million deaths per year estimated worldwide, lung cancer is ranked highest with respect to morbidity and mortality among malignant neoplasms. In the year 2002, lung cancer made up 12.4% of cancer cases and accounted for 17.6% of all cancer-related deaths on the world scale [1].

Survival from lung cancer has shown no discernible improvement for more than 20 years. This is because the majority of patients have advanced disease when they are diagnosed and curative treatment is not possible. Five-year survival rates for lung cancer are consistently poor at 7–21%. The average survival in Europe is 10%, not much better than the 8.9% observed in developing countries [1].

The incidence and mortality rates of lung cancer vary among countries and follow the pattern of tobacco smoking a few decades earlier. The highest values can be noted in highly developed countries, particularly in Eastern Europe, and among Afro-Americans in the United States. In women, the highest incidence rates are recorded in North America and Northern Europe [1,2]. Although the rate of men dying from lung cancer is declining in western countries, it is actually increasing in women due to the increased take-up of smoking by this group.

Lung cancer is the major neoplastic disease in men; however, a rapid increase in incidence of cancer at this site has recently been observed in the population of women. This tendency can be attributed to lifestyle changes in this group, mostly to increasing prevalence of tobacco smoking [3]. The World Health Organization has estimated that lung cancer deaths will rise in virtually all industrialized countries, largely due to smoking and unhealthy diet [4].

Although cigarette smoking accounts for the vast majority of lung cancer cases, different factors may also play a role. Other risk factors involved in lung cancer development include environmental tobacco smoke, social class, dietary habits, alcohol consumption, physical activity, air pollution and occupational exposures (Table 1).

This article presents a review of the association between certain modifiable characteristics and

Table 1. Modifiable risk factors for lung cancer.

Factor	Evidence linking factor with lung cancer
Cigarette smoking	Strong
Occupational exposure	Strong
Environmental tobacco smoke	Strong
Alcohol consumption	Possible
Low fruit and vegetable intake	Possible
High-fat diet	Possible
Physical inactivity and excess body weight	Possible
Urban air pollution and indoor smoke from coal fires	Possible

the risk for lung cancer in humans, using information derived primarily from epidemiological studies. Recently published reviews and large well-designed original articles were preferred to form the basis of the present paper.

Data sources were MEDLINE from January 1950 to November 2006, title in the field. Search terms included: lung cancer, tobacco smoke, social class, diet, alcohol consumption and physical activity terms. Book chapters, monographs, relevant news reports and Web material were also reviewed to find articles.

MODIFIABLE RISK FACTORS FOR LUNG CANCER

Social class

Over many years, social determinants of health have aroused much interest among epidemiologists. In this domain, we can also encounter publications on the relationship between lung cancer and the level of education. The majority of those reports show higher lung cancer morbidity in persons with a lower social status, and thus with a lower level of education.

It is likely that unhealthy lifestyle, especially smoking habit (frequency and intensity of inhalation), much more common among less educated people, may explain this observation. It is difficult to separate the true effect of socioeconomic factors from the confounding effects that they introduce, especially from smoking habits that are highly related to social class [5,6].

Tobacco smoking

According to estimates made by the World Health Organization, one third of the world adult population (about 1.1 billion people), including 200 million women, smoke. It is also estimated that this world-wide tobacco epidemic takes every year a heavy toll of 3.5 million human lives.

In the 1950s, a group of researchers in the United States conclusively demonstrated the link between cigarette smoking and the growing number of deaths from lung cancer. Nowadays, it is well established that about 85–90% of all new lung cancer cases followed by deaths are caused by smoking [7]. Lung cancer risk associated with smoking depends on numerous factors such as age at starting to smoke, duration of smoking, number and type of cigarettes smoked (tar and nicotine contents, filter and non-filter cigarettes), and smoking behaviour (degree and frequency of tobacco smoke inhalation) [8]. In general, a person who has smoked all their life has a 20–40 times higher risk of developing lung cancer than a nonsmoker. Duration of smoking is more important than the amount smoked in determining the risk for cancer. Smoking 2 packs/day for 20 years is far less hazardous than smoking one pack/day for 40 years [9]. Further, the earlier the age at inhalation of smoking and the longer continuation of smoking in adulthood, the greater the risk. The risk is higher in smokers of hand-rolled and black tobacco cigarettes [10]. Risk of lung cancer is also proportional to the number of cigarettes smoked, increasing with increasing cigarette use [11].

Tobacco smoking is conducive to the generation of all types of neoplasm. Squamous carcinoma is the most common histological type of lung cancer, to date accounting for 40–50% of lung cancers. For some years however, the situation has been changing and adenocarcinoma has taken the lead, becoming the predominant histological type of lung cancer [12]. This is mostly due to constantly modified cigarette contents. Over several decades, nicotine and tar yields of cigarettes have been reduced and smokers have switched from non-filter to filter cigarettes, which has contributed to modified smoking behaviour. The evolution of cigarette manufacturing toward changes in chemical composition (lower tar and nicotine) and filtered cigarettes may have a potentiating effect in modifying the predominant histological type of lung cancer from central squamous cell carcinomas to peripheral adenocarcinoma.

Smokers of low-yield filter cigarettes have a tendency to take more puffs on a cigarette, smoke more cigarettes and inhale more deeply to fulfil their needs for nicotine than smokers of high-yield non-filter tipped cigarettes do. That enables carcinogenic tar particles to settle in the deeper, peripheral regions of the lung, leading to the development of a more aggressive type of lung cancer – adenocarcinoma [13,14].

There is a long interval between quitting smoking and elimination of lung cancer risk.

A smoker's risk of developing cancer decreases after quitting, and continues to decrease every year thereafter. The amount of time that must elapse before the level of risk faced by ex-smokers reverts to that of non-smokers is controversial. The preventive effect of smoking cessation is dependent on the intensity and duration of the prior smoking history. The decline in relative risk after stopping smoking is greater in those who had smoked for shorter periods, less often or deeply and had stopped smoking at a younger age. Stopping smoking before middle age reduced the risk for lung cancer by more than 90% [15].

Environmental tobacco smoke

Environmental tobacco smoke (also called ETS, secondhand smoke or passive smoke) is the combination of two forms of smoke from burning tobacco products: *sidestream smoke (SS)*, or smoke emitted between the puffs of a burning cigarette, pipe or cigar, and *mainstream smoke (MS)*, or the smoke exhaled by the smoker. ETS is a complex mix of over 4 000 compounds and contains many known or suspected human carcinogens and toxic agents. The smoke emitted from ETS has been documented to contain virtually all of the same carcinogenic compounds that have been identified in the mainstream smoke inhaled by smokers, but in different amounts [16]. Carcinogens that occur in secondhand tobacco smoke include: benzene, 1,3-butadiene, benzo[a]pyrene, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and many others. The available data indicate that sidestream smoke contains higher levels some of these toxic compounds. For example, N-nitrosodimethylamine, a probable human carcinogen, is emitted in quantities 20 to 100 times higher in SS than in MS. Benzene, a known human carcinogen, has about tenfold higher emission. Concentrations of some of the other PAHs in frequently exceed the values in mainstream

smoke. Sidestream smoke is also a source of 30 times higher rates of 2-naphtyloamine, a definite human carcinogen, and releases a 13 to 30 times higher amount of nickel and about seven-fold higher rates of cadmium, known lung carcinogens [17].

Epidemiological evidence of an association between passive smoking and lung cancer first appeared 20 years ago in Japan and Greece; both concluded that lung cancer incidence and mortality in nonsmoking women were higher for women married to smokers than for those married to nonsmokers [18,19].

In 1992 the U.S. Environmental Protection Agency (EPA) published a major assessment of the respiratory health risks of passive smoking. The report concludes that exposure to environmental tobacco smoke (ETS) is responsible for approximately 3,000 lung cancer deaths each year in nonsmoking adults and impairs the respiratory health of hundreds of thousands of children. In January 1993 the EPA declared environmental tobacco smoke a known human carcinogen. It was classified as an environmental toxin equivalent to asbestos and other hazardous substances [17]. A recently published meta-analysis revealed a 26% increase in lung cancer risk in nonsmokers whose partners are active smokers [20].

Dietary risk factors

Diet has been shown to have a dual effect on the appearance of lung cancer, including both protective and harmful elements. Many of the studies on diet and lung cancer aetiology have been motivated by the hypothesis that diets high in antioxidant nutrients may protect against oxidative DNA damage and thereby protect against cancer [21]. Many cohort and case-control study data have shown an inverse relationship between fruit and vegetable consumption and lung cancer, although several more recent studies have cast doubt on these findings. The results of case-control and prospective studies have shown that individuals with high dietary intake of fruits and vegetables have a lower risk of lung cancer than those with low fruit or vegetable intake [22]. A diet rich in fruit and vegetables reduces the incidence of lung cancer by approximately 25%. In a pooled analysis of cohort studies the protective association was stronger for fruits than for vegetable consumption [23]. The evidence that diets high in vegetables and fruit protect against lung cancer is convincing, but it is not clear

what constituents are responsible for this effect. Antioxidant vitamins were observed to have no clear protective effect, though there was some evidence pointing to a protective role for vitamins C and E [24].

Unfortunately, data investigating the effects of antioxidant supplementation in individuals who smoke have not demonstrated a reduction in cancer risk. In fact, it appears that supplemental (but not dietary) antioxidants may actually increase the risk of cancer in smokers. Three large-scale intervention trials among the high-risk populations (namely smokers and persons exposed to asbestos), the Beta-Carotene and Retinol Efficacy Trial (CARET) [25], the ABC Cancer Prevention Study [26] and the Physicians' Health Study [27], have reported no protective effect for intake of beta-carotene, retinol and alpha-tocopherol. In addition, the results indicated excess mortality among subjects who were taking these supplements.

Diet can also contain risk factors for lung cancer, particularly in the form of saturated fats. The risk rises with intake of red meat, dairy products and saturated fats (particularly from animal sources), lipids in general and cholesterol [28]. A risk has also been observed for foodstuffs and drinks containing nitrates and other preservatives added to food [29].

Alcohol consumption

Alcohol is thought to be a strong carcinogen, a compound that enhances the effect of other agents, showing strong synergism with tobacco smoking. To become aware of this fact is of great importance since over 90% of persons abusing alcohol are heavy smokers. Mechanisms by which alcohol exerts its carcinogenic effect have not yet been conclusively elucidated. It is likely that alcohol as a solvent can disturb the integrity of cellular membranes, and thus facilitate cellular penetration of noxious substances. Alcohol may raise cancer risk also by acting as an irritant (resulting in increased cell turnover) or possibly a transporter carrying carcinogens to the basal layer of the mucosa [30].

Some epidemiological studies suggest a causal relationship between alcohol consumption and lung cancer risk. Unfortunately, most of them did not reflect the actual risk because of the strong correlation between alcohol consumption and cigarette smoking. Therefore, the association observed between lung cancer aetiology and alcohol intake

was apparently insignificant after controlling for cigarette smoking. Studies carried out in a population of non-smokers, rather rare because of the low incidence of lung cancer in this group of subjects, did not reveal a statistically significant alcohol-related risk of this neoplasm [31].

Physical activity, body weight

There are relatively few studies on physical activity and lung cancer prevention. The available data suggest that physically active individuals have a lower risk of lung cancer; however, it is difficult to completely account for cigarette smoking [32]. A recent analysis of nine studies found that high physical activity reduced the risk of lung cancer by about 30% [33].

Investigators hypothesize that improvement in pulmonary function and ventilation in active compared to inactive individuals may explain the possible association between lung cancer and reduced physical activity. Being active may reduce lung cancer risk by improving the lung's efficiency. This might reduce the time that cancer-causing chemicals spend in the lung, as well as lowering their concentration. Regular exercise also helps to keep body weight at a healthy level [34].

Other modifiable risk factors

Other potentially modifiable risk factors for lung cancer include same infections, previous respiratory diseases and exposure to carcinogens in the workplace or environment. Occupational exposures also increase lung cancer risk, with an estimated 3% to 40% of all lung cancer attributable to occupational exposures [35,36].

Strongly associated occupational lung cancer risk include exposure to arsenic compounds, hexavalent chromium compounds, asbestos, beryllium, cadmium compounds, ionizing radiation, crystalline silica, soots, talc containing asbestos fibres, bis(chloromethyl)ether and chloromethyl methyl ether (technical grade). Other occupational exposures strongly associated with lung cancer are aluminium production, coke production, coal gasification, underground hematite mining (radon), iron and steel founding, nickel refining (nickel oxides and sulphides) and painting [37].

CONCLUSIONS

Effective prevention programmes against some of the lifestyle-related factors for lung cancer, es-

pecially against smoking, must be developed to minimize potential health risks and prevent the future cost of health. Although smoking is the strongest risk factor for lung cancer, greater intake of foods and vegetables may modestly lower the risk, supporting the conclusion that dietary but not supplemental carotene may be beneficial in smokers.

Large-scale prospective cohort studies attribute to effect to intake of fruit and vegetables (in general as well as specific foodstuffs), alcohol consumption, physical inactivity and excess body weight may explain the association with lung cancer incidence and could help reduce future lung cancer incidence and mortality. For lung cancer prevention it is recommended not to smoke, to choose a predominantly plant-based diet limited in red meat and animal fat, to reduce the intake of alcohol and to be physically active. Unfortunately, it is likely to be many years before the full benefit of improvements in cancer risk factors will be evident by a reduction in cancer rates in all populations.

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