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Review Article

A Brief Review on Lung Cancer

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ABSTRACT

Lung cancer is one of the most leading causes of cancer death in the world. Lung cancer, also known as lung carcinoma, is a malignant lung tumor characterized by uncontrolled cell growth in tissues of the lung. If left untreated, this growth can spread beyond the lung by process of metastasis into nearby tissue or other parts of the body. Most cancers that start in the lung, known as primary lung cancers, are carcinomas that derive from epithelial cells. The main primary types are small-cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (NSCLC). The vast majority (85%) of cases of lung cancer are due to long-term exposure to tobacco smoke. About 10–15% of cases occur in people who have never smoked. These cases are often caused by a combination of genetic factors and exposure to radon gas, asbestos, or other forms of air pollution, including second-hand smoke. This review gives a detailed idea on the epidemiology, causes, types, signs & symptoms, and treatment of lung cancer.

Keywords: Lung cancer, Cause, Types, Treatment.

1. INTRODUCTION

Cancer is defined as an abnormal growth of cells which tend to proliferate in an uncontrolled way and, in some cases, to metastasize (spread). Cancer is not one disease. It is a group of more than 100 different and distinctive diseases. Cancer can involve any tissue of the body and have many different forms in each body area. Most cancers are named for the type of cell or

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organ in which they start. If a cancer spreads (metastasizes), the new tumor bears the same name as the original (primary) tumor.

Lung cancer is a disease of uncontrolled cell growth in tissues of the lung. This growth may lead to metastasis, invasion of adjacent tissue and infiltration beyond the lungs. The vast majority of primary lung cancers are carcinomas of the lung, derived from epithelial cells. Lung cancer, the most common cause of cancer-related death in men and the second most common in women,[1, 2] is responsible for 1.3 million deaths worldwide annually.[3] The most common symptoms are shortness of breath, coughing (including coughing up blood), and weight loss.[4]

Tumors can be benign or malignant; Benign tumors can usually be removed and do not spread to other parts of the body. Malignant tumors, on the other hand, grow aggressively and invade other tissues of the body, allowing entry of tumor cells into the bloodstream or lymphatic system which spread the tumor to other sites in the body. This process of spread is termed metastasis; the areas of tumor growth at these distant sites are called metastases. Since lung cancer tends to spread, or metastasize, very early in its course, it is a very life-threatening cancer and one of the most difficult cancers to treat. While lung cancer can spread to any organ in the body, certain organs—particularly the adrenal glands, liver, brain, and bone—are the most common sites for lung cancer metastasis.

The lung is also a very common site for metastasis from tumors in other parts of the body. Tumor metastases are made up of the same type of cells as the original, or primary, tumor. For example, if prostate cancer spreads via the bloodstream to the lungs, it is metastatic prostate cancer in the lung and is not lung cancer.

Lung cancer is responsible for the most cancer deaths in both men and women throughout the world. The American Cancer Society estimates that 213,380 new cases of lung cancer in the U.S. will be diagnosed and 160,390 deaths due to lung cancer will occur in 2007. Lung cancer is predominantly a disease of the elderly; almost 70% of people diagnosed with the condition are over 65 years of age, while less than 3% of cases occur in people under age 45.

Lung cancer has also surpassed breast cancer in causing the most cancer-related deaths in women in the United States.

2. EPIDEMIOLOGY

Worldwide, lung cancer is the most common cancer in terms of both incidence and mortality with 1.35 million new cases per year and 1.18 million deaths, with the highest rates in Europe and North America.[5] The population segment most likely to develop lung cancer is over-fifties who have a history of smoking. Lung cancer is the second most commonly occurring form of cancer in most western countries, and it is the leading cancer-related cause of death.

Not all cases of lung cancer are due to smoking, but the role of passive smoking is increasingly being recognized as a risk factor for lung cancer, leading to policy interventions to decrease undesired exposure of non-smokers to others' tobacco smoke. Emissions from automobiles, factories and power plants also pose potential risks.[6-8]

Lung cancer incidence is currently less common in developing countries.[9, 10] With increased smoking in developing countries, the incidence is expected to increase in the next few years, notably in China[9] and India.[10]

Lung cancer incidence (by country) has an inverse correlation with sunlight and UVB exposure. One possible explanation is a preventative effect of vitamin D (which is produced in the skin on exposure to sunlight).[11]

3. TYPES OF LUNG CANCER

Table 1: Types of lung cancer

Frequency of histological types of lung cancer	
Histological type	Frequency (%)
Non-small cell lung carcinoma	80.4
Small cell lung carcinoma	16.8
Carcinoid[13]	0.8
Sarcoma[14]	0.1
Unspecified lung cancer	1.9

The vast majority of lung cancers are carcinomas—malignancies that arise from epithelial cells. There are two main types of lung carcinoma, categorized by the size and appearance of the malignant cells seen by a histopathologist under a microscope: *non-small cell* (80.4%) and *small-cell* (16.8%) lung carcinoma.[12] This classification, based on histological criteria, has important implications for clinical management and prognosis of the disease.[12]

3.1 Non-small cell lung carcinoma (NSCLC)

The non-small cell lung carcinomas are grouped together because their prognosis and management are similar. There are three main sub-types: squamous cell lung carcinoma, adenocarcinoma and large cell lung carcinoma.

Accounting for 31.1% of lung cancers,[13] squamous cell lung carcinoma usually starts near a central bronchus. Cavitation and necrosis within the center of the cancer is a common finding. Well-differentiated squamous cell lung cancers often grow more slowly than other cancer types.[17]

Adenocarcinoma accounts for 29.4% of lung cancers.[14-17] It usually originates in peripheral lung tissue. Most cases of adenocarcinoma are associated with smoking. However, among people who have never smoked ("never-smokers"), adenocarcinoma is the most common form of lung cancer.[18] A subtype of adenocarcinoma, the bronchioloalveolar carcinoma, is more common in female never-smokers, and may have different responses to treatment.[19]

Accounting for 10.7% of lung cancers,[12] large cell lung carcinoma is a fast-growing form that develops near the surface of the lung.[20] It is often poorly differentiated and tends to metastasize early.[13]

Table 2: Sub-Types Of Non-Small Cell Lung Cancer

Sub-types of non-small cell lung cancer		
Histological sub-type		Frequency of all lung cancers (%)
Squamous cell lung carcinoma		31.1
Adenocarcinoma	Adenocarcinoma (not otherwise specified)	23.2
	Bronchioloalveolar carcinoma	3.0
	Adenosquamous carcinoma	1.2
	Papillary adenocarcinoma	0.7
	Mucoepidermoid carcinoma[15]	0.1
	Adenoid cystic carcinoma[16]	0.04
	Other specified adenocarcinoma	1.1
Large cell carcinoma		10.7
Giant cell and spindle cell carcinoma		0.4
Other/unspecified non-small cell lung carcinoma		8.9

3.2 Small cell lung carcinoma (SCLC)

Small cell lung carcinoma (SCLC, also called "oat cell carcinoma") is less common. It tends to arise in the larger airways (primary and secondary bronchi) and grows rapidly, becoming quite large.[21] The "oat" cell contains dense neurosecretory granules (vesicles containing neuroendocrine hormones) which give this an endocrine/paraneoplastic syndrome association.[22] While initially more sensitive to chemotherapy, it ultimately carries a worse prognosis and is often metastatic at presentation. Small cell lung cancers are divided into Limited stage and Extensive stage disease. This type of lung cancer is strongly associated with smoking.[23]

3.3 Metastatic cancers

The lung is a common place for metastasis from tumors in other parts of the body. These cancers are identified by the site of origin, thus a breast cancer metastasis to the lung is still known as breast cancer. They often have a characteristic round appearance on chest x-ray.[24] Primary lung cancers themselves most commonly metastasize to the adrenal glands, liver, brain, and bone.[17]

4. SIGNS AND SYMPTOMS OF LUNG CANCER

Symptoms that suggest lung cancer include:[25]

- dyspnea (shortness of breath)
- hemoptysis (coughing up blood)
- chronic coughing or change in regular coughing pattern
- wheezing
- chest pain or pain in the abdomen
- cachexia (weight loss), fatigue and loss of appetite
- dysphonia (hoarse voice)
- clubbing of the fingernails (uncommon)
- dysphagia (difficulty in swallowing).

If the cancer grows in the airway, it may obstruct airflow, causing breathing difficulties. This can lead to accumulation of secretions behind the blockage, predisposing the patient to pneumonia. Many lung cancers have a rich blood supply. The surface of the cancer may be fragile, leading to bleeding from the cancer into the airway. This blood may subsequently be coughed up.

Depending on the type of tumor, so-called paraneoplastic phenomena may initially attract attention to the disease.[26] In lung cancer, these phenomena may include Lambert-Eaton myasthenic syndrome (muscle weakness due to auto-antibodies), hypercalcemia or syndrome of inappropriate antidiuretic hormone (SIADH). Tumors in the top (apex) of the lung, known as Pancoast tumors,[27] may invade the local part of the sympathetic nervous system, leading to changed sweating patterns and eye muscle problems (a combination known as Horner's syndrome), as well as muscle weakness in the hands due to invasion of the brachial plexus.

Many of the symptoms of lung cancer (bone pain, fever, weight loss) are nonspecific; in the elderly, these may be attributed to comorbid illness.[17] In many patients, the cancer has already spread beyond the original site by the time they have symptoms and seek medical attention. Common sites of metastasis include the bone, such as the spine (causing back pain and occasionally spinal cord compression), the liver and the brain. About 10% of people with lung cancer do not have symptoms at diagnosis; these cancers are incidentally found on routine chest x-rays.[4]

5. CAUSES OF LUNG CANCER

The main causes of lung cancer (and cancer in general) include carcinogens (such as those in tobacco smoke), ionizing radiation, and viral infection. This exposure causes cumulative changes to the DNA in the tissue lining the bronchi of the lungs (the bronchial epithelium). As more tissue becomes damaged, eventually a cancer develops.[17]

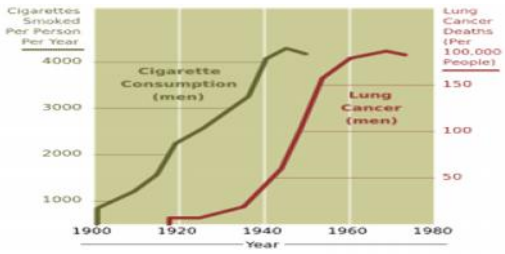

Fig 1: Twenty year Lag time between Smoking & Lung cancer

5.1 Smoking

Smoking, particularly of cigarettes, is by far the main contributor to lung cancer.[28] Across the developed world, almost 90% of lung cancer deaths are caused by smoking.[29] In the United States, smoking is estimated to account for 87% of lung cancer cases (90% in men and 85% in women).[30] Among male smokers, the

lifetime risk of developing lung cancer is 17.2%. Among female smokers, the risk is 11.6%. This risk is significantly lower in non-smokers: 1.3% in men and 1.4% in women.[31] Cigarette smoke contains over 60 known carcinogens [32] including radioisotopes from the radon decay sequence, nitrosamine, and benzopyrene. Additionally, nicotine appears to depress the immune response to malignant growths in exposed tissue.[33]

The length of time a person smokes as well as the amount smoked increases the person's chance of developing lung cancer. If a person stops smoking, this chance steadily decreases as damage to the lungs is repaired and contaminant particles are gradually removed.[34] In addition, there is evidence that lung cancer in never-smokers has a better prognosis than in smokers,[35] and that patients who smoke at the time of diagnosis have shorter survival than those who have quit.[36]

Passive smoking—the inhalation of smoke from another's smoking—is a cause of lung cancer in non-smokers. Studies from the U.S.,[37] Europe,[38] the UK,[39] and Australia[40] have consistently shown a significant increase in relative risk among those exposed to passive smoke. Recent investigation of sidestream smoke suggests it is more dangerous than direct smoke inhalation.[41]

5.2 Radon gas

Radon is a colorless and odorless gas generated by the breakdown of radioactive radium, which in turn is the decay product of uranium, found in the earth's crust. The radiation decay products ionize genetic material, causing mutations that sometimes turn cancerous. Radon exposure is the second major cause of lung cancer after smoking.[42] Radon gas levels vary by locality and the composition of the underlying soil and rocks. The United States Environmental Protection Agency (EPA) estimates that one in 15 homes in the U.S. has radon levels above the recommended guideline of 4 picocuries per liter (pCi/L) (148 Bq/m³).[43] Iowa has the highest average radon concentration in the United States; studies performed there have demonstrated a 50% increased lung cancer risk with prolonged radon exposure above the EPA's action level of 4 pCi/L.

5.3 Asbestos

Asbestos can cause a variety of lung diseases, including lung cancer. There is a synergistic effect between tobacco smoking and asbestos in the formation of lung cancer.[46] In the UK, asbestos accounts for 2–3% of male lung cancer deaths.[47] Asbestos can also cause cancer of the pleura, called mesothelioma (which is different from lung cancer).

5.4 Viruses

Viruses are known to cause lung cancer in animals[48, 49] and recent evidence suggests similar potential in humans. Implicated viruses include human papillomavirus,[50] JC virus,[51] simian virus 40 (SV40), BK virus and cytomegalovirus.[52] These viruses may affect the cell cycle and inhibit apoptosis, allowing uncontrolled cell division.

6. LUNG CANCER TREATMENT

The most widely used therapies for lung cancer are surgery, chemotherapy, and radiation therapy.

6.1 Medical Treatment

Chemotherapy and radiation therapy

- Chemotherapy and radiation may lead to a cure in a small number of patients. These therapies result in shrinking of the tumor and are known to prolong life for extended periods in most patients.
- Chemotherapy and radiation are very effective at relieving symptoms.
- Of all cases of advanced-stage lung cancer (spread outside the chest cavity), approximately 50%-60% of SCLC and 15%-

40% of NSCLC will go in to remission with chemotherapy.

- If relapse occurs, a different type of chemotherapy regimen may offer symptom relief and modest survival benefit.
- Chemotherapy uses chemicals that travel through the bloodstream. It affects both cancerous and healthy cells. This accounts for the many well-known side effects of chemotherapy, including nausea and vomiting, hair loss, skin problems, mouth sores, and fatigue.

Radiation therapy does not affect cells throughout the body the way chemotherapy does. However, it does affect healthy tissues overlying or directly adjacent to the tumor. To a certain extent, the side effects of radiation depend on which part of the body is targeted with radiation.

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