



Review Article

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## Lung cancer, an update

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### ABSTRACT

Cancer is known as a disease in which cells divide abnormally. They can involve various parts of the body. Many people annually die due to cancer. Yet, there are several reasons for the emergence of this disease. Cancer costs so much for society and patients in economic and social terms. Lung cancer malignity is known as the main mortality factor related to cancer. Lung cancer is divided into various types. Among them, Squamous cell carcinoma and Adenocarcinoma have the highest rate of prevalence. This malignity may be due to a variety of reasons. Generally, they are reported into groups including environmental factors (e.g. life style and cigarette) and genetic factors. Among the symptoms of the disease, followings can be implied: cough, chest pain, hoarseness due to the involvement of laryngeal nerve, whizzing in breath, respiratory distress, various syndromes like Horner, Pancoast's syndrome, Superior vena cava syndrome, Paraneoplastic syndrome, fingers Clubbing, headache and lymph nodes involvement, sweating, weight loss, etc. This disease can be diagnosed in different ways. The most elementary methods can be exploited; for example, preparing an appropriate medical history of the patient regarding his life style and coping with risk factors as well as examining symptoms. Other methods like examining biomarkers, imaging and/or biopsy are also used. CT scan is known as the most important imaging tool used for examining lung cancer. Similarly, there are a variety of treatments for this disease. They can be done in terms of medical therapies and/or surgery. Chemotherapy and radiotherapy are also applied depending on the trend of the disease and physician diagnosis.

**Keywords:** Lung Cancer; Epidemiology; Etiology; Diagnosis; Treatment

### INTRODUCTION

Cancer is the term used for a disease in which cells divide abnormally and able to invade other tissues. Cancer cells can expand to other parts of body through blood and lymph system (1). Cancer is increasing across the world due to several reasons. Among them, age increase and global population growth, and further cancer-inducing behaviors (especially, smoking) (2). Now, it is expected that over a million people in the US and more than 10 millions across the world are diagnosed as having cancer (3). It can be due to genetic dysfunctions (4, 5) and/or due to environmental reasons like diet (6), and/or life style and the like (7, 8). The main behavioral and environmental reasons concerned with the morality of individuals with cancer across the world include diet and lack of physical activity, using addictive drugs, sexual health and fertility, being exposed to air pollution, and using infected needles (9). Malignancy infection brings about various consequences. For instance, it can reduce the quality of people's life (10) and/or can impose treatment costs which are increasing (11, 12). This study aims to examine lung cancer as one of the most prevalent malignancies with high mortality. In this study, the epidemiology, diagnosis, treatment, and ... of this disease will be explored.

**Etiology and Epidemiology:** Lung cancer is the main cause of cancer-induced deaths across the world (13). In general, lung cancer is divided into Small Cell Carcinoma, Non-Small Cell Carcinoma, Squamous cell carcinoma, Adenocarcinoma, and large cell carcinoma (14) and metastatic type (15). About 85% of the basic lung malignancies belong to Non-Small Cell Carcinoma and the rest to Small Cell Carcinoma (16). The prevalence of Squamous cell carcinoma and Adenocarcinoma is higher as compared to other lung malignancies (17). Based on WHO reports, it is

estimated that about 1.8 millions of new people were added to people with lung cancer across the world. Over a half of them were from less developed areas. This malignancy has the highest prevalence among men in the world (18). Various factors can affect this type of cancer. Among them, cigarette can be implied (19). Occupational risk factors and pneumonia history may be lung cancer risk factors in women who do not smoke. A diet rich with fresh vegetables and cheese can have a protective role (20). Among other risk factors, followings can be implied: being exposed to radon, environment pollution, occupational encounters, gender, race, and history of pulmonary diseases (21). Tobacco smoking is one of the most important risk factors that is a part of cultural and economic structure of countries. Tobacco smoking is the primary cause of chronic obstructive pulmonary disease and lung cancer. Gender is another risk factor. Women may have more susceptibility to the carcinogenic effects of tobacco. Also lung cancer occurs in non-smoker women more than men (22). Genetic factors are of other reasons causing malignancies so that some studies have shown that gene variants prevalent in 5p15.33, 6p21-6p22, and 15q25.1 can be related to lung cancer (23).

**Signs and Symptoms:** A patient with lung malignancy may refer by symptoms such as coughing, chest pain, and hoarseness due to the involvement of laryngeal nerve in each stage of disease; whether early stages or final stages. As in other malignancies, these patients can also have symptoms such as fatigue, weakness and lethargy, weight loss, and sweating (24). In respiratory examinations, some dysfunctions may also be seen; for instance, whizzing in breath (25). Or, in metastatic stages, further symptoms such as bone pain and/or the involvement of lymph nodes can appear (26, 27). Respiratory distress may also emerge as a life threatening factor in these patients (28). Fingers clubbing can also be one of lung cancer symptoms. Yet, its prevalence is different in various types of this disease (29). Horner syndrome is also among other symptoms of lung cancer. It is caused by the involvement of sympathetic nerve path. It is known by a triad, pupillary miosis, Ptosis, and lack of sweating on the same side of the face and neck (30). This syndrome together with shoulder and arm pain, weakness and atrophy in hand muscles causes Pancoast's syndrome. They may be seen in upper lobe lung cancer patients (31). Superior vena cava syndrome is among other symptoms which may be seen in patients with lung malignancies. It is caused due to the compressive effect of tumor on Superior vena cava path. It is accompanied with organs edema and other symptoms (32). Generally, lung cancer is the most prevalent cause of this syndrome (33). Paraneoplastic syndrome is also another symptom frequently seen in these patients. It is accompanied with endocrine, neurological, musculoskeletal, and other manifestations (34).

**Diagnosis and Screening:** Taking history and examination are important in lung cancer diagnosis (35). "Concentrating on risk factors such as Cigarette smoking and underlying disease, show the possibility of lung cancer incidence patients. The next step is screening tests that contain Chest radiography, Sputum cytology, bronchoalveolar biomarkers and serum serology. Depending on accessibility and indications, these methods would be used but the most common way to screen is chest radiography. Also in recent studies some new methods are examined to screen patient that mentioned later. To diagnose the lung cancer, sputum cytology, fiberoptic bronchoscopy, transthoracic needle aspiration, Positron Emission Tomography (PET) Scan, bolus contrast compound tomography, video assisted thoracoscopic surgery and thoracotomy" (22). PET scan plays a role in staging the disease (36). CT Scan is among the main diagnostic methods for lung cancer (37). As used for staging, this diagnostic tool can be applied to diagnose the metastatic cases of lung cancer (38). Fluorescence endoscopy and spectrofluorometry are other methods for diagnosing the disease (39). Ultrasound methods are also among other diagnostic tools. They affect staging like some other diagnostic techniques (40). Examining the level of tumor markers and molecular genetics are among the diagnostic methods of lung cancer. Her-2/neu is a gene located on chromosome 17q21. It codifies 185KD membrane glycoprotein having tyrosine kinase activity. The level of this test sensitivity is reported between %5 and %64 in studies. This factor together with other diagnostic markers such as carcinoembryonic antigen (CEA), neuron specific antigen, and tissue polypeptide specific antigen has high sensitivity (41). It is proved that cytokeratins such as CYFRA21-1 and tissue polypeptide specific Ag (TPS) are useful in diagnosing non-small cell lung carcinoma. Neuron specific enolase (NSE) is a good tumor marker for the periodical monitoring of small cell lung carcinoma. The maximum range of normal level for tumor markers TPS, CYFRA21-1, NSE, and CEA were 80U/L, 3.3ng/ml, 13g/l, and 5ng/ml, respectively. Any amounts higher than these numbers are suspicious of tumor. It is also shown that tumor markers TPS, CYFRA21-1, and NSE have sensitivity %94 and specificity %95. Yet, for CEA, sensitivity and specificity are %54 and %56, respectively. Followings are among other diagnostic markers: retinol binding protein,  $\alpha$ 1- antitrypsin, Squamous cell carcinoma antigen, free circulating DNA & RNA, Exosomal microRNA, and Annexing A1 (42-44). Among other methods applied to diagnose lung cancer, biopsy can be implied. It is used in various forms for diagnosing this disease (45). Finally, besides being capable of playing the role of a diagnostic tool, bronchoscopy can be a tool for staging the disease. (46)

**Treatment and Prognosis:** In general, several factors can play a role in lung cancer treatment; for instance, patients' social and economic status (47). Yet, treatments considered for these patients include surgery and non-surgery (radiotherapy, chemotherapy, pharmaceutical therapy) treatments as well as combined treatments (48). Among surgery procedures, open surgery treatment to remove tumor can be implied; for example, thoracotomy (49). Again,

lobectomy using VATS can be implied (50). Some studies have shown that if lobectomy together with VATS is used in early stages, it will be more effective and appropriate (51). It must be noted that there is divergence between anatomic and complete resections, in surgical treatments (52). Generally, surgical treatments can have a different effect on the quality of these patients' life. It is demonstrated that the quality of life has increased in patients undergone thoracotomy (53). The type of surgery also affects respiratory status, and its relevant factors, and patient's ability in exercising (54). Pharmaceutical treatments are also used for patients. Today, methods like chemotherapy are used. For example, to slow the disease in some stages or in some cases before surgery, chemotherapy gets started (55, 56). Some treatments like radiotherapy are used for tranquilizing cases in the final stages of the disease (57). Patient's histology, age, gender, etc can affect the prognosis of the disease (58). That is, the lower the patient's age is, the better the prognosis of the disease can be. (59).

## CONCLUSION

Based on selected studies and reviewing them, environmental risk factors of lung cancer are the most prevalent and effective causes of lung cancer. Therefore reducing these factors can prevent people to develop to lung cancer, also reduce the severity of that.

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