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An Overview of Lung Cancer Comprehensive Review

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ABSTRACT: Lung cancer is the most common type of cancer in many countries and is the leading cause of cancer-related deaths worldwide, affecting both men and women. Tobacco use is the primary cause of lung cancer, which influences where and when the disease occurs in populations. Lung cancer often goes undetected until it reaches an advanced stage, contributing to its high occurrence. Therefore, early detection is crucial, especially for screening groups at high risk, such as smokers and those exposed to harmful substances in their work environments. Currently, diagnosing lung cancer involves various imaging techniques and analysing tissue samples through biopsies. However, these methods may not detect early stages of the disease. Patients suspected of having lung cancer typically undergo tests to confirm the diagnosis, determine the extent of the cancer (staging), and evaluate their overall health. Methods such as sputum cytology, thoracentesis, lymph node biopsy, bronchoscopy, needle aspiration, thoracoscopy and thoracotomy can all help in diagnosing lung cancer by examining tissue samples. In this review, we will discuss the advantages and disadvantages of current lung cancer diagnosis methods, as well as the potential of biomarker screening for improving detection and treatment.

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INTRODUCTION:

Breast, lung and colorectal cancers make up over 50 % of all cancer cases in women and are highly prevalent overall [1]. Lung cancer is the leading cause of cancer death in the United States [2]. The 5-year survival rate following diagnosis is 15.6 %, which is lower than the survival rates for breast, colon, and prostate cancer [2]. Despite advancements in treatment options such as surgery, medicine, and radiotherapy, the long-term survival rate of patients with primary lung cancer remains low [2]. Lung cancer is the leading cause of cancer-related deaths in North America and other developed countries. According to the 2020 special report on lung cancer, this disease is the most frequently diagnosed cancer and the leading cause of cancer death

in Canada [3]. Statistics show that lung cancer kills more Canadians than colorectal, pancreatic, and breast cancers combined. For example, approximately 30,000 Canadians will be diagnosed with lung cancer, with an estimated 21,000 deaths in 2020. Globally, the cancer burden is expected to double by 2050, with lung cancer topping the list [3]. Smoking is best known for causing chronic obstructive pulmonary disease [4-6] and lung cancer [7, 8]. It has also been linked to the development of interstitial lung disease; respiratory bronchiolitis-associated interstitial lung disease (RB-ILD) was first described in 1986 [9], with a follow-up report in 1989 [10]. Cigarette smoking has long been linked to pulmonary Langerhans cell histiocytosis (PLCH) and desquamative interstitial pneumonia (DIP) [10, 11]. Low-dose CT (LDCT) is now widely used for lung cancer screening. Furthermore, a trial (NELSON) demonstrated that this screening has 85 % selectivity and 99 % specificity when compared to no screening [12]. A recent study found that the overall false-positive rate was 81 % [13]. This extremely high number necessitated additional imaging or testing to confirm the findings.

SCREENING POPULATION:

Over the last 15 years, numerous trials have been conducted to determine which groups of people would benefit, if any, from lung cancer screening. The NLST is the only trial to show a decrease in mortality as a result of lung cancer screening [14].

NATIONAL LUNG SCREENING TRIAL:

The National Cancer Institute released the NLST results in August 2011 [14]. The NLST was a randomized control trial that began in 2002, screening at-risk smokers using Low-dose CT or standard chest radiography [15]. The majority of the NLST sites were designated National Cancer Institute centers, and over 80 % were large, multidisciplinary academic centers with more than 400 beds [16]. The study included a total of 53,454 participants [14]. Eligible participants included current or former smokers with no personal history of cancer, those who had smoked the equivalent of one pack of cigarettes per day for at least 30 years, and former smokers who had quit less than 15 years before participating in the study and were between the ages of 55 and 75 [14]. Participants were randomly assigned to receive three annual screening examinations using either low-dose CT or chest radiography. They were then followed for another five years after the screening exams were completed [14]. Overall, when comparing the two groups, the low-dose CT group had a 13 % higher detection rate of lung cancer than the chest radiography group [14]. Both screening modalities detected malignancies at earlier stages (IA and IB), but low dose CT detected them more effectively. The majority of the malignancies found were adenocarcinoma and squamous cell lung cancers, which could be attributed to the lesions' peripheral location.

DIAGNOSIS:

Tissue diagnosis:

There are several techniques that can help physicians make an accurate tissue diagnosis. Consultation with a pulmonologist, interventional radiologist, or thoracic surgeon is usually required to determine the most appropriate test. Thoracotomy is the recommended test for tissue diagnosis and staging in patients who have obvious early non-small cell carcinomas and are surgical candidates. In patients with suspected small cell or metastatic non-small cell carcinomas, the diagnosis should be made using the most convenient and least invasive method available (e.g., thoracentesis of a pleural effusion, excisional biopsy of an accessible node, bronchoscopy, transthoracic needle aspiration) [17]. When the type and stage of cancer are unclear, several options exist, including sputum cytology, flexible bronchoscopy, and transthoracic needle aspiration. Sputum cytology is a noninvasive test that may be useful in detecting centrally located tumors. The test detects 71 % of central tumors but less than 50% of peripheral tumors, requiring additional testing if the result is negative. Flexible bronchoscopy (using bronchial washings, brushings, and biopsies) is frequently the test of choice in patients with central tumors, with a combined sensitivity of 88 % [18]. Despite the addition of fluoroscopic and computed tomography (CT) guided transbronchial needle aspiration, bronchoscopy's sensitivity drops to 70 % in patients with peripheral tumors, and even lower in patients with tumors less than 2 cm in diameter [18,19]. Pneumothorax and bleeding are serious but rare complications of transbronchial needle aspiration [18]. Transthoracic needle aspiration has been shown to be more sensitive than bronchoscopy in patients with peripheral lung tumors, and it may be used when transbronchial needle aspiration is inconclusive or the patient is not a surgical candidate [18]. Fluoroscopy or CT are commonly used to guide transthoracic needle aspiration, and the presence of a cytopathologist improves diagnostic yield. The most common

complication of transthoracic needle aspiration is Pneumothorax (25 to 30 %), but the procedure rarely necessitates chest tube insertion [19]. Video-assisted thoracoscopy is a newer technique that can be used to sample small peripheral tumors (less than 2 cm in diameter), pleural tumors, or pleural effusions for diagnostic or staging purposes [20].

APPLICATIONS OF BIOMARKERS IN CLINICAL SAMPLES:

The following clinical samples are available for biomarker measurements:

Sputum:

Although cytological examination of sputum is an effective screening tool for early detection of lung cancer, peripheral tumors, such as adenocarcinoma of the smaller airways, may be missed. PCR techniques have been used to identify potential molecular biomarkers for early lung cancer. This was highlighted in a study conducted on fifteen patients. from a project called The Johns Hopkins Lung Project (JHLP) [21, 22]. In this study, approximately 50% of the recruited patients (n = 15) with adenocarcinoma or large-cell carcinoma were detected by mutations in sputum cells prior to clinical diagnosis (1 to 13 months), indicating that traditional methods would have missed them. Another gene of interest is the p16 gene, which is frequently deactivated or mutated in lung cancer [23]. The measurement of hypermethylation of the CpG islands in the sputum of lung cancer patients showed a strong correlation with early stages of NSCL cancer, implying that p16 CpG hypermethylation could aid in the early detection of lung cancer.

Bronchoalveolar lavage (BAL):

Over the years, routine cytopathological examination of Bronchoalveolar lavage (BAL) specimens has been used as a common diagnostic tool. Currently, BAL is another specimen sample where molecular biomarkers are used for early diagnosis. BAL is the infusion and respiration of a sterile saline solution into distal segments of the lung using a fiberoptic bronchoscope [24].

Peripheral Blood:

A comparison of microsatellite changes in tumor and plasma DNAs was performed in SCLC patients. The results revealed that 93% of patients with microsatellite alterations in tumor DNA also had modifications in plasma DNA [25]. These findings indicate that modifications to circulating DNA can be used as an early detection biomarker. Aberrant DNA methylation is another type of modification seen in circulating DNA. Hyper ethylated DNA was found in all stages of cancer, suggesting that it could be used as an early lung cancer detection marker. Other gene mutations, such as p53 and RAS gene mutations, which have been identified as markers in the plasma and serum of patients with other cancers such as colorectal and pancreatic cancers, have yet to be established in lung cancer [26]. In addition, gene expression changes in circulating white blood cells have been discovered in lung tumors.

Urine:

Urine is rarely examined in the search for biomarkers. However, urine has the potential to be used as a biomarker for lung cancer. Several analytes, including a signature of volatile organic compounds (VOCs) and proteomic analyses, have been proposed as potential biomarkers for lung cancer detection. Urine samples were collected and analyzed with a urine cartridge sensor that had an array of 73 spots [27]. The results showed that accuracies with sensitivities and specificities ranged from 36 to 95.5 and 60 to 97.6 %, respectively. These differences were observed when various cancers were compared to controls [27].

Metabolomics:

Metabolomics data have the advantage of providing information on metabolite levels, which can help determine the stage of the disease. Metabolomics has recently been used to predict cancer development in various fluids, including serum, sputum, urine, and sweat, with promising results [28–32]. Metabolomics studies using serum revealed that the discriminating metabolites aspartic acid and Pyruvic acid distinguished individuals with lung cancer from healthy controls [29]. Another study found a different set of discriminating metabolites, such as glycerophospho-β-arachidonoyl ethanolamine and sphingosine, with sensitivity and specificity of 77 and 93 %; 97 and 90 %, respectively [31].

CONCLUSIONS:

In diagnosing lung cancer, bronchoscopy and biopsies are common methods. Bronchoscopy requires skill from the bronchoscopist for an accurate diagnosis despite being minimally invasive; it can cause discomfort and complications. Screening for early lung cancer is crucial for effective treatment. Biomarker research in human fluids such as sputum, blood and urine, shows promise.

These biomarkers, often detected using PCR or Metabolomics, allow for rapid intervention. Notably, urine samples can detect lung cancer metabolites quickly. In conclusion, bronchoscopy and biopsies are key for diagnosing lung cancer, but the expertise of the bronchoscopist is vital. Screening for early detection is essential and biomarker research offers promising methods, including urine samples for quick and effective intervention.

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