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Delayed Diagnosis in Lung Cancer

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Abstract

Lung cancer is cancer that develops from the airway epithelium. It is one of the leading causes of cancer mortality worldwide, accounting for up to 13% of all cancer diagnoses. The problems that exist are also the result of a large number of cases that have not been effectively recognized, a lack of systematically documented reports, and delays in diagnosis, all of which result in delays in treatment and a worse prognosis. There are numerous factors that contribute to the problem of lung cancer diagnosis delays. As a result, the precise time of lung cancer patient management must be taken seriously.

Keywords: lung cancer, delayed diagnosis, factors

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Introduction

Lung cancer is a type of cancer that originates from the airway epithelium. It is one of the leading causes of mortality from malignancy worldwide, contributing for up to 13% of all cancer diagnoses. According to World Health Organization (WHO) data, lung cancer is the leading cause of cancer death in males and second in females.[1] According to the findings of a hospital-based study, of 100 hospitals in Jakarta, Indonesia, lung cancer is the leading cause of death in males and the fourth leading cause of death in females. Persahabatan General Hospital reported that lung cancer accounted for more than half of all cases of cancer. Cancer registration statistics of Dharmais Cancer Hospital from 2003 to 2007 showed that airway malignancies originating in the trachea, bronchi, and thoracic cavity were the second most common malignancy in males (13.4%) after nasopharyngeal cancer (13.6%). They were also the leading causes of malignancy mortality in males (28.9%).[2]

Smoking is a major concern that is currently increasing the incidence of lung cancer. There were approximately 1.1 billion smokers worldwide, and 8 million people died as a result of diseases caused by inhaling cigarette smoke. Approximately 1.2 million people died as a result of secondhand smoke exposure from smokers.[3] Lung cancer rates increased by 10–15% in the early 1900s, and smoking was responsible for more than 921,000 fatalities globally. This figure is undoubtedly rising as a result of industrial developments and high levels of air pollution, and what is rarely highlighted is radon gas exposure in a confined space. Radon is the world's second leading cause of cancer, after cigarettes. Radon exposure caused around 14% of lung cancer cases in the United States, especially when paired with smoking behaviors. Radon has long been recognized as a carcinogen in the environment, and considerable levels were obtained from within the home, particularly in areas with insufficient air circulation.[4]

Males over the age of 40, heavy smokers, and individuals who have been exposed to cigarette smoke and harmful gas pollutants for a long time are the main risk factors for lung cancer, and exposure to radon gas in an enclosed environment must still be considered. The problems that exist in developing countries appear to be lesser than those in developed countries. This is not necessarily attributed to a fewer number of affected people, but it can also be due to the number of instances that have not been effectively-recognized, the absence of systematically documented reporting, and delays in diagnosis, all of which result in delays in treatment and a worse prognosis.[5]

Addressing the Issues of Delayed Diagnosis of Lung Cancer in Indonesia

Diagnosis Delay Caused by Clinical Symptoms

Lung cancer symptoms occur in certain cases and frequently mirror those of other diseases. Coughing, shortness of breath, chest discomfort, and weight loss are the most common symptoms that predominate the complaints of lung cancer patients. Other symptoms include pleural effusion, pericardial effusion, superior vena cava syndrome, dysphagia, superior sulcus tumor syndrome, and diaphragmatic paralysis, which are caused by cancer cells pressing on intrathoracic organs. Short-term weight loss, decreased appetite, intermittent fever, and paraneoplastic symptoms are the most prevalent systemic clinical symptoms that often accompanied.[6]

Research data from the United Kingdom reported that coughing, chest pain, and shortness of breath occur in 60-70% of cases, as well as hemoptysis in 41% of cases. These symptoms could manifest even in the initial stages or non-malignant cases. Most lung cancer symptoms have a 2% positive predictive value, indicating that they can also appear in other diseases affecting the airways and cannot be used to rule out lung cancer. Cough, which is frequently a sign of airway disorders, is only clinically significant 77% of the time if it occurs three times in one period of illness.[7] Coughing up blood has a strong positive predictive value from the start when compared to other symptoms. Approximately 21.6% of lung cancer patients suffered from frequent hemoptysis as the initial symptom. This means that patients who present with this symptom might be referred to the possibility of lung cancer and can immediately be advised to carry out diagnostics such as chest radiographs.[8] Shortness of breath, the most common symptom of airway disorders, was not substantially significant in the early stages of lung cancer; this symptom can be used as a predominate benchmark if obtained in conjunction with other respiratory symptoms, and studies showed that the positive predictive value is only 41% even when this appears for the second time during the same disease period.[9]

Data on the time interval between the onset of symptoms and treatment have been collected in several countries through various studies. The average time between the onset of symptoms and the diagnosis of cancer is approximately two months.[10] The average treatment delay from the time symptoms first appeared was about 3.6 months in the United Kingdom and about 4.6 months in Sweden.[8] The optimal period to identify symptoms until the cancer is diagnosed, is no more than two weeks, with a treatment decision (operative or non-operative) due within four weeks.[11]

Diagnosis Delay due to Radiological Interpretation

The plain chest radiograph, alone or in combination with other modalities, has become the primary support for lung cancer management.[12] One of the factors that cause delays in the management of lung cancer associated with radiological examinations is the image of the tumor in a particular site that is difficult to distinguish because it is obscured by images of other organs. The second factor is a discrepancy between the radiologist's and pulmonologist's interpretations, which implies that the supporting images are often not used to establish the diagnosis. The final factor emerges as a consequence of dubious or unequivocal interpretations, which might make therapeutic decisions challenging.[13]
Studies showed that approximately 4% of radiologists were prone to make an inaccurate assessment in diagnosing lung cancer. An error rate of 49% was associated with the appearance of tumor abnormalities on plain chest radiographs, and this problem occurs due to difficulties in recognizing any irregularities on the chest radiograph images due to the disease's unusual location from its predilection. 14 Second, due to the early stages of lung cancer, the conclusion of the readings frequently appeared as something normal and was not concluded as a pathological process. The last mistake that radiologists often make is that they only pay attention to the primary abnormality and

overlook other abnormalities or satellite lesions that can hint at developing a differential diagnosis.[15]

Errors in the CT scan can also occur, as detailed in White's 1999 study, in which 15 cases of lung cancer were not detected because the lesions were located endobronchial in the lower lobe.[16] CT scanning is rapidly evolving, and one technique for reducing errors is to employ high-resolution slices (1.25 mm). Li et al discovered that it was difficult to detect small tumors (7 mm) using low-resolution CT scans, especially if there were other comorbidities or overlap with other organ images.[17]

The CT scan characteristics of the tumor are critical in determining the conclusion. The dimensions, clarity, and location of the tumor all influence the reading results. The detection rate for tumors 10 mm in size is 29%. Sizes 10-30 mm have a 28% error rate, sizes 30-40 mm have a 12% error rate, and sizes >40 mm are practically entirely discernible. The contrast between the tumor and the surrounding tissue, as well as the firm wall boundaries, determines the level of clarity of the tumor image.[14]

Diagnosis Delay Caused by Histopathology Interpretation

Histopathology evaluation is the gold standard for the diagnosis of lung cancer to determine the treatment regimen. Careful consideration is essential to decide whether a cell is malignant because the following phase of therapy will have to be aggressive. False-positive results will harm the patient due to the side effects of chemotherapy. Pathologists classify the problem of diagnosing lung cancer into three categories: overdiagnosis, underdiagnosis, and misdiagnosis. This issue frequently arises as a result of the tumor being misinterpreted as a false positive when it is actually a reactive process or a benign tumor, and vice versa. It is critical in reaching a conclusion about microscopic findings based on clinical examination, radiology, and the underlying process. The accuracy of the diagnosis is determined by the accuracy of the sampling location, the method of sample transportation, the description of tissue samples that show malignant characteristics, the number and size of the samples taken, and the pathologist's experience in determining the results of the examination.[18]

It is also necessary to understand the sampling method, because studies reported that samples taken blindly often generate more false-negative results.[19] The differences between studies showed that the blind sampling method frequently produced false-positive values in cases of benign tumors and false-negative values in cases of early malignancy. Other errors were frequently caused by the uneven distribution of cells. According to the findings, approximately 16% of false positives were caused by misinterpretation of cytological examination due to changes in cell shape caused by inflammation, squamous cell metaplasia, and atypical cell shape in fibrosis. Then there were the false-negative results, which accounted for approximately 33.8 percent of the total, due to the confounding of inflammatory cells surrounding the lesion, the number of samples that were not good due to damage during storage, and fluid containing very few cells.[20]

Diagnosis Delay due to the Health Care System

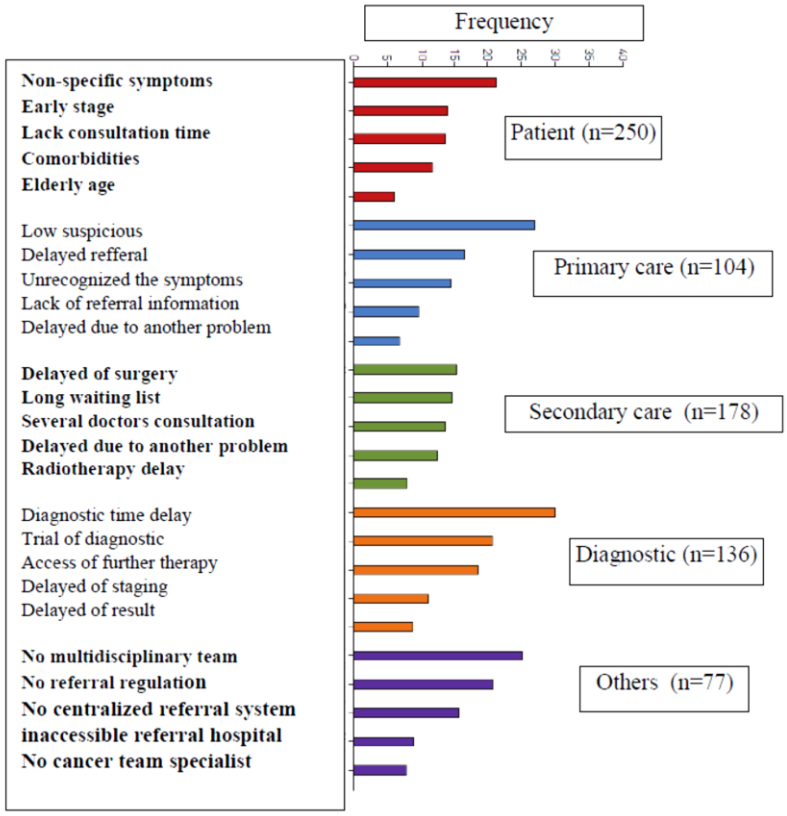
Patients suspected of having lung cancer must receive immediate treatment to determine whether the disease is malignant or not. Because the distribution of health workers with expertise in the field of lung cancer is not uniform throughout the region, many cases are missed. According to a study conducted at Persahabatan General Hospital in Jakarta, many cases of lung cancer were first treated as non-cancerous but were not appropriately followed, resulting in therapy being maintained without review. A clinician will typically perform an adequate evaluation and see improvement in symptoms if the treatment is appropriate for the diagnosis.[10]

Referral factors that do not work correctly from primary health care facilities to secondary and tertiary health care facilities also contribute to the delay. In the United

Kingdom, health services have implemented a two-week waiting period for referrals from primary care doctors to pulmonary specialists. The maximum time to provide therapy for patients who have established a diagnosis has been determined to be 31 days. America has even stricter management standards, which are applied approximately 10 days after a patient is suspected of having lung cancer.[21] In addition, Australia has established a 14-day referral system for patients diagnosed in primary care to receive therapy at specialist services.[13] According to a total of 26 studies, the referral period from primary to specialist services ranged from 0 to 33 days, with a median value of 7-8 days. As many as 52 studies looked into the duration of therapy and found that 6-80 days, with an average of 28 days, became the standard reference for the maximum time of therapy for patients with confirmed cancer diagnosis.[22]

There are five major factors that contribute to lung cancer treatment delays. Patient factors, primary health care factors, secondary health care factors, diagnostic issues, and other groups are included. Patients' factors were found to account for 34% of the challenges that caused delays in lung cancer detection. Non-specific clinical symptoms (53.21%) generate patient ignorance concerning the conditions caused by lung cancer, and the advent of cancer in the early stages frequently causes patients to fail to recognize changes in their bodies (35.14%). Meanwhile, education level and socioeconomic factors played only a minor role (0.4% and 2%). Many people who experienced respiratory disease symptoms misunderstood it for a simple disease and did not receive adequate treatment. Health insurance is a finance aspect on which the community has relied, thus when patients are referred to advanced facilities, those without insurance may cause delays in receiving appropriate treatment.[11]

The primary health care issue that would be the most prevalent cause was the physician's ignorance that the patient's symptoms were caused by lung cancer (27%), so they only received symptomatic therapy and did not follow up on referrals to secondary facilities. Referral delays were also caused by the lack of information about the locations of hospitals with pulmonary experts. The most common problem in secondary care was subsequent treatment delay (17%), the length of waiting time to see a specialist (15%), and the patient's reluctance to consult several related departments (14%). Subsequent delays in treatment were caused by diagnostic procedures, such as long waiting times for scheduled diagnostic procedures (30%), failure of early diagnostic procedures, which required them to try other methods (22%), and waiting time for post-diagnostic results (10%). Other issues arise as a result of the absence of multidisciplinary collaboration at the referred hospital (25%), unclear referral systems and requirements that must be met (20%), and insufficient referral hospital facilities, requiring patients to transfer to other referral locations (18%).[13]



Picture 1. Graph depicting the delay caused by the referral system
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Conclusions

Lung cancer cases continued to be affected by the issue of diagnosis delays. The delay was caused by a combination of factors that can occur concurrently. The most common causes of delay in diagnosis were clinical symptoms, radiological examinations, histopathology examinations, as well as referral system policies and health services, all of which needed to be improved.

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