Description of Lung Cancer Occurrence Characteristics at Siloam MRCCC Semanggi Hospital in 2020 Due to the Covid-19 Pandemic

Efhata Surya Diapari Pohan[1], Joyna Getruida Sopaheluwakan[1], Vidi Posdo A. Simarmata[2]

[1]Department of Surgery, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta
[2]Department of Medical Community, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta

Corresponding Author: Efhata Surya Diapari Pohan

ABSTRACT

Lung cancer is one of the most common types of cancer worldwide and the number one cause of death in Indonesia. As the name implies, lung cancer is a disease activity in which cells in the body develop out of control and are localized in the lungs. Lung cancer has many underlying etiologies and risk factors, but the majority is due to smoking habits which are still high. Now, the world is being hit by the COVID-19 pandemic, which makes lung cancer patients have to be vigilant because they have a high risk of severity if infected. This study aims to describe the characteristics of the incidence of lung cancer at Siloam MRCCC Semanggi Hospital in 2020 during the COVID-19 pandemic. This research is a type of descriptive analytic research. The use of data comes from secondary data from archives of anatomical pathology laboratories, with the inclusion criteria for the sample being all patients diagnosed with lung cancer in the 2019-2020 period and having complete archives and data on the results of anatomical pathology examinations. Based on the results of the analysis, it was found that 35.5% of cases were distributed in the age group of 60-69 years, 58.6% were male, 70.4% were of the Adenocarcinoma type, 45.5% were advised to carry out further examination of the target of therapy, 15.9% used tissue biopsy as a histopathological examination technique and 32.5% used pleural effusion specimens for cytological examination.

Keywords: Lung cancer, characteristics, therapeutic targets, COVID-19

INTRODUCTION

In daily life, humans have a system that plays an important role in breathing, namely the respiratory system. The lungs are one of the vital organs that run this system. When air reaches the lungs, there will be an exchange between oxygen from outside the body and carbon dioxide from the blood. Therefore, it is important to maintain the health of our lungs. The system cannot work as it should if abnormal cell growths develop and attack the lungs. This condition in the medical world is called cancer.

Cancer is a general term that refers to a large group of body cells that grow uncontrollably and can attack any body part. Usually, human body cells grow and develop through cell division to form new cells according to the body's needs. When cells become old or damaged, they die and are replaced by new cells. But sometimes, this process can get damaged and become disorganized, allowing abnormal cells to grow and develop. These cells can form a tumor, which is a lump of tissue. Tumors can be cancerous (malignant) or noncancerous (benign). [1]

Cancer can spread or invade adjacent tissues and even travel to distant places in the body to form new tumors (a process called metastasis) by the rapid growth of abnormal cells beyond their usual boundaries. Other terms used are malignant tumors and neoplasms. [1] Data from the Global Burden of Cancer (GLOBOCAN) released by the World Health Organization (WHO) states that countries in Asia have the largest contribution to cancer cases worldwide. And until 2020, it was found that lung, breast, colorectal, prostate, and stomach were the most common types of cancer. Meanwhile, data from Riskesdas compared in 2013 and 2018 showed increased cancer incidence (prevalence) in Indonesia from 1.40/00 to 1.490/00. [2] Lung cancer is a type of cancer or malignant tumor that threatens the lives of most of the world's population. Lung cancer certainly occurs because abnormal cell growth occurs in the lung tissue. Lung cancer includes two main types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Smoking is the most frequent cause of lung cancer; even passive smokers can be attacked by lung cancer. [3]

Based on statistical data from the Global Burden of Cancer (GLOBOCAN) in 2020, the global incidence of lung cancer is in second place after breast cancer (11.7%), namely 11.4%, while the number of new cases of lung cancer in Indonesia is ranked third after breast cancer and cervical cancer, namely 8.8% with a mortality rate in the first position of 13.2% of a total of 30,843 cases. [4] Data on the proportion of cancer cases (%) were also obtained for all residents (male and female) in the hospital. Dharmais cancer in 2018, the breast was ranked first at 19.18%, cervical at 10.69%, and lung at 0.90%, followed by colorectal at 6.08%, and nasopharynx at 5.92%. Suppose reviewed by gender, data from RS. Dharmais cancer was reported in men contributing the most cases of lung cancer, namely 16.77%, while in women, the most was breast cancer, 34.40%. [5] So this is the main focus, especially during the COVID-19 pandemic. Lung cancer requires fast and targeted management and action.

Lung cancer diagnosis certainly requires skills and facilities as well as multidisciplinary cooperation. Diagnosis of lung cancer at an early stage will greatly help sufferers, and finding a diagnosis in a faster time allows sufferers to obtain a better quality of life in the course of their disease, namely by selecting therapies that can be carried out immediately even though the disease cannot be cured. [6]

Lung cancer is a health problem because it is still a type of cancer with a high incidence rate, known as the cancer burden in Indonesia. It is caused by the smoking behavior of people in Indonesia, which is intolerable, especially in men. Even now, patients with lung cancer have a high risk of being infected with COVID-19 because of their body condition, which requires a comprehensive treatment system, the immunocompromised state of cancer or its therapy, supporting drugs such as steroids, and most importantly, old age and co-morbidities. Patients with lung cancer consistently report an increased risk of death compared with other cancers. It may be due to a combination of certain pathophysiological aspects, including underlying pulmonary impairment due to smoking history and the specific increase in urgency in respiratory health services caused by the COVID-19 pandemic. [7] So it became an interest for the authors to conduct a study entitled "Description of the Characteristics of Lung Cancer Occurrence at Siloam MRCCC Semanggi Hospital in 2020 During the COVID-19 Pandemic".

Based on the description in the background of the problem above, the formulation of the problem is obtained, namely, how to describe the characteristics of lung cancer at Siloam MRCCC Semanggi Hospital in 2020 during the COVID-19 pandemic. The research objective was to describe the characteristics of lung cancer at Siloam MRCCC Semanggi Hospital in 2020 during the COVID-19 pandemic.

LITERATURE REVIEW

The lungs in humans are located in the chest cavity (thorax) and include the lower respiratory tract, which consists of two, one on the right side (pulmo dextra) and one on the left side (pulmo sinistra). The right pulmo is larger than the left pulmo because the heart is on the left side of the thorax. The heart expands the mediastinum to the left so that the volume of the left pulmo is 10-20% smaller than the right pulmo. Inside the thorax is a cavity called cavitas pleurales lined by parietal pleura, divided into three parts: pars mediastinalis, pars costalis, and pars diapraghmatica. The pleural cavity has four pleural recesses where the lung expands during deep inspiration and is radiographically diagnostic when there is an effusion. The four recesses are the costodiaphragmatic, costomediastinal, phrenicomediastinal, and vertebro-mediastinal. [8]

Each lung has a lung apex (apex pulmonis), a cranial or upper part of the lung, and a caudal or lower part (pulmonic base). The lungs have many sides/edges called anterior, posterior, and inferior margins. The outer surface of the lung is covered by a thin layer, namely the visceral pleura, which consists of three surfaces, namely (1) the costalis surface, which is located laterally and continues as (2) the diaphragmatic surface at the inferior border, (3) the mediastinal surface towards the mediastinum. Between the parietal and visceral pleura is a capillary space filled with serous fluid to lubricate the pleural surface and reduce friction during inspiration and expiration. On the medial side of the lung, there is also the entry point of the main bronchus called the hilum pulmonic, and the neurovascular area of the lung called the root pulmonic. The root pulmonic consists of the pulmonary arteries, veins, and lymph nodes (nodi lymphoidei tracheobronchiales). The lungs have two systems of blood vessels connected by their terminal branches in the walls of the alveoli (alveolar septa). A A. Pulmonales and Vv. The pulmonales in the pulmonary circulation consist of the vasa publica, which functions for gas exchange, and the vasa privatea, to supply the lung tissue. A A. Pulmonales pass, sending deoxygenated blood from the right heart to the alveoli, whereas Vv. Pulmonales send oxygenated blood to the left atrium. [8]

Pulmo dextra has three lobes, namely the superior lobe, middle lobe, and inferior lobe, with four bronchi branching from the trachea or windpipe, including principal bronchi and superior middle lobar bronchi, and inferior lobar bronchi. Two horizontal and oblique fissures separate the three lobes on the right pulmo. Anteriorly, the horizontal fissure separates the superior and middle lobes, while the oblique fissure separates the middle and inferior lobes. Pulmo dextra has two sulcus/indentations: sulcus arteriae subclaviae and sulcus venae brachiocephalicae. This indentation is caused by blood vessels adjacent to the lungs. [8; 9]

While the left lung has two lobes, namely the superior lobe and the inferior lobe, with three bronchi: the principal bronchi, the superior lobar bronchi, and the inferior lobar bronchi, and only has one fissure, namely the obliqua fissure which separates the superior and inferior lobes. Pulmo sinistra has three sulcus, namely sulcus arteriae subclaviae, sulcus venae brachiocephalicae, and sulcus aorticus, and there is a depression/pressure of the esophagus called impressio oesophagea and impressio cardiaca (place of the heart). [8; 9]

The angle between the large bronchi (bronchus principalis dextra et sinistra) is as high as 55-65o. Where the right main bronchus is larger and lies almost vertically. So because of this position, foreign bodies more often enter the pulmo dextra during inspiration. Compared to the left pulmo, the position of the main bronchi is more horizontal. [9] Following the trachea, there will be a branch to the pulmo dextra et sinistra, namely the main bronchi, then the branch again to become lobar bronchi, then segmental bronchi. In the right pulmo, there are three lobar bronchi: superior (divided

into three segmental bronchi), medius (3 segmental bronchi, one posterior to the inferior lobe), and inferior (4 segmental bronchi). And in the left lung are two lobar bronchi, namely superior (divided into three segmental bronchi and two lingular bronchi) and inferior (5 segmental bronchi). Especially in the left lung, the superior lobar bronchus combines two segmental bronchi into one called the apicoposterior, and in the inferior lobar bronchus, there is a combination of two segmental bronchi into one called the antromedalis basalis. [9]

The lungs act as a vital organ in carrying out the respiratory system. Breathing is a process that occurs automatically and is usually controlled by the brain subconsciously. Also called involuntary respiration, namely any form of respiratory control that is not under direct control. [10] Breathing is necessary to sustain life, so involuntary respiration allows it to occur when voluntary respiration is impossible, such as during sleep. Involuntary respiration also has a metabolic function that works even when a person is conscious. In this condition, the brain will determine how much oxygen and the speed of the respiration pathway is needed to be supplied to vital organs such as the brain, heart, kidneys, liver, stomach, and intestines, as well as the muscles and joints in the body to carry out their respective functions. Meanwhile, the types of voluntary respiration are all types of respiration that are under conscious control. This type of breathing is important for higher functions involving air supply, such as voice control or blowing out candles. Similar to how the function of involuntary respiration is controlled by the lower brain, namely the brainstem or brainstem which consists of the medulla oblongata and pons varolli, the function of voluntary respiration is controlled by the upper brain, which is part of the cerebral cortex. [11] The lungs' main function is to exchange oxygen (O_2) and carbon dioxide (CO_2) gases in the blood. The gas exchange aims to provide oxygen to the tissues and expel carbon dioxide. The

need for oxygen and carbon dioxide is adjusted to the level of activity and metabolism of the body so that it will not settle down, but the respiratory system must remain constant to maintain the oxygen and carbon dioxide content in the body. [12] There are four main components in respiration, namely (1) pulmonary ventilation, regarding the inflow and outflow of air between the atmosphere and the alveoli in the lungs; (2) the diffusion of oxygen (O_2) and carbon dioxide (CO_2) that occurs between the alveoli and the blood; (3) transport of oxygen (O_2) and carbon dioxide (CO_2) in the blood and body fluids to and from the body's tissue cells; and (4) ventilation arrangements. [13]

Especially in the respiratory system, air will be distributed into the lungs through the trachea, bronchi, and bronchioles. When the system is running, what must be maintained is to keep the channels open so that air can enter and leave the alveoli easily. It is supported by a tracheal structure with a ring of cartilage surrounding it so that the trachea does not collapse; there are also curved and small cartilage plates on the walls of the bronchi to maintain rigidity and still allow movement for the lungs to expand or contract. The lungs can expand and contract in two ways, namely (1) by moving up and down the diaphragm to enlarge or reduce the chest cavity and (2) by lifting and pressing the ribs to increase or decrease the anteroposterior diameter of the chest cavity. [13]

Histologically, this system is divided into the conducting and respiratory parts. The conducting portion includes the outer (extrapulmonary) and internal (intrapulmonary) airways that conduct air for gas exchange to and from the lungs. In contrast, the respiratory portion consists of the respiratory passages within the lungs, which conduct air and allow respiration or gas exchange. [14]

The extrapulmonary airways consist of the nasal cavities, pharynx, larynx, trachea, extrapulmonary bronchi, and intrapulmonary bronchioles of diminishing

diameter ending in the terminal bronchioles, lined by ciliated pseudostratified epithelium (epithelium pseudostratificatum ciliatum) containing many goblet cells. On reaching the lungs, the bronchi form many branches and progressively decrease in diameter. Likewise, epithelial height, the number of cilia, and the number of goblet cells decrease gradually in the canal. The epithelium gradually shortens until it becomes a simple ciliated epithelium (epithelium simplex ciliatum), and until it reaches the terminal bronchioles, there are no more goblet cells. The smaller bronchioles are lined only by simple cuboidal epithelium (epithelium simplex cuboideum). In the terminal bronchi and respiratory tract, there are other types of cells instead of goblet cells, namely clara cells (exocrinocytus caliciformis). Clara cells are cuboidal cells without cilia whose number increases as ciliated cells decrease. [15]

The respiratory portion is the distal continuation of the conducting portion and begins with the respiratory tract, where gas exchange or respiration occurs. Starting from the terminal bronchioles, they branch into respiratory bronchioles, characterized by thin-walled air sacs and the alveoli. The respiratory bronchioles are the transitional zones between the conducting and respiratory portions. Gas exchange in the lungs occurs in the alveoli, the terminal air sacs in the respiratory system. There are no goblet cells in the alveoli, and the type of epithelium lining them is the simple squamous epithelium. Other intrapulmonary structures where respiration occurs are the alveolar ducts and alveolar sacs. In addition to cells in the respiratory tract, there are other types of cells in the lungs. The most abundant cells are squamous alveolar or type I pneumocytes (pneumocytus typus I). These squamous cells line the entire surface of the alveoli. Type II pneumocytes (pneumocytus typus II) are tucked singly or in groups between these squamous alveolar cells. The lung macrophage cells (macrophagocytus alveolaris), derived from blood monocytes, are also found in the connective tissue of the alveolar walls or interalveolar septum and the alveoli (dust cells). Within the interalveolar septum are numerous capillary beds, pulmonary arteries, pulmonary veins, lymph ducts, and nerves.

According to the Centers for Disease Control and Prevention (CDC, 2020), cancer is a disease in which cells in the body grow out of control. When cancer starts in the lungs, it is called lung cancer. The cell of origin for lung cancer is still largely unknown. It is, however, speculated that different tumor histopathological subtypes arise from different cell origins and are localized in a defined microenvironment. According to Abo KM et al., the results of their research said that alveolar type II cell (pneumocyte type II) contributes as a cancer cell for lung cancer of the Adenocarcinoma type. [16] In general, lung cancer occurs when the epithelial cells line the airways.

Lung cancer starts in the lungs and can spread to the lymph nodes or other organs in the body. Cancer from other organs can also spread to the lungs. When cancer cells spread from one organ to another, it is called metastasis. Lung cancer is usually grouped into two main types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). This type of lung cancer grows differently and is treated differently. Non-small cell lung cancer is more common than small cell lung cancer. [26]

Cancer is the leading cause of death worldwide, accounting for nearly 10 million deaths in 2020. The most common new cases of cancer in 2020 were: breast (2.26 million cases); lungs (2.21 million cases); colon and rectum (1.93 million cases); prostate (1.41 million cases); skin (non-melanoma) (1.20 million cases); and stomach (1.09 million cases). Meanwhile, the most common causes of death from cancer in 2020 are lung (1.80 million deaths); colon and rectum (935,000 deaths); followed by liver (830 000 deaths); stomach (769,000 deaths); and breast (685,000

deaths). [18] Therefore lung cancer is a type of cancer or malignant tumor that threatens the lives of most of the world's population. Most lung cancer statistics include small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). About 13% of all lung cancers are SCLC, and 84% are NSCLC. [19] It is interesting to note that in the early 20th century, lung cancer was a relatively rare disease. However, the significant increase in the following decades was largely due to increased smoking among men and women.

Based on statistical data from the Global Burden of Cancer (GLOBOCAN) in 2020, the global incidence of lung cancer is ranked second after breast cancer (11.7%), namely 11.4%, while the number of new cases of lung cancer in Indonesia is ranked third after breast cancer, breast and cervical cancer, namely 8.8% with a mortality rate in the first position of 13.2% of a total of 30,843, with new cases reaching 34,783 cases. Meanwhile, if the statistics are based on gender, in men, the incidence of lung cancer reaches 20.1%. [4] Data on the proportion of lung cancer cases (%) in all male and female residents were obtained from registration data at the Dharmais Cancer Hospital in 2018, lung cancer cases ranked third at 9.89%, and the proportion of cancer cases specifically in men For men, lung cancer is ranked first, namely 16.77%, it can be said that the lung cancer mortality rate is higher in men than women. [20]

Smoking is the most common cause of lung cancer. It is estimated that 90% of lung cancer cases are caused by smoking. So this risk is highest in men who smoke. Exposure to other carcinogens, such as asbestos, further exacerbates this risk. There is no correlation between lung cancer and the number of packs of cigarettes smoked per year due to the complex interaction between smoking, environmental and genetic factors. The risk of lung cancer caused by second-hand smoke increases by 20% to 30%. Other factors include radiation for treating non-lung cancers, particularly non-Hodgkins lymphoma and breast cancer.

Exposure to metals, such as chromium, nickel, arsenic, and polycyclic aromatic hydrocarbons, has also been linked to lung cancer. Lung diseases such as idiopathic pulmonary fibrosis increase the risk of lung cancer regardless of smoking. [21]

Several compounds have been implicated as a cause of lung cancer. However, in reality, it is difficult to establish a causal relationship due to several other confounding factors, such as differences in the amount of exposure time, smoking status, and so on.

Several risk factors can cause lung cancer, namely smoking, genetics, gender, race and ethnicity, diet and obesity, industrial contact, air pollution, viral infections, and oncogenes and oncogene suppressors.

General classification according to the location of the onset of the tumor, then in general, lung cancer can be divided into (1) central type: namely, tumors arising in the proximal bronchi of the segmental bronchial ostium, (2) peripheral type: tumors arising in the bronchi distal to the bronchial ostium segmental, that is, from the subsegmental bronchi to the alveoli. Meanwhile, in terms of histopathological division of lung cancer, according to WHO are: Squamous Cell Carcinoma, adenocarcinoma, large cell carcinoma, adenosquamous cell carcinoma, small cell carcinoma, and other types of lung carcinoma, non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC).

The pathophysiology of lung cancer is complex and not fully understood. It is hypothesized that repeated exposure to carcinogens, particularly cigarette smoke, causes pulmonary epithelial dysplasia. If exposure continues, it will cause genetic mutations and affect protein synthesis. And in the end, it can disrupt the cell cycle and increase carcinogenesis. The most common genetic mutations responsible for lung cancer development are MYC, BCL2, and p53 for small cell lung cancer (SCLC) and EGFR, KRAS, and p16 for non-small cell lung cancer (small cell lung cancer). The SCLC and NSCLC classifications represent more than 95% of all lung cancers.

Histologically, SCLC is characterized by small cells with scant cytoplasm and no obvious nucleoli. SCLC is almost always caused by smoking. It suggests a higher doubling time and earlier metastatic rate; therefore, it is always considered a systemic disease at diagnosis. The central nervous system, liver, and bones are the most common areas of metastases. Certain tumor markers can help differentiate SCLC from NSCLC. The tumor markers tested most frequently were thyroid transcription factor-1, CD56, synaptophysin, and chromogranin. Meanwhile, NSCLC is typically associated with paraneoplastic syndromes, which can describe this disease when the body's immune system cells produce hormones or other substances that can change the surrounding tissue. [22]

There are no specific signs and symptoms of lung cancer. Most patients have advanced disease at presentation. Symptoms of lung cancer occur due to local effects of tumors, such as cough due to bronchial compression by tumor, due to distant metastases, stroke-like symptoms secondary to brain metastases, paraneoplastic syndromes, and kidney stones due to persistent hypercalcemia. In particular: cough, dyspnea, and hemoptysis are common symptoms. Cough is the most common symptom, accounting for 50% to 75% of cases. It is sensitive but not specific. Squamous cell and small cell cancers usually cause coughing early due to the involvement of the central airways. Dyspnea or shortness of breath is lung cancer in 25% to 40% of cases. Hemoptysis is an important symptom in anyone with a history of smoking. However, bronchitis is the most common cause of hemoptysis, 20% to 50% of patients with underlying lung cancer present with hemoptysis. Although rare, patients may also present with shoulder pain, Horner's syndrome, and hand muscle atrophy. This constellation of symptoms is called the Pancoast syndrome. It is due to lung cancer arising in the superior sulcus. [23]

Lung cancer clinical manifestations vary according to location, size, pathological type, presence or absence of infiltration and pressure to surrounding organs, and presence or absence of metastases. Clinical manifestations that are often found are divided into (a) local and systemic symptoms due to tumors, (b) symptoms of external invasion and metastasis, and (c) accompanying symptoms. [24] Local and systemic symptoms due to tumor. Local and systemic symptoms include cough, hemoptysis, chest fullness and pain, dyspnea, fever, and nonspecific systemic symptoms (anorexia, weight loss, and cachexia in advanced stages). In addition, there are signs of invasion and metastasis, such as superior vena cava obstruction syndrome, Horners syndrome, Pancoast syndrome, and other symptoms of invasion and metastases that are often found, among others. As well as accompanying symptoms such as pulmonary hypertrophic osteoarthropathy, carcinoid syndrome (Cassid's syndrome), and gynecomastia, other accompanying symptoms include hypercalcemia due to ectopic, ectopic parathormone-like substances, neuropathy and myopathy, dermatomyositis carnomatous, eosinophilia syndrome, Cushing's syndrome, and ADH hypersecretion syndrome.

After the diagnosis of lung cancer, the most important step is to determine the stage of the disease to quickly determine treatment options, considering morbidity and chances of survival. It is important to do this very carefully. Staging is primarily performed for NSCLC using the TNM classification (tumor, node, metastasis). SCLC can also be staged similarly, but the approach is much easier for limited and extensive diseases. [25]

The TNM classification of tumor (T), node (N), and metastasis (M) is the internationally accepted way of staging NSCLC. It comprehensively determines tumor size and extent, location, and distant spread, which helps clinicians draw meaningful conclusions about the best

treatment, avoids unnecessary surgery, and provides timely referral to palliative care when a cure is not an option. [26]

First, tumors. Primary tumors are divided into five categories, and each category is further subdivided depending on tumor size, location, and invasion of surrounding structures. [26] The histopathological appearance of lung cancer will be classified based on two major groups: NSCLC and SCLC.

Based on the WHO report, on December 31, 2019, coronavirus 2 (SARS-Cov-2) cases were first detected in Wuhan, China, spreading worldwide. This outbreak was designated a COVID-19 pandemic through the WHO declaration in March 2020. This case is known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The spread of this virus through the mouth or nose of infected sufferers in small liquid particles when they cough, sneeze, talk, sing, or breathe. These particles range from larger respiratory droplets to smaller aerosols. [27]

Each individual's clinical manifestations differ according to their immunological condition, so patients can experience mild to moderate respiratory disease symptoms and recover without special treatment. Some patients are asymptomatic, contributing to the spread of SARS-Cov-2 uncontrollably. The most common symptoms include fever, cough, tiredness, and loss of taste or smell/smell. While less common symptoms: are sore throat, headache, aches and pains, diarrhea, rash on the skin, discolored fingers or toes, and red or irritated eyes. And serious symptoms include difficulty breathing, shortness of breath, loss of speech or mobility, confusion, and chest pain. Treatment for patients with mild symptoms who are otherwise healthy is said to independently manage their symptoms at home. On average, it takes 5-6 days from the time someone is infected with the virus to show symptoms, but it can take up to 14 days. [28]

It is known that patients with cancer are more susceptible to infection than individuals without cancer due to their systemic immunosuppressive state induced by malignancy and anticancer treatment. Therefore, cancer patients may be at higher risk of developing pulmonary complications due to COVID-19. SARS-CoV-2 can sometimes cause an exaggerated and ineffective host immune response associated with severe, potentially fatal lung injury, and patients may develop acute respiratory distress syndrome (ARDS). [29] Based on research, it was found that COVID-19 caused severity in lung cancer patients with the result that 62% were hospitalized, and 25% died. During the pandemic, COVID-19 accounted for a small share of overall lung cancer deaths, namely 11%. Determinants of the severity of COVID-19 are largely based on patient-specific characteristics, including smoking status and chronic obstructive pulmonary disease. According to the study results, cancer-specific features, including previous thoracic surgery/ radiation and recent systemic therapy, did not affect severity. [30] This research is a study that investigates the significant impact of the COVID-19 crisis in indirectly detecting lung cancer cases during the pandemic.

With the pandemic, the government is actively directing the public to carry out tests such as Rapid Tests or PCR Swab Tests when symptomatic or after contact with positive patients so they can determine the next steps, such as self-isolation. It is also a screening for COVID-19 cases in Indonesia. In addition, examinations from the field of radiology are also needed to support patients with suspected COVID-19 infection, namely thorax screening. The thorax area is the main target of infection from this virus, so the screening results are expected to support and strengthen the diagnosis because it can show an image of the lungs in patients suspected of COVID-19. [31]

LDCT or Low dose CT-Scan Thorax has been widely used as an option because it can minimize unnecessary radiation doses. [31] It was said by Maximilian et al. patients

who have symptoms of COVID-19, with the use of LDCT, the diagnosis can be made with sensitivity comparable to RT-PCR testing. In addition, LDCT also has high specificity for differentiating COVID-19 from other diseases associated with the same or similar clinical symptoms. So that the use of LDCT is proposed as a mandatory examination besides RT-PCR because it helps correct false-negative RT-PCR results, and the results are also obtained faster than RT-PCR. They can provide additional diagnostic information that is useful for additional diagnoses regardless of the type of infectious agent. [50] One of them can help detect nodules suspicious of lung cancer.

Moreover, because the most at-risk population is the elderly, an LDCT Thorax Scan can reduce the effects of too high radiation. [31] It is also in line with the provisions of the U.S. The United States Preventive Services Task Force (USPSTF) recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years with a history of smoking 20 packs per year currently smoking smoke or have quit in the past 15 years. [32] So with the thoracic screening examination during this pandemic and in high-risk populations, it can be assumed that many lung cancer cases can be detected.

RESEARCH METHOD
This type of research is descriptive. Descriptive research is research conducted to describe a phenomenon that occurs in society. This research will describe the characteristics of the incidence of Lung Cancer at the Siloam MRCCC Semanggi Hospital in 2020 during the COVID-19 pandemic; this research was conducted at the Siloam MRCCC Semanggi Hospital, South Jakarta. The time of research was conducted from November to December 2021. The population is a generalized area consisting of objects or subjects with certain qualities and characteristics determined by the researcher to then study and draw

conclusions. The population of this study is lung cancer patients treated at Siloam MRCCC Semanggi Hospital in 2019-2020. The sample is part of the population selected with a certain sampling technique to represent the population. The sample in this study is all lung cancer patients treated at Siloam MRCCC Semanggi Hospital in 2019-2020. In this case, the sampling is done by total sampling: the number of samples equal to the population. The research instrument used in this study was secondary data which is an archive of the Anatomical Pathology Laboratory of patients with a lung cancer diagnosis at the Siloam MRCCC Semanggi Hospital from January 2019 - December 2020. Research data processing was carried out through 3 stages: data editing, data tabulation, and data analysis; research ethics aims to protect or maintain the rights and obligations of respondents and researchers. In this study, researchers applied the principles contained in research ethics by disseminating informed consent and confidentiality.

RESULT AND DISCUSSION
Based on the Anatomical Pathology laboratory archives of the Siloam MRCCC Semanggi Hospital in the 2019-2020 period, 169 patients had undergone histopathological and cytological examinations. They met the inclusion criteria, including the variables used in this study, including age, gender, and type of lung cancer, specimen collection techniques, follow-up examinations for therapeutic targets, and histopathological diagnosis. Following the research that will be conducted to see comparisons between years before and after the pandemic, the total records were divided into 56 records in 2019 and 113 files in 2020. The following table shows the percentage of age-related lung cancer in 2019 and 2020.

Table 1. Characteristics of Lung Cancer Patients by Age in 2019.

Age Group	Frequency	Percentage (%)
< 20 years old	None	-
20-29 years old	None	-
30-39 years old	3	5,4
40-49 years old	9	16,1
50-59 years old	11	19,6
60-69 years old	22	39,3
≥ 70 years old	11	19,6
Total	56	100

Table 2. Characteristics of Lung Cancer Patients by Age in 2020.

Age Group	Frequency	Percentage (%)
< 20 years old	None	-
20-29 years old	1	0,9
30-39 years old	6	5,3
40-49 years old	11	9,7
50-59 years old	36	31,9
60-69 years old	38	33,6
≥ 70 years old	21	18,6
Total	113	100

In terms of a year, the table describes an increase in lung cancer incidence in certain age groups, namely in the 60-69 year age group. In 2019, there were 22 cases which then increased to 38 cases in 2020. The 50-59 year age group from 11 cases to 36 cases, and the age group ≥ 70 years from 11 to 21 cases. These results indicate that lung cancer mainly occurs in the elderly group, and most patients are diagnosed at the age of ≥ 65 years, while a small proportion is diagnosed at ≤ 45 years. 35 This is supported because the ability to diagnose lung cancer is very difficult. Usually, these symptoms do not appear until it has reached an advanced stage as well as there are no specific early symptoms in lung cancer patients sufferers who rarely come to the doctor when the disease is still in its early stages because the course of the disease is also long and does not show early symptoms. Or another possibility because the number of visits of lung cancer patients at the Siloam MRCCC Semanggi Hospital in that year is not fixed. No explanation or correlation exists that the COVID-19 pandemic underlies the change in age-related cases.

The following is a table of percentage results based on gender in 2019 and 2020, which can be seen as follows:

Table 3. Characteristics of Lung Cancer Patients by Gender in 2019 – 2020.

Year 2019		
Gender	Frequency	Percentage (%)
Male	29	51,8
Female	27	48,2
Total	56	100
Year 2020		
Gender	Frequency	Percentage (%)
Male	70	61,9
Female	43	38,1
Total	113	100

In terms of the year, the table describes an increase in lung cancer incidence in both men and women; namely, in 2019, there were 29 cases which then increased to 70 cases in 2020. Likewise, in women, from 27 cases to 43 cases. These results are consistent with various studies where men still dominate the incidence of lung cancer in terms of smoking behavior as a cause of nearly 90% of lung cancer cases globally, even though there is no record of the history of the patient's habits in the archives. Meanwhile, according to Kiyohara et al.'s research, lung cancer in women occurs due to its relationship with hormones that affect the susceptibility to the process of lung carcinogenesis and a DNA approach where the DNA repair capacity (DNA repair) in women is lower than in men. Of course, this is outside the case of women who smoke. [33] It also shows that there is no explanation or correlation that there COVID-19 pandemic that underlies the change in the number of cases related to sex. The following table shows the percentage of lung cancer according to its type in 2019 and 2020.

Table 4. Characteristics of Lung Cancer patients by type in 2019.

Types of Lung Cancer	Frequency	Percentage (%)
NSCLC Adenocarcinoma	43	76,8
NSCLC Cell Carcinoma Squamous	6	10,7
NSCLC Atypical Carcinoma	2	3,6
SCLC Carcinoma	2	3,6
Neuroendocrine Carcinoma	1	1,8
Lungs	2	3,6
Total	56	100

Table 5. Characteristics of Lung Cancer patients by type, specifically for men, 2019-2020.

Year 2019

Types of Lung Cancer	Frequency	Percentage (%)
NSCLC Adenocarcinoma	19	65,5
NSCLC Squamous Cell Carcinoma	6	20,7
NSCLC Adenosquamous Carcinoma	1	3,4
SCLC Carcinoma	2	6,9
Neuroendocrine	1	3,4
Total	29	100

Year 2020

Types of Lung Cancer	Frequency	Percentage (%)
NSCLC Adenocarcinoma	40	57,1
NSCLC Squamous Cell Carcinoma	19	27,1
NSCLC Atypical Carcinoma	1	1,4
NSCLC Adenosquamous Carcinoma	3	4,3
SCLC Karsinoma Neuroendocrine	6	8,6
Carcinoma Lungs	1	1,4
Total	70	100

Table 6. Characteristics of Lung Cancer patients by type, specifically for women, 2019-2020.

Year 2019

Types of Lung Cancer	Frequency	Percentage (%)
NSCLC Adenocarcinoma	24	88,9
NSCLC Adenosquamous Carcinoma	1	3,7
Total	27	100

Year 2020

Types of Lung Cancer	Frequency	Percentage (%)
NSCLC Adenocarcinoma	36	83,7
NSCLC Squamous Cell Carcinoma	2	4,7
NSCLC Atypical Carcinoma	1	2,3
NSCLC Adenosquamous	3	7,0
Lung Carcinoma	1	2,3
Total	43	100

Because of the results in the table show that the most common type of lung cancer in 2019 and 2020 is the non-small cell lung carcinoma (NSCLC) adenocarcinoma subtype, followed by the squamous cell carcinoma subtype. There was also an increase in the incidence of lung cancer in 2020, namely adenocarcinoma, from 43 cases to 76 cases, and squamous cell carcinoma, from 6 cases to 20 cases. While other types only range from 1-8 cases of the total. Among them are small-cell lung carcinoma (SCLC) types, atypical carcinomas, adenosquamous carcinomas, neuroendocrine carcinomas, and other (unspecified) lung carcinomas. Likewise, with the specifications for types of lung cancer based on sex, both men and women

in 2019-2020 showed that most cases were NSCLC with the Adenocarcinoma subtype.

A study by Siddiqui et al. explained that the adenocarcinoma type is found in approximately 35-40% of lung cancer and is the most common histological subtype of NSCLC [26]. This type of cancer occurs most commonly in women and non-smokers but can also appear in current or former smokers. Meanwhile, squamous cell carcinoma, the second most common type of lung cancer, is found around 30-35% and histologically belongs to non-small cell lung cancer (NSCLC). And related to smoking habits that mainly occur in men. [26] This also supports data from the American Cancer Society in 2021 that around 84% of lung cancer in the world is NSCLC, 13% is SCLC, and the rest are other types of lung cancer.

Adenocarcinoma is generally localized to the outside or periphery of the lung, and this follows the distribution of carcinogens which explains that smoking cigars and pipe tobacco produces relatively large particles that only reach the upper airways, unlike smoking, which produces small particles, smooth, and easily reach the distal airways. [34] The delay between smoking onset and cancer onset is usually long, requiring 20–25 years for cancer to form. So even though theoretically adenocarcinoma generally occurs in women and passive smokers, there is still a possibility of being exposed to various carcinogens in cigarettes during recent years, where E Brambila et al. also said that lung cancer in people who have never smoked is caused by environmental tobacco smoke, it is a relatively weak carcinogen. It can only explain a small proportion of lung cancers in non-smokers. [35] It is, of course, coupled with genetic risks (family history), EGFR mutations, and environmental exposures that have been identified to be mostly related to occupational exposure, such as asbestos, tar, soot, and several metals such as arsenic, chromium, and nickel. [34] As for squamous cell carcinoma, the second most common case, its location is more common

in the central part of the lung. Unlike adenocarcinoma, this type mainly occurs in active smokers or highly addictive smoking habits. This is closely related to inhaling cigarette smoke's duration, intensity, and depth. And other lung cancer cases are rare, such as SCLC, atypical carcinoma, neuroendocrine carcinoma, and other (unspecified) lung carcinoma. SCLC has a higher metastatic rate due to its degree of malignancy. SCLC and NSCLC differ in terms of the cells affected. There is no explanation or correlation that the COVID-19 pandemic underlies the change in the number of cases related to the type of lung cancer. However, it is more likely that the patient's level of vigilance increased during the COVID-19 pandemic, so they carried out examinations or vice versa because they were accidentally found during periodic medical check-ups. Based on the histopathological diagnosis of lung cancer in 2019 and 2020, the following percentage results table is obtained:

Table 7. Characteristics of Lung Cancer patients based on Histopathological Diagnosis.

Year 2019		
Histopathological Diagnosis	**Frequency**	**Percentage (%)**
Adenocarcinoma positive	15	26,8
NSCLC positive leans towards Adenocarcinoma	14	25,0
Squamous Cell Carcinoma Positive	2	3,6
NSCLC positive leaning Squamous Cell Carcinoma	4	7,1
SCLC positive	2	3,6
Positive for Neuroendocrine Carcinoma	1	1,8
Positive for Carcinoid Tumor	2	3,6
Lung Carcinoma Metastases	15	26,8
Lung Carcinoma Positive	1	1,8
Total	56	100
Positive for Neuroendocrine Carcinoma	4	3,5
Positive for Carcinoid Tumor	2	1,8
Lung Carcinoma Metastases	16	14,2
Lung Carcinoma Positive	9	7,9
Total	113	100
Year 2020		
Histopathological Diagnosis	**Frequency**	**Percentage (%)**
Adenocarcinoma positive	46	40,7
NSCLC positive leans towards Adenocarcinoma	15	13,3
Positive, Squamous Cell Carcinoma	12	10,6
NSCLC positive leaning Squamous Cell Carcinoma	9	8,0

Based on the results in the table, it is described that the most histopathological diagnoses of lung cancer in 2019 and 2020 were non-small cell lung carcinoma (NSCLC) adenocarcinoma subtype, followed by squamous cell carcinoma subtype. While the SCLC type only amounted to 2 of the total cases. And quite a few other cases also show lung cancer metastases. This aligns with the characteristics based on the type of cancer obtained, namely NSCLC subtype adenocarcinoma, which ranks first, then squamous cell carcinoma. Following global data evidence, NSCLC accounts for around 84% of all lung cancer cases worldwide, and the rest are SCLC.

Adenocarcinomas are described by their acinar/tubular structure or mucin production. Suppose poorly differentiated carcinoma lacks microscopic evidence of glandular differentiation. In that case, it is demonstrated by immunohistochemistry to express "adenocarcinoma markers," such as TTF-1 and/or Napsin A. [36] So in addition to assays for therapeutic targets such as EGFR, ALK, or PD-L1, in confirming the histopathological diagnosis of adenocarcinoma is also accompanied by an examination of TTF-1 and Napsin A as stated in the archive attachment. Meanwhile, squamous cell carcinoma (SqCC) is described as a carcinoma recognized by the appearance of keratinization or intercellular bridges. The 2015 WHO classification divides them into keratinizing SqCC, non-keratinizing SqCC, and basaloid SqCC. Before this

classification, basaloid SqCC was categorized as a variant of large-cell carcinoma. However, basaloid SqCC immunohistochemically shows "SqCC markers" (e.g., p40, CK5/6, and p63) and is therefore categorized as SqCC. [36] As attached in several patient files with suspected SqCC, it will be followed by a p40 or p63 examination. According to the 2015 WHO classification, neuroendocrine carcinoma is defined as a "neuroendocrine tumor" with several subtypes. Invasive neuroendocrine tumors consist of three subtypes: SCLC, large cell neuroendocrine carcinoma (LCNEC), and carcinoid tumors (typical/atypical). Idiopathic pulmonary neuroendocrine cell hyperplasia is extremely rare and non-invasive, therefore,

of low clinical importance. On the other hand, the distinction between high-grade neuroendocrine tumors (HGNETs), which comprise SCLC and LCNEC, and carcinoid tumors is of great importance in pathological and clinical practice. HGNET is one of the most aggressive subtypes and is characterized by a history of heavy smoking in patients, whereas carcinoid tumors usually carry a benign prognosis and frequently occur in patients without a smoking history. [36]

Based on the specimen collection technique in the anatomical pathology archive for histopathological examination types in 2019 and 2020, the percentage results table is as follows:

Table 8. Characteristics of Lung Cancer patients based on the 2019 Histopathological Examination Specimen Collection Technique.

Year 2019

Retrieval Technique	Frequency	Percentage
Specimen		(%)
Core biopsy	1	6,3
TTB	2	12,5
CT-*guided* TTB	1	6,3
A frozen section (VC)	4	25,0
Tissue biopsy	8	50,0
(lungs/bronchi/KGB/femur)		
Total	16	100

Year 2020

Specimen Collection Techniques	Frequency	Percentage (%)
Sputum cytology	1	2,0
Core biopsy	14	28,6
CT-*guided core biopsy*	2	4,1
TTB	1	2,0
A frozen section (VC)	11	22,4
Tissue biopsy (lung/bronchus/KGB/femur)	19	38,8
Resection	1	2,0
Total	49	100

Judging from the table's results, it can be described that the most specimen collection technique for histopathological examination in 2019 was tissue biopsy from the lung/bronchi/KGB/femur, followed by frozen section (VC). And the remaining cases are core biopsies, TTB, and CT-guided TTB. In 2020, the three most common techniques are still the same: tissue biopsy, a core biopsy, and a frozen section. Tissue biopsy is the main technique used in taking specimens for histopathological examination. Biopsy techniques, especially for the lungs, generally consist of needle, transronchial, thoracoscopic, and open

biopsies. However, the specific biopsy techniques used in some examination files are not listed due to several limitations. Even so, it can still be characterized that in a histopathological examination, the most specimen collection techniques are needle biopsies (core biopsies) and frozen sections, which are diagnostic tests to see the accuracy of the specimens taken to be compared with existing paraffin blocks (cell blocks). It is the gold standard. [37]

In addition, several cases are examined by transthoracic biopsy (TTB). Sampling with this technique is more effective, and when compared to surgical procedures, TTB is

more minimally invasive. TTB will provide more informative specimen diagnosis results. However, indications for use depend on the results of previous specimens because TTB is usually continued when FNAB results are inadequate. After all, the diagnostic rate for TTB is higher than for FNAB. [41] Certainly, TTB, with CT guidance, will be more helpful in the accuracy of specimen collection and diagnosis. As for the types of cytology examinations in the 2019 and 2020 archives, the percentage results table is as follows:

Table 9. Characteristics of Lung Cancer patients based on the Cytological Examination Specimen Collection Technique.

Year 2019		
Specimen Collection Techniques	**Frequency**	**Percentage (%)**
Fluid cytology (pleural effusion,	Pleural effusion = 19	38,8
pericardial fluid, and	Pericardium = 2	4,1
ascites)	Ascites = 2	4,1
FNAB	4	8,2
TTNA	1	2,0
BSO (sweep)	3	6,1
BSO (rinse)	1	2,0
TTB	5	10,2
CT-*guided* TTB	2	4,1
Tissue smear	1	2,0
Total	40	100
Year 2020		
Specimen Collection Techniques	**Frequency**	**Percentage (%)**
Fluid cytology (pleural effusion, pericardial	Pleural effusion = 36	56,3
pericardial fluid, and	Pericardium = 2	3,1
ascites)	Ascites = 3	4,7
FNAB	7	10,6
TTNA	4	6,3
BSO (sweep)	4	6,3
BSO (rinse)	1	1,6
TTB	6	9,4
A frozen section (VC)	1	1,6
Total	64	100

Judging based on the table results, it can be described that the specimen collection technique for most cytological examinations in 2019 and 2020 is the same, namely pleural effusion. Then followed by FNAB, TTB, fiberoptic bronchoscopy (rinsing/brushing), TTNA, frozen section, and tissue smear preparation. In contrast to histopathology, a cytological examination will only show the cells' shape without the tissue structure's involvement. In short, the specimens obtained in this examination aim to detect lung cancer growth before clinical manifestations appear. Pleural effusion cytology examination is an examination that is easy to do; apart from not requiring a large amount of money, this examination is also minimally invasive in patients. According to the results, it is likely that most lung cancer patients who carry out examinations have clinical manifestations in the form of pleural effusion after X-rays/CT, so this examination is the choice.

After pleural effusion, various techniques are also used for cytological examination. Starting from the second most common, namely FNAB, it is also the most frequently used in anatomical pathology examination because of its minimally invasive technique using a thin hollow needle to remove fluid/small pieces of tissue from the tumor. After that, other collection techniques that are also recorded, such as TTB, fiber-optic bronchoscopy, to TTNA, may be chosen according to the indications and results of previous examinations that are uncertain or the localization of tumors that cannot be reached. Again, the best technique may be partly determined by the availability of local resources and their expertise in the biopsy technique and for interpreting samples in lung cancer patients. Because diagnosing a patient with lung cancer is not easy, bearing in mind that some patients can also perform pathological anatomy examinations up to >3 times to get a definite diagnosis, an

adequate and comprehensive examination is necessary.

Based on follow-up examinations carried out for target therapy in 2019 and 2020, patients who continue for EGFR, ALK, and/or PD-L1 examinations are obtained in the percentage results table as follows:

Table 10. Characteristics of Lung Cancer patients based on follow-up examination for therapeutic targets.

Year 2019		
Follow-Up Examination of Therapeutic Targets	**Frequency**	**Percentage (%)**
EGFR	26	46,4
ALK	None	-
PD-L1	None	-
EGFR, ALK	1	1,8
EGFR, PD-L1	3	5,4
Year 2020		
Follow-Up Examination of Therapeutic Targets	**Frequency**	**Percentage (%)**
EGFR	13	11,5
ALK	None	-
PD-L1	1	0,9
EGFR, ALK	None	-
EGFR, PD-L1	1	0,9
ALK, PD-L1	3	2,7
EGFR, ALK, PD-L1	22	19,5
No referrals	73	64,6
Total	113	100
ALK, PD-L1	None	-
EGFR, ALK, PD-L1	7	12,5
No referrals	19	33,9
Total	56	100

Research on lung cancer has continued to develop over the last few decades, especially in the biomolecular field, intending to find effective steps or options for better treatment plans for lung cancer patients. With that, the identification results indicate the existence of specific pathway mutations (molecular level) that play a role in the growth and replication of cancer cells. Based on that, targeted therapy was developed to block the mutation pathway in the hope of increasing the survival rate of lung cancer patients, especially for the type of NSCLC. [38] Targeted therapy will block the growth and spread of cancer cells by intervening with specific molecular targets involved in the growth, progression, and spread. These targets include EGFR and ALK, according to research by Hirsch et al., who identified overexpression of the EGFR protein (62%) in squamous cell NSCLC and ADC subtypes. Overexpression of EGFR is often associated with a poor prognosis. Other research is also reinforced by Tian X et al., who said that the sustained expression of EGFR is important not only in tumor development but also for its stability, and again EGFR-targeted therapy for EGFR-mutated lung adenocarcinoma is dramatically effective, thus demonstrating that EGFR mutations are directly involved in tumor maintenance. [39]

Regarding ALK, Inamura K et al. identified that a repeated gene fusion between EML4 (EML4; sometimes with other fusion partners) and ALK occurs in 7% of NSCLC, resulting in strong activation of the ALK fusion protein. The ALK fusion protein is usually found in subjects who have never smoked. Although relatively rare, a relative deficiency of fusion proteins is known to contribute to the pathogenesis of lung cancer. However, the current understanding of the ALK fusion protein is limited. Thus, it may support ADC histology and never-smoker status. [40] Whereas PD-L1 is a target in immunotherapy methods which simply enhances the immune system by reducing autoimmunity or autodestruction. PD-1 plays an important role in regulating T-cells and increasing self-tolerance. However, it also makes the immune system less effective against tumor cells. PD-1 interacts with two proteins: PD-L1 and PD-L2. And this binding causes the inactivation of T cells. [17] Thus blocking PD-L1 is one

way to prevent cancer cells from inactivating T cells in the tumor microenvironment. In the end, doctors or hospitals began to gradually implement follow-up examinations for these therapeutic targets. Following a recent publication by Nicholson et al., systemic therapy between 2013 and 2016 showed that the mortality rate due to NSCLC decreased significantly from the incidence. This decrease has been associated with an increase in survival rate according to the time of approval of targeted therapy. It reflects the impact of the clinical application of EGFR and ALK-blocking agents in patients whose tumors have specific genomic disorders. Also, related immunotherapy is expected to further improve the five-year survival rate of NSCLC in the next few years. [41] The table above shows that Siloam MRCCC Semanggi Hospital has also implemented follow-up examinations for therapeutic targets; in 2019, 56 records of anatomical pathology examination were obtained, and 37 of them were advised to carry out EGFR, ALK, and PD-L1 examinations. In 2020, out of 113 archives, 40 were also recommended for a therapeutic target examination. It is certainly a positive thing to increase the effectiveness of treatment plans for lung cancer patients through targeted therapy. Of course, not all of them perform follow-up examinations for therapeutic targets. It can be ascertained because one of the important factors that also influence it is the availability of specimens or the number of cells that are insufficient to carry out further examinations, especially EGFR, or also ALK, and PD-L1. Furthermore, another factor was due to histopathological diagnosis, which found not only the type of NSCLC but also SCLC or other types of lung cancer because SCLC has different treatment options, namely surgery or chemotherapy. Compared with chemotherapy, targeted therapy works on specific molecular targets, while chemotherapy works on all cells that replicate rapidly, both cancer and normal cells.

CONCLUSION

A lung cancer diagnosis is not easy, especially in early lesions. There is no explanation or correlation that the COVID-19 pandemic underlies the change in the number of lung cancer cases. So based on the objectives, results and discussion of research conducted at Siloam MRCCC Semanggi Hospital in 2019-2020 regarding the description of the characteristics of lung cancer during a pandemic with a total of 169 files or samples in patients, it can be concluded as follows: a) Lung cancer incidence by age most widely distributed in the age group of 60-69 years as many as 60 cases (35.5%); b) The majority of lung cancer cases based on gender were male, namely 99 cases (58.6%); c) The highest incidence of lung cancer by type was the subtype of non-small cell lung carcinoma, Adenocarcinoma with 119 cases (70.4%); d) Based on histopathological diagnosis, the most frequently diagnosed lung cancer was positive adenocarcinoma in 61 cases (36.1%); e) The incidence of lung cancer based on specimen collection technique was mostly tissue biopsy for histopathological examination in 27 cases (15.9%) and pleural effusion on cytological examination in 55 cases (32.5%); f) The incidence of lung cancer based on follow-up examinations for therapeutic targets, namely EGFR, ALK, and PD-L1, there were 77 cases that were recommended to continue the examination (45.5%); and g) The incidence of lung cancer diagnosed at Siloam MRCCC Semanggi Hospital has increased from 56 cases in 2019 to 113 cases in 2020 during the COVID-19 pandemic. There is no direct connection with the virus infection, but because the patient's sense of alertness has increased during a pandemic or diagnosed during COVID-19 screening tests or periodic medical check-ups, which have also increased.

Declaration by Authors

Ethical Approval: Approved
Acknowledgement: None
Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Dictionary ND. National Cancer Institute at the National Institutes of Health.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2018 Nov;68(6):394-424.
3. Gomez DR, Liao Z. Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). InTarget Volume Delineation and Field Setup: A Practical Guide for Conformal and Intensity-Modulated Radiation Therapy 2012 Aug 4 (pp. 87-103). Berlin, Heidelberg: Springer Berlin Heidelberg.
4. World Health Organization. International Agency for Research on Cancer 2021: Estimated Number of New Cases in 2020, Worldwide, Both Sexes, All Ages. World Health Organization: Geneva, Switzerland. 2021.
5. Pangribowo S. Beban Kanker di Indonesia. Pusat Data Dan Informasi Kesehatan Kementerian Kesehatan RI. 2019:1-6.
6. Nasional KP. Pedoman nasional pelayanan kedokteran kanker paru. Hasil dan diskusi. Edisi pertama. Jakarta: Kementerian Kesehatan Republik Indonesia. 2017:1-75.
7. Passaro A, Bestvina C, Velez MV, Garassino MC, Garon E, Peters S. Severity of COVID-19 in patients with lung cancer: evidence and challenges. Journal for ImmunoTherapy of Cancer. 2021;9(3).
8. Paulsen F, Waschke J. Sobotta Atlas of Anatomy, Vol. 2, English/Latin: Internal Organs. " Elsevier, Urban&FischerVerlag"; 2018 Aug 20.
9. Netter FH. Netter Atlas of Human Anatomy: Classic Regional Approach-Ebook. Elsevier Health Sciences; 2022 Feb 19.
10. Mukunda Rao M. Influence of Controlled Breathing (Pranayama) on Dermal Perfusion. Studies in Skin Perfusion Dynamics: Photoplethysmography and its Applications in Medical Diagnostics. 2021:33-50.
11. Dickinson JW, Hull JH, editors. Complete Guide to Respiratory Care in Athletes. Routledge; 2020 Jul 21.
12. West JB, Luks AM. West's Respiratory Physiology. Lippincott Williams & Wilkins; 2020 Sep 10.
13. Hall JE, Hall ME. Guyton and Hall textbook of medical physiology e-Book. Elsevier Health Sciences; 2020 Jun 13.
14. Harkema JR, Wagner JG. Pathology of the respiratory system. Toxicologic Pathology for Non-Pathologists. 2019:311-54.
15. Baldassi D, Gabold B, Merkel OM. Air−liquid Interface cultures of the healthy and diseased human respiratory tract: promises, challenges, and future directions. Advanced nanobiomed research. 2021 Jun;1(6):2000111.
16. Abo KM, de Aja JS, Lindstrom-Vautrin J, Alysandratos KD, Richards A, Garcia-de-Alba C, Huang J, Hix OT, Werder RB, Bullitt E, Hinds A. Air-liquid interface culture promotes maturation and allows environmental exposure of pluripotent stem cell–derived alveolar epithelium. JCI insight. 2022 Mar 3;7(6).
17. Noviana R, Rasal I, CL EU. Implementasi Algoritma Watershed untuk Segmentasi Nodul Kanker pada Citra CT Scan Kanker Paru. Skripsi. 2016.
18. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F. Global cancer observatory: cancer today. International Agency for Research on Cancer. Lyon, France. 2020.
19. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA: a cancer journal for clinicians. 2022 Jan;72(1):7-33.
20. Gondhowiardjo S, Christina N, Ganapati NP, Hawariy S, Radityamurti F, Jayalie VF, Octavianus S, Prawira Putra A, Sekarutami SM, Prajogi GB, Giselvania A. Five-year cancer epidemiology at the national referral hospital: hospital-based cancer registry data in Indonesia. JCO global oncology. 2021 Feb;5(1):190-203.
21. Choi H, Park HY, Han K, Yoo J, Shin SH, Yang B, Kim Y, Park TS, Park DW, Moon JY, Ra SW. Non–cystic fibrosis bronchiectasis increases the risk of lung cancer independent of smoking status. Annals of the American Thoracic Society. 2022 Sep;19(9):1551-60.
22. Cabry Jr R, Ballyamanda S, Kraft M, Hong E. Understanding paraneoplastic syndromes in athletes. Current Sports Medicine Reports. 2013 Jan 1;12(1):33-40.
23. Skowronek J. Brachytherapy in the treatment of lung cancer–a valuable solution. Journal of Contemporary Brachytherapy. 2015 Aug 1;7(4):297-311.

24. Latacz E, Van Dam PJ, Vanhove C, Llado L, Descamps B, Ruiz N, Joye I, Grünhagen D, Van Laere S, Dirix P, Mollevi DG. Can medical imaging identify the histopathological growth patterns of liver metastases?. InSeminars in Cancer Biology 2021 Jun 1 (Vol. 71, pp. 33-41). Academic Press.
25. Rudin CM, Brambilla E, Faivre-Finn C, Sage J. Small-cell lung cancer. Nature Reviews Disease Primers. 2021 Jan 14;7(1):3.
26. Siddiqui F, Siddiqui AH. Lung Cancer. StatPearls.
27. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it. Brazilian Journal of Implantology and Health Sciences. 2020 Mar 24;2(3).
28. World Health Organization. Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations: scientific brief, 29 March 2020. World Health Organization; 2020.
29. Addeo A, Obeid M, Friedlaender A. COVID-19 and lung cancer: risks, mechanisms and treatment interactions. Journal for immunotherapy of cancer. 2020;8(1).
30. Peng X, Long G, Yan P, Tang W, Clarke A. COVID-19 Impact Analysis on Patients with Complex Health Conditions: A Literature Review.
31. Rizkiansyah I. *Prosedur Pemeriksaan LDCT Scan Thorax pada Pasien OTG dengan Hasil Rapid Test Reaktif (Studi Kasus di Rumah Sakit Islam Jombang)* (Doctoral dissertation, UNIVERSITAS AIRLANGGA).
32. Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, Davis EM, Donahue KE, Doubeni CA, Kubik M, Landefeld CS. Screening for lung cancer: US Preventive Services Task Force recommendation statement. Jama. 2021 Mar 9;325(10):962-70.
33. Kiyohara C, Ohno Y. Sex differences in lung cancer susceptibility: a review. Gender medicine. 2010 Oct 1;7(5):381-401.
34. Cruz CS, Tanoue LT, Matthay RA. Lung cancer: epidemiology, etiology, and prevention. Clinics in chest medicine. 2011 Dec 1;32(4):605-44.
35. Brambilla E, Gazdar A. Pathogenesis of lung cancer signalling pathways: roadmap for therapies. European Respiratory Journal. 2009 Jun 1;33(6):1485-97.
36. Inamura K. Lung cancer: understanding its molecular pathology and the 2015 WHO classification. Frontiers in oncology. 2017 Aug 28;7:193.
37. Preeti A, Sameer G, Kulranjan S, Abhinav SA, Preeti R, Sunita Y, Mati GM. Intra-operative frozen sections: experience at a tertiary care centre. Asian Pacific journal of cancer prevention: APJCP. 2016;17(12):5057.
38. Yuan M, Huang LL, Chen JH, Wu J, Xu Q. The emerging treatment landscape of targeted therapy in non-small-cell lung cancer. Signal transduction and targeted therapy. 2019 Dec 17;4(1):61.
39. Tian X, Gu T, Lee MH, Dong Z. Challenge and countermeasures for EGFR targeted therapy in non-small cell lung cancer. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer. 2022 Jan 1;1877(1):188645.
40. Inamura K. Update on immunohistochemistry for the diagnosis of lung cancer. Cancers. 2018 Mar 14;10(3):72.
41. Nicholson AG, Tsao MS, Beasley MB, Borczuk AC, Brambilla E, Cooper WA, Dacic S, Jain D, Kerr KM, Lantuejoul S, Noguchi M. The 2021 WHO classification of lung tumors: impact of advances since 2015. Journal of Thoracic Oncology. 2022 Mar 1;17(3):362-87.

******