An Overview of the Clinical Management and Challenges of Treatments for the Patients Diagnosed with COVID-19 and Lung Carcinoma

By

Israt Zerin Bristy

ID: 17346053

A project submitted to the Department of Pharmacy in partial fulfillment
of the requirements for the degree of
Bachelor of Pharmacy (Hons.)

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Declaration

It is hereby declared that

1. The project submitted is my own original work while completing Bachelor of Pharmacy at Brac University.
2. The project does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The project does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

Israt Zerin Bristy
17346053

Approval

The project titled "An Overview of the Clinical Management and Challenges to Treat the Patients Diagnosed with COVID-19 Patients and Lung Carcinoma" submitted by

1. Israt Zerin Bristy, ID: 17346053

Of Summer 2020, has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on 10th June.

Examining Committee:

Thesis Supervisor:

____

Md. Tanvir Kabir
Senior Lecturer
Department of Pharmacy,
Brac University

Program Coordinator:

____

Professor Dr. Hasina Yasmin
Department of Pharmacy,
Brac University

Departmental Chairperson:

____

Professor Dr. Eva Rahman Kabir
Chairperson, Department of Pharmacy,
Brac University

Ethics Statement

This is to certify that this project titled "An Overview of the Clinical Management and Challenges to Treat the Patients Diagnosed with COVID-19 Patients and Lung Carcinoma" is submitted for the partial fulfilment of the requirements for the degree of Bachelor of Pharmacy (Hons.) from the Department of Pharmacy, BRAC University constitutes my own work under the supervision of Md. Tanvir Kabir, Senior Lecturer, Department of Pharmacy, BRAC University and I have given appropriate credit where I have used language, ideas or writings of another. No animals were used or harmed in this project.

Abstract

During the COVID-19 disease outbreak, the main objective of lung carcinoma treatment is to reduce the risk of contamination to patients and workers while simultaneously controlling all life-threatening elements of the illness. The pathophysiology of the development of lung cancer includes multiple genetic mutations, chromosomal abnormalities, and the presence of viruses. Nucleic acid SARS-CoV-2 detection & nasopharyngeal swab is used in the diagnosis of COVID-19 as well as an image-guided biopsy low-dose computed tomography is utilized for lung cancer identification. Furthermore, the challenging task of the management of chemotherapy, immunotherapy, therapeutic objectives, or optimal support services should be adjusted to the tumour types of the patient, the biomarkers, taking into consideration the risk of adverse effects and the potential of COVID-19 contamination. So, the overall treatment strategy of these patients is very prudent to avoid any further delay that could compromise survival with the challenges they are facing now.

Keywords: COVID-19, Lung carcinoma, Genetic mutation, Chemotherapy, Immunotherapy.

Dedication

Dedicated to the Chairperson of Department of Pharmacy, Prof. Dr. Eva Rahman Kabir and my supervisor Md. Tanvir Kabir

Acknowledgement

All honors belong to Allah for strengthening me with patience to complete my project work along with the courses necessary to complete the Bachelor of Pharmacy (B.Pharm) program. I am grateful to my respected supervisor, Md. Tanvir Kabir, Senior Lecturer, Department of Pharmacy, BRAC University for supporting me continuously and giving me the motivation to complete the project paper. Without his support it was not possible to finish my project work. I am also grateful to Prof. Dr. Eva Rahman Kabir, Honorable Chairperson, Department of Pharmacy, and BRAC University for giving me the support and opportunity to complete my project work and B.Pharm program.

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List of Acronyms

SARS-CoV-2	Severe Acute Respiratory Syndrome Corona virus 2
ACE2	Angiotensin converting enzyme 2
MERS	Middle East respiratory Syndrome
EBV	Epstein-Barr virus
TMPRSS2	Transmembrane protease, serine 2
RBD	Receptor Binding Domain
TNF- alpha	Tumor necrosis factor -alpha
MCP	Monocyte chemotic protein
PAH	Polycyclic aromatic hydrocarbons
ECMO	Extracorporeal membrane oxygen delivery
AT2	Angiotensin receptor 2
SCC	Squamous cell lung cancer
SCLC	Small cell lung cancer
SABR	Stereotactic ablative body radiotherapy
WBRT	Whole brain radiotherapy
ICIs	Immune checkpoint inhibitors
CCRT	Complementary chemoradiation
NACT	Neoadjuvant chemotherapy

TKI	Tyrosine kinase receptor
G-CSF	Granulocyte-colony-stimulating factor
CTLA	Cytotoxic T-lymphocyte Antigen
PD	Programmed cell death protein
NSCLC	Non-small cell lung carcinoma
CT	Computed Tomography
ECMO	Extracorporeal membrane oxygen delivery
SABR	Stereotactic ablative body radiology
ICI	Immune-checkpoint inhibitors

Chapter 1

Background

The COVID-19 coronavirus pandemic, an acute respiratory syndrome, is the highest public health concern of the current time. It made its first appearance in December 2019 in Wuhan, China. At first, this endemic disease spread in China's Wuhan, then extend to the entire world and was called a pandemic disease. COVID-19 has linked to about 14.9 million confirmed cases and over 610,000 fatalities globally as of July 22, 2020, causing widespread concerns (WHO, 2020). Also, COVID-19 harms the worldwide health system with substantial morbidity and mortality. COVID-19 has affected millions of people worldwide and, at unprecedented rates, has emerged as an epidemic, killing around 4.5 million people till now (Bakhribah et al., 2020).

Since it is a contagious disease, it poses a high risk to individuals who have auto-immune diseases in the lungs, or other respiratory problems, that are a significant cause of lung carcinoma. Patients with lung carcinoma are more likely to develop COVID-19 during the present disease outbreak and, more significantly, undergo a greater severity of the condition. They may also be at such an increased risk of COVID-19 respiratory depression. Lung carcinoma continues to be the most common cancer in terms of both prevalence and fatalities, with approximately 2.1 million individuals and 1.8 deaths worldwide in 2018 (Bray et al., 2018).

Patients with lung carcinoma and COVID-19 have worse clinical conditions than individuals with COVID-19 only, contrary to common opinion. Based on the prior experiences with this disease outbreak and the underlying issues that Lung carcinoma patients are confronting throughout this pandemic, some assumptions can be drawn about the challenges that patients with Lung carcinoma are facing, the emerging therapeutic scenario, and during the current

COVID-19 disease outbreak (Russano et al., 2020), successful clinical treatment of patients with lung carcinoma is critical. Due to the similarity of radiologic results, pulmonary effects, and the prevalence of systemic immunocompromised, there are numerous problems in the practice of medicine with lung carcinoma. Monoclonal antibody blockers are also commonly being used to cure lung carcinoma that is progressing. Even so, the substantial improvement in cancer care was a crucial move made globally, and patients who recovered from COVID-19 must be in the observation for tumour growth (Malkani & Usman, 2021).

Chapter 2

Introduction

The earth is now seeing the birth of a new disease outbreak, which is now wreaking havoc on people's lives, destroying property, and disrupting regular life. A disease outbreak is unique in its way. Ambiguity and fear are lessened by the knowledge what we are learning is new and mysterious. On the other hand, this pandemic contagious disease has posed a serious threat to humans across history. The progression of the disease pathogenesis has been classified as Severe Acute Respiratory Syndrome Coronavirus 2 by the International Virus Classification Commission (Gorbalenya et al., 2020). Coronaviruses are members of the Coronavirus genus, which is part of the *Coronaviridae* family and is a part of the Nidovirales order. Pathogens that live inside a single-stranded RNA membrane framework are known as single-stranded RNA envelope variants. SARS-CoV-2 is the seventh coronavirus to harm people as joining the Middle East respiratory syndrome-associated coronavirus (MERS-CoV) and the extreme acute respiratory syndrome-associated coronavirus (SARS-CoV) (Peiris et al., 2004).

Transmission of COVID-19 is reported by certain symptomatic and asymptomatic individuals, according to the WHO. Since bats are reported as the hosts of this virus's reservoir, the zoonotic is the origin of this virus (MacKenzie & Smith, 2020). Tang et al. found two distinct types of SARS-CoV2 in 103 clinical specimens: The L type that is thought to be much more offensive, and the one which is thought to evolve from the L type is the S type but has less combative characteristics (Tang et al., 2020). This highly contagious pathogen is transmitted by coughing or sneezing and aerosols, also close contact with mucosal surfaces, and possibly the faecal matter process (Xiao et al., 2020). The primary mode of transmission is the virus affects the human host's respiratory system mainly. For this virus, there is an incubation time of about five days. Throughout the lungs, the infection rate is quite high in that time. After 14 days of infection, there will be symptoms (Lauer et al., 2020). As a consequence, before being symptomatically established, SARS-CoV-2 is capable of massively propagating (Malkani & Usman, 2021). Temperature, coughing, nausea, anorexia, shortness of breath, mucus formation, and myalgia seem to be the most common signs of the illness, according to the Centers for Disease Control and Prevention (CDC), although a significant percentage of affected patients (43.8 percent) do not exhibit fever or radiological indications (Xiao et al., 2020).

No therapeutics that are successful against COVID-19 have been discovered yet. Regardless of the lack of clinical information, the US FDA permitted the use of chloroquine, as well as hydroxychloroquine in COVID-19 focused on in vitro experiments and a small, non-randomized study. According to laboratory findings, ACE 2 receptors interfere with antimalarial compounds by raising the pH of the recipient organism and inhibiting viral endocytosis (Cortegiani et al., 2020). The World Health Organization (WHO) briefly postponed the hydroxychloroquine risk management study in May 2020. Regardless of new facts, Remdesivir is indeed an antiviral medication that has shown in vitro efficacy towards SARS-CoV-2 by inhibiting RNA polymerase. The FDA has approved it for use in extreme COVID-19. The medicinal values of Remdesivir towards COVID-19 are debatable. Remdesivir's potential effectiveness in reducing by cure time for certain severe COVID-19 infections has been demonstrated in clinical trials (Beigel et al., 2020). Remdesivir, on the other hand, is still not proven to reduce infection rates in infected patients' nasal scrapings (Wang et al., 2020). The precise fatality rate from SARS-CoV-2 contamination is unknown. Although it varies from 0.3 per cent to 8.4 per cent globally. Therapeutic progress was found in 36 of the individuals in a previously reported cohort of 62 extreme COVID-19 individuals, (Grein et al., 2020).

Researchers in China examined the therapeutic effectiveness and pathogenesis of type 5 airborne COVID-19 adenovirus vaccines in 108 people and after only four weeks of vaccination (Folegatti et al., 2020) an immune response reaction to the vaccine has found on day 28 after vaccinations. The mRNA-1273 vaccine has had promising initial effects in the United States, and it is going to be implemented in Second Phase (Jackson et al., 2020).The old aged people and the ones having the presence of underlying health conditions, such as cancer increases the severity of the illness. The treatment of cancer patients is very complicated under these conditions as having weakened immunity increases the chances of being affected by COVID-19 (Ballout et al., 2020). Lung cancer develops lung cells to regrow or alter. This modification can be triggered by several factors. People breathing in toxic, dangerous substances, might trigger this type of transformation in lung cells often and when anyone is being prone to these contaminants for many years getting infected by lung carcinoma has a high possibility (Rubinstein et al., 2020). Tobacco utilization is indeed one of the leading causes of lung carcinoma due to the prevalence of carcinogens that promote cell conversion. Other factors that have been recently identified in lung carcinogenesis involve systemic inflammatory gene expression, hormonal imbalance, and pathogens, such as those caused by a virus or bacterial pathogens (Ordóñez-Mena et al., 2016).

Lung cancer is still the leading cause of death for both men and women in the United States with over 158,900 deaths in 1999. Every year, tobacco is thought to be the leading cause of 90% of male lung carcinoma cases deaths and 75-80% of female lung carcinoma cases deaths (Hecht, 2011). The risk of developing lung carcinoma from tobacco consumption varies by ethnicity: African American and Native Hawaiian smokers have a greater risk of getting cancer than white smokers, while Latino and Japanese smokers have a much-reduced chance. Besides that, lung carcinoma happens to be a gender-specific disease (Stapelfeld et al., 2020).

While men were shown to have the majority of lung tumours, a steady increase in women was observed (Witschi, 2001). In the last ten years, patient's lives have been prolonged due to improved treatment choices, and the number of cancer patients with high resistance capability has also increased. Because respiratory infections predominantly affect lung tissues, patients with advanced cellular breakdowns in the lungs who already have a weakened pneumonic capacity and a weakened immune system are more vulnerable to SARS-CoV-2 infections. Furthermore, lung cancer kills two people every minute, resulting in the deaths of over one million people each year around the world (Witschi, 2001). During the present pandemic, these patients are in danger of contracting COVID-19, a severe respiratory disease (SARS-CoV2). In malignant growth patients compared to the general people, SARS-CoV-2 infection is twice (Hsu & Wang, 2020). According to Yu et al., disease patients have a higher risk of being infected with SARS-CoV-2 than non-malignant growth patients (0.37 %), especially patients with the cellular breakdown in the lungs (7 out of 12 patients) and patients with cellular destruction in the lungs (0.79 %), who are at least 60 years old (Malkani & Usman, 2021).

Nonetheless, considering the multidisciplinary endeavours that were gathered, one should concede that the pandemic immensely affected the malignant growth of patients. The weakness of this patient group remains a concern when virtually every 30 days of mortality in patients with neoplasms and COVID-19 are considered to be greater. This mortality is specifically linked to risk parameters that are only available in cancer patients rather than general risk factors (Kuderer et al., 2020). One thing that should be taken into consideration is the need for specialized treatment in countries with medium-to-low incomes, where the number of cancer patients is also reduced due to financial limitations (Lemjabbar et al., 2015a). It has been generally debated that patients with cancer and COVID-19 had poorer health results than patients with COVID-19 alone (Kuderer et al., 2020). The COVID-19 differential test is used in patients with cellular breakdown in the lungs to see whether there are any other causes of fever and respiratory symptoms to screen out diseases other than COVID-19. It is prescribed to think about tumour movement or different conclusions like pneumonic edema in the differential determination (Xu et al., 2020).

Generally speaking, in this pandemic, conveying therapy to immunocompromised malignancy patients has ended up being really troublesome not due to raised danger of disease and demise, yet also because of an expanded requirement for ventilation or ICU section, accompanying with limited outpatient administrations, including authoritative faculty and trained professionals. Most lung cancer patient’s cellular decomposition is studied at the most advanced stages, and any further delay will harm the results. (Kattan et al., 2020; Wang et al., 2020). For this reason, evaluation is required in lung treatment when it comes to cell disintegration. Successful treatment of cellular breakdown in the lungs takes more than half a month and includes routine clinic visits and confirmation for tests, radiotherapy, chemotherapy, and other procedures, putting SARS-CoV-2 patients at risk of developing an immunocompromised condition. The board of patients with the cellular breakdown in the lungs during the COVID-19 pandemic isn't just a daunting challenge for oncologists, but also patients, because random visits to emergency clinics are limited to determining the distribution of SARS-CoV-2 (Shankar et al., 2020). In this review, we have focused on those vulnerable cancer patients who are exposed to COVID-19 about their cumulative care, and overall management to overcome the challenges during this pandemic.

Chapter 3

Pathophysiology of COVID-19

Following microbial dissemination, SARS-CoV-2 attaches to the layer of the nasopharynx epithelial layer, conjunctival mucosal borders, or the optical canal. Angiotensin-converting enzyme 2 (ACE 2) protein is upregulated on a range of psychological cell types, particularly type II alveolar cells (AT2), stomach, oropharyngeal, and ileal epithelium, cardiac tissue organelles, proximal renal tubule cell lines, and urothelial bladder tissues, and is thought to act as a mediator SARS-CoV2 incorporation (Zou et al., 2020). The pathogenic envelope plays an important part in the pathogenesis of the virus by assisting in viral aggregation development, and propagation (Schoeman et al., 2020). The viral RNA manipulates the infected cell's mechanism to start the development of the genetic material and membrane protein chains, as well as the replication-transcription complex (RCT), which is necessary to make both sub-genomic RNAs and cell membrane components envelope (outer shell and nucleoshell) (Khodor, 2020).

3.1 The Structure of Coronavirus

The subgroups of coronavirus include four primary groups (alpha, β, and μ). Coronaviruses include six members, including Cov-229E and CoV-HKU1, which are both associated with mammals. The human diseases CoV-OC43, SARS-CoV, and MERS-CoV are all part of the coronavirus family (Lefkowitz et al., 2018). SARS-CoV-2 is a coronavirus, and the amino acid patterns that within seven preserved regions inside the genetically accessible reading framework 1ab (ORF1ab) are 94.6 % similar to those of the actual SARS-CoV (Zhou et al., 2020b). Moreover, the coronavirus virion molecule is usually circular or multi-shaped. It has a triple Spike (S) protein petal-shaped extension, which is a normal coronavirus characteristic and extends 120-160 nm in diameter.

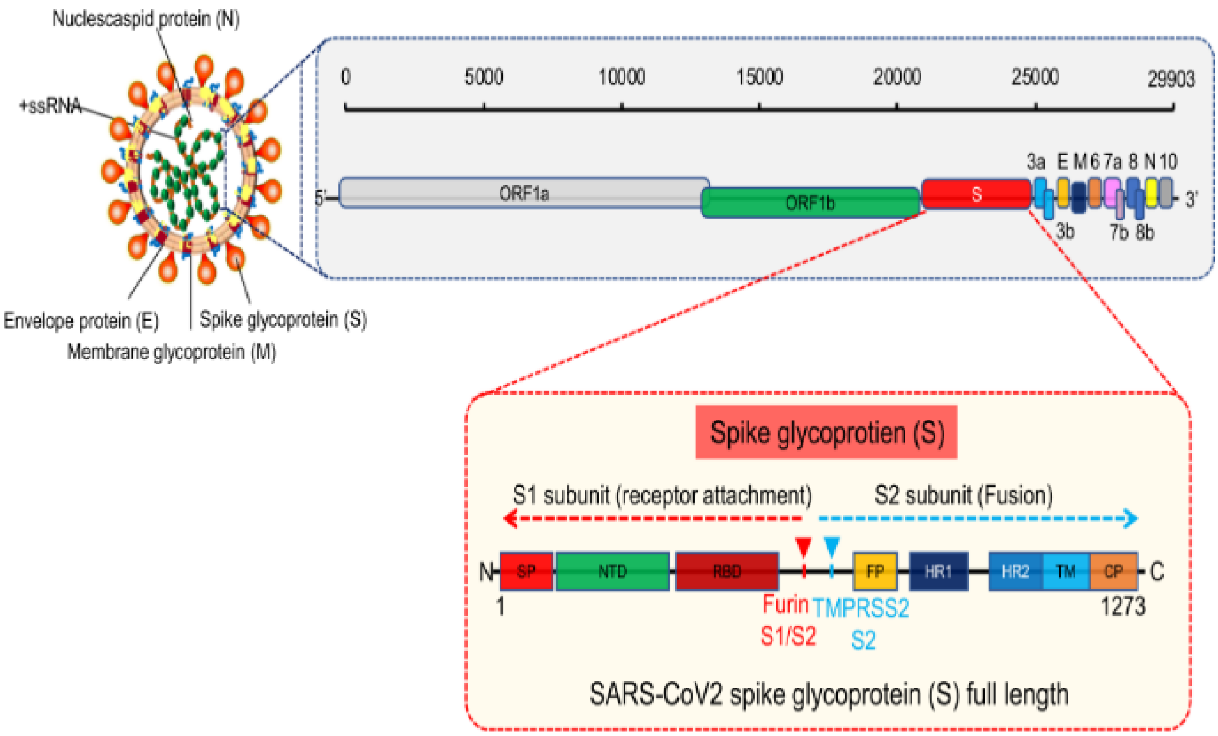

Figure 1: Representation of The Structure of SARS-CoV-2(Kumar & Al Khodor, 2020).

The S protein is involved in virus adhesion and cell fusion during contamination. Coronavirus genomes normally produce three primary protein molecules, such as the Membrane (M) protein, the Envelope (E) protein, and the Nucleocapsid (N) protein, in regards to the well-known S protein. The coronavirus M protein has a hydrophilic C-terminal tail and an O- or N-glycan-modified N-terminus. The E protein, which has a length of 74-109 amino acids and has about 20 copies per virion, can play a role in fostering pathogenicity. The coronavirus N protein, which has 349 to 470 amino acids, is a phosphorylated RNA-bound polypeptide that aids in the optimal replication of the virus. The coronavirus N protein, which has 349 to 470 amino acids, is a phosphorylated RNA-bound polypeptide that helps genomic RNA fold properly into the nucleocapsid (King et al., 2012).

3.2 SARS-CoV-2 S Receptor Binding Mechanism

The SARS-CoV-2 S protein amino acid sequence only shares minimal homology with that of SARS-CoV; the level of relatedness among the S1 domain is incredibly poor (64%) and comparatively large among the S2 domain (up to 90%). In both the S1 domain and the RBD (receptor binding domain) subdomain, the N-terminal area is normally less preserved (51%), whereas the C-terminal RBD subdomain is comparatively preserved (74%), providing for associations with a certain ACE2 cellular receptor (Jaimes et al., 2020). Inside the S1 RBD region of SARS-CoV-2, there are 4 - 5 distinctive amino acid sequence changes compared to SARS-CoV. X442, F472, C479, and N487 are amino acids present in the S protein series of SARS-CoV-22 (P. Zhou et al., 2020b). Inside a crucial sequence in the S1 RBD region, these modifications can impact receptor-mediated linking. Many organizations have already addressed this major issue Layer plasmon resonance electromagnetic biosensing, for example, was used to detect the linking of amounts as low as 15 nmol/L of the S1 region of SARS-CoV-2 in ACE2. These results suggest that the protein of SARS-S CoV-2 has a 10-20-fold greater specificity for this site than SARS-CoV. It is important to note that in silico studies of the ACE2 and S protein interactions of SARS-CoV-2 led to various conclusions, although these findings remain to be verified by in vitro and in vivo experiments (Huang & Herrmann, 2020; Lan et al., 2020).

3.3 SARS-CoV-2 Virulence Factors as a Result of Implantations in the S Nucleotide Sequences

SARS-CoV-2 is a highly transmissible coronavirus; transmission rate assessments indicate that it could be 3 and 10 times higher than SARS-CoV and MERS, respectively (Jiang & Shi, 2020). The S protein series, which contains one of the gene placements observed in the SARS-CoV-2 genomes, is closely linked to SARS-CoV-2 infectivity (Heurich et al., 2014; Millet & Whittaker, 2015). The S protein has a four-residue penetration immediately parallel to the cleavage region (Meng et al., 2020). Both SARS-CoV and MERS-CoV pathogens have been linked to TMPRSSs; TMPRSS and TMPRSS11a will precipitate the cleavage of the S protein into S1 and S2 (or S2') regions at the R667 and R797 residues (Heurich et al., 2014;

Millet, 2015). When the four amino acids in the insertion, P681, R682, R683, and A684, are combined with R685, they build an exposed ring, which increases protease resistance. The insertion series also created a protease cleavage site, and furin reported that TMPRSS1 and TMPRSS2 are S protein initiating proteases that contribute to SARS-CoV-2 linking and cell entrance (Hoffmann et al., 2020; Jaimes et al., 2020; Meng et al., 2020). Furthermore, they said that the loops formed by the injected residues made S proteins more susceptible to the protease-mediated midriff, making SARS-CoV-2 contamination easier. The entry pattern is special and has not been used in some other coronaviruses, including the bat coronavirus RaTG12 (Jaimes et al., 2020; P. Zhou et al., 2020b).

Chapter 4

Pathophysiology of Lung Cancer

Lung carcinoma is a disease that already has a high mortality rate, as well as a reduced overall survival of people who have been diagnosed. Novel genetic markers, including such exosomes, would be seen as possible screening methods for cancers, especially lung cancer. The nanovesicles are used as better molecular, diagnostic, and medicinal genetic markers in the treatment of lung cancer patients. Exosomes are being researched as drug molecules and targeted therapy in comparison to their therapeutic roles (Amiri et al., 2021). Lung cancer is the second most prevalent cancer in both genders and it is the highest health issue, accounting for 75–80% of cancer-related fatalities (Ferlay et al., 2019).

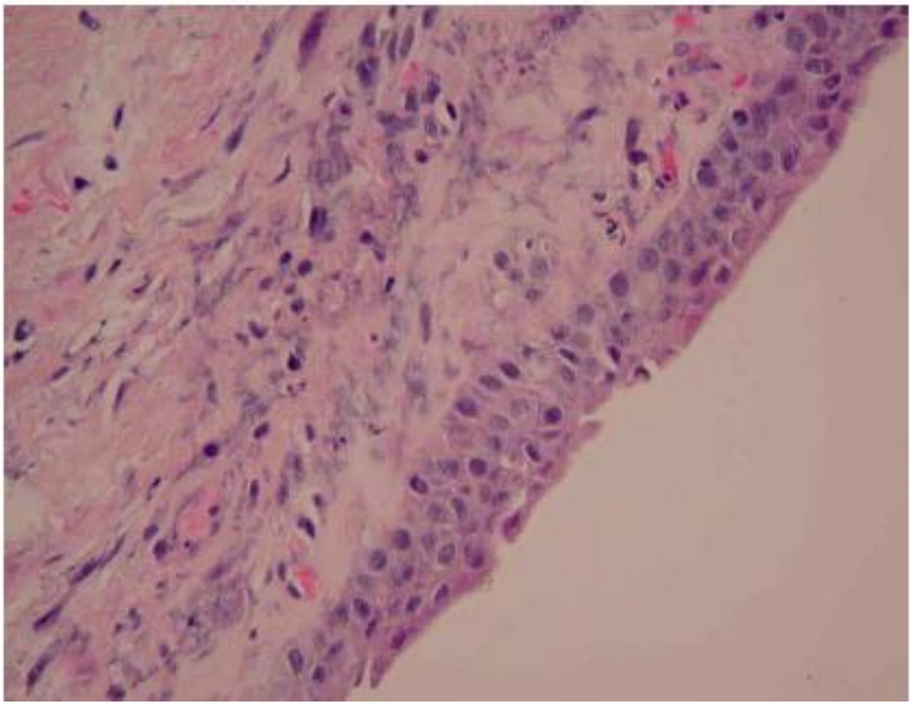

Figure 2: Lung Carcinoma in Situ (Microscopic Characteristics) (Ruffini et al., 2004).

4.1 Categorization of Lung Cancer

Lung cancer is a heterogeneous disorder that may occur in several locations all along the bronchial tree, specific features are associated depending on the tissue type and are divided into four groups (Steen, 2000). Squamous cell lung cancers (SCC) occur in the primary alveoli and extend to the carina, accounting for 25–30% of all lung cancer cases, whereas adenocarcinomas arise throughout the periphery alveoli and account for 40% of all lung cancers (Lemjabbar et al., 2015a). Small-cell lung carcinomas (SCLC) are cancers that suppress the standard glandular or squamous phenotype but show neuroendocrine differentiation, accounting for 15–20% of all lung malignancies (Lemjabbar et al., 2015b). SCC, adenocarcinomas, and large tumor carcinomas are all known as non-small cell lung carcinomas (NSCLC) because they vary from SCLC in terms of anatomy, molecular biology, and clinical features. Lung cancer is thought to be caused by a mixture of genes and environmental factors, including family background and polymorphisms. Cigarette smoking is the leading cause of lung cancer (Sasco et al., 2004; Youlden et al., 2008). Viral infections such as microorganisms (Lanoix et al., 2011; Littman et al., 2005; Stapelfeld et al., 2020) have been reported as elevated factors in some recent research (Cheng et al., 2001; Kheir et al., 2019; Robinson et al., 2016; Syrjänen, 2002).

4.2 The Causes and Prognosis of Lung Cancer

The pathophysiology of lung cancer necessitates the accumulation of multiple genetic mutations over a long time (Massion & Carbone, 2003). The genomic disorder is systematically formed during the accumulation of these results (Lawrence, 1991). At the point of genetic suppression, the adjustments may take the form of methylation, Genomic DNA variations, DNA section multiplication or removal, or even whole chromosome benefits or losses. These alterations begin rapidly in standard specimens that lack cancer-like characteristics. Microdissection of bronchial epithelium abnormalities, and also intrusive cancers, produced standardized specimens for the analysis of genetic alterations (*Europepmc*, n.d.), chromosomal deletions (Sundaresan et al., 1992), microsatellite instability (Mao et al., 1994; Miozzo et al., 1996), and DNA methylation trends (Belinsky et al., 1996).

4.2.1 Changes in the Gene

Somatic genes have been described and related to the growth of tumours over the last twenty years. These tumour suppressor genes or oncogene variations might not be rate-limiting incidents. Observational studies evidence suggests that some kinds of tissues develop a variety of main variations (Steen, 2000). According to Loeb's concept including its mutator genes, tissues contain a proclivity for genetic variations earlier in existence (L A Loeb, 1991). While this phenomenon can be inherited, the primary mutations are still to be established. DNA disruption throughout the lungs can lead to disincorporated nucleotides and, as a consequence, alterations occur. DNA polymerase-caused random recombination mistakes occur in the process of 1/10,000 to 1/100,000 DNA sequence, relying on the polymerase. These intrinsic variations in K-ras, p53, and p16 can play a role in tumours progression and, finally, cancer progression.

If mutations occur K-ras may change respiratory epithelium by triggering the ERK-MAP kinase pathway (Lacal et al., 1986; Nikliński et al., 2001). It may be a crucial step in the development of this lung cancer subgroup. This theory is reinforced by the fact that genetically mutated K-ras genes acquire lung malignancies (Cooper et al., 1997). Squamous and small-cell carcinomas of the lungs are now the most prominent tumours with p53 genetic variation which is very prominent in tumour progression (Harris, 1995). Once p53 is mutations occur, it becomes a tumour suppressor gene that accumulates in the cell membrane (Pietenpol, 2001). Since mutant p53 has a long 1/2 life, immunohistochemistry can detect it associated with mutations in around 1/2 of malignant tumours on the lungs (Carbone et al., 1994). NSCLCs have inactivated p16, an oncogene. It includes the DNA methylation of the genome include different techniques of inhibition, according to earlier reports (Belinsky, 1998). As a cause of the lack of p16 features, genetic variants or homozygous deletions are even more commonly observed in lung cancer cells occurring in cigarette smoking. The correlation between cigarettes and p16 losses indicates that cigarettes can play a role in lung carcinoma pathogenesis in alternative forms (Cespedes et al., 2001).

4.2.2 Disruption in the Genome

The heterogeneity of the gene is a central aspect of cancer formation and development. Instability can be caused by several causes. Mutation induces chromosomal dysfunction at the gene sequences stage in a tiny proportion of lung tumour cells. In many other cancers, adrenal hyperplasia (abnormal number of chromosomes amount) is the most common characteristic (Lengauer et al., 1997). The emergence of anatomy, lack of cell death oversight and regulation of tumour growth, and the aggregation of alterations are all related to deteriorating dysplasia gene variants and may represent underlying dysfunction of pathways that control genetic conformity. The meaning of particular DNA restoration deficiencies in lung cancer is much less apparent than mitochondrial dysfunction. Polymorphisms in the DNA mismatch repair gene XPD (codon 312 Asp/Asp vs Asp/Asn) have previously been related to reduced DNA mismatch repair performance and cell death activity in lung carcinoma (Butkiewicz et al., 2001). Nevertheless, recent technologies enable us to examine these improvements in single or small groups of preneoplastic cells. FISH detectors can detect differences in copy numbers in single cells. Target mutations (Chung et al., 1995), chromosomal removals (Sundaresan et al., 1992), chromosomal dysfunction (Mao et al., 1994; Miozzo et al., 1996), and DNA methylation trends have all been analysed using isolated specimen collected through microdissection of dysplastic epithelial cells (Cespedes et al., 2001). As a consequence, a systematic sequence of growth for genetic disorders in preneoplastic respiratory epithelium can be derived.

4.2.3 Variations in the Chromosome

Cancerous cells have a variety of chromosomal abnormalities, namely removals and errors in cell division processes, in addition to genetic variations (Mitelman et al., 1997). The chromosomal areas with its most widespread damages are those that code for important tumour suppressors and DNA repair genes, which may play a pathogenic role in a variety of malignant tumours (Knuutila et al., 1999). Lung carcinoma genomes also contain huge regions of removals (e.g., chromosome 3p, 9p) or modifiers (e.g., 1q, 3q). SqCa has been shown to have a higher incidence of genetic modifications than adenoma of the lung, as measured by depletion of heterozygosity (Sato et al., 1994; Wistuba et al., 2000).

4.3 Viruses in the Development of Lung Cancer

The evolution of transgenic models utilizing viral antigens, such as SV40 mass Percentage antigen and polyomavirus (PyV) broad and mid T antigens, has resulted in a greater prevalence of tumours due to a better knowledge of lung cancer genomic strategies. Although the pulmonary virus has not been definitively linked to lung carcinoma, some have been suspected. For example, the human papillomavirus (HPV) has been linked to lung cancer, especially lung carcinoma in females (Cheng et al., 2001).

In response to the current coronavirus outbreak 2019 (COVID-19), other pathogens along with coronaviruses have been involved in multiple pulmonary infectious diseases such as pneumonia, upper respiratory tract disorders, severe acute respiratory syndrome (SARS), and Middle-East respiratory syndrome (MERS) (Vijayanand et al., 2004). Simian Virus 40 has been implicated in the pathogenesis of mesothelioma (Testa et al., 1998), and Epstein-Barr Virus (EBV) has been connected to the presence of papilloma, mesotheliomas, and pulmonary malignancies. Some PCR-based tests, on the other hand, have failed to link bronchogenic tumours to viral pathogens. That involvement of viral infection in respiratory epithelium transformation could be examined using significant advancements in proteomics. The discovery of peptides relevant to infections that are sometimes neglected in tumour growth could be possible using genome sequencing of cancers. Pathogens are most often used in in vivo regenerative medicine of mammalian lung carcinoma using adventurous p53 transmitted by a retrovirus (e.g., adenovirus-mediated gene transfer) (Carbone & Minna, 1994).

Chapter 5

COVID19 Progression, Pathological Characteristics, and Effects on Lung Carcinoma Patients

The involvement of the SARS-CoV-2 coronavirus in lung carcinoma patients is indeed unknown. Cancer patients, particularly lung carcinoma, are at an increased risk of suffering serious health problems as a result of SARS-CoV-2 disease, so critical steps to reduce the risk of disease for this number of participants must be addressed. Furthermore, comprehensive biomolecular research is necessary to know the virus's mode of action, which could lead to a better understanding of the pathways linking SARS-CoV-2 to cancer, particularly lung carcinoma, as well as the therapeutic effects of numerous SARS-CoV-2 blockers (Vijayanand et al., 2004).

5.1 Primary Access Genes of SARS-CoV-2 and Lung Carcinoma

In several cases, β-coronavirus is the causal factor, which leads to the discovery of SARS-CoV-2 (Zhou et al., 2020a). The genetic study placed SARS-CoV-2 in the genus Beta coronavirus and subgenus Sarbecovirus (lineage B), establishing its relation to bat coronavirus (BatCoV RaTG13) (Zhou et al., 2020a; Zhu et al., 2020). Additional investigation revealed even a specific amino acid discrepancy amongst SARS-COV as well as the pangolin Coronavirus, indicating a possible intermediate host (Zhang et al., 2020). The coronavirus S protein has 2 key domain names: S1 is the ligand region, and S2 is a specific region that aids in the plasma membrane (Shen et al., 2017). Another of the unique characteristics including its coronavirus S protein is whether it contains several proteolytic cleavage sites; the very first identified cleavage place is situated at the S1/S2 border, whereas the second is located in the S2 upward of the prospective viral envelope (Millet & Whittaker, 2015). Until cleavage of the spike glycoprotein, the S1 and S2 regions retain non-covalently connected; since cleavage of the spike glycoprotein, the S1 domain separates itself against the protein's S2 stem region (Belouzard et al., 2012; Millet & Whittaker, 2015; Reguera et al., 2014).

Only at the molecular level, the epithelium is recognized by a metallopeptidase and penetrates the pulmonary tract's host epithelial membrane. SARS-CoV-2, like SARS-CoV-2, requires angiotensin conversion enzyme II (ACE-2) for virus replication; ACE-2 is a cytoplasmic regulator that regulates the renin-angiotensin mechanism by breaking angiotensin II (RAS) (Riordan, 2003). To facilitate cell membrane breakdown and endocytosis, the microbial S protein communicates with the ACE-2 regulator; this process is regulated by type II intracellular serine proteases and appears to be dependent on S protein (TTSPs) (Iwata-Yoshikawa et al., 2019; Matsuyama et al., 2010). TTSPs, such as TMPRSS2 and TMPRSS11D, are associated with spiked polymer cleavage and activate SARS-CoV-2, enabling cytoplasmic entry into the body part far enough (Heurich et al., 2014). This implies that TTSPs can contribute to SARS-CoV-2 disorder and spread. Enhanced proteases have been found in both SARS-CoV-2 and non-SARS-CoV-2 distribution, most of which are FURIN. There are four simultaneous FURIN cut sites in the SARS-CoV-2 protein, namely SARS-CoV-2 (PRRA motif) (Coutard et al., 2020). Even after ligand binding, the FURIN protease allows for efficient cleavage of the SARS-CoV-2 enzyme (Coutard et al., 2020), which enhances viral replication in the infected individual (Burkard et al., 2014; Millet & Whittaker, 2014).

SARS-CoV-2 is transmitted primarily via person pulmonary epithelial tissue. A loss of TMPRSS2 activity in the respiratory system caused by SARS-CoV-2 infection resulted in intense lung injury (Shen et al., 2017). According to an in-vivo study, TMPRSS2 caused the spread of SARS-CoV-2 in infected mice (Zhou et al., 2015). SARS-CoV-2 transcription was missing in the respiratory and bronchioles in TMPRSS2-deficient mice, according to a recent report. Besides that, in TMPRSS2-deficient mice, CoV-2 diffusion and inflammatory aggregation were observed in the respiratory tract, as well as the formation and action of many other serine proteases, as well as the transition of SARS-CoV-2 and MERS-CoV-2 to bronchial areas (Shen et al., 2017). TMPRSS4 is detected in lung carcinoma (Jung et al., 2008) and the mammalian trachea (Yamaya et al., 2015), whereas TMPRSS11D is identified in mammals' alveoli and the trachea (Yamaoka et al., 1998; Yamaya et al., 2015; Yasuoka et al., 1997).

In the existence of lung carcinoma and COVID-19, proteolytic breakdown of cellular membranes (collagens, laminins, and elastin) causes extreme breathing problems (Zhao et al., 2010). People with lung carcinoma are more vulnerable to COVID–19 because they are usually likely to smoke and elderly patients may develop therapy immunologic dysfunction (Passaro et al., 2020; Zhao et al., 2020). People who smoke are more susceptible to COVID-19 and are at an increased incidence of respiratory illness, particularly lung carcinoma. Studies show the histopathologic modifications and inflammation in ARDS caused by smoking-induced lung damage are most likely caused by the difference in the ACE/ACE-2 cascade (Yilin et al., 2015).

5.2 SARS-CoV-2 Scanning Characteristics and Significance for Lung Carcinoma

Compaction with limited situations of pleural effusion is a common chest radiographic characteristic in COVID-19 people (Wong et al., 2020). With a resolution of 30% to 70%, chest radiographs are therefore effective in detecting COVID-19 (Yoon et al., 2020). Besides that, due to existing experimental shortcomings and kit results, the generally positive level of RT-PCR from nasopharyngeal smears has been confirmed to be 59% at the beginning of the group demonstration (Ai et al., 2020). In this context, European radiologists evaluated its use of 1st screening diagnostic radiographs using contemporary research (Wong et al., 2020). An International Consensus Declaration on Recording Chest Computed Tomography (CT) Observations Relevant to COVID-19 was previously released by the Radiological Society of North America (Simpson et al., 2020). It, therefore, tries to classify COVID-19 pneumonia CT results into four categories: typical, indeterminate, atypical, and negative for pneumonia (Simpson et al., 2020). Peripheral, bilateral ground-glass opacities (GGOs) both with and without accumulation or clear intralobular lines (crazy paving), multifocal GGO or rounded cellular structure with or without accumulation or recognizable intralobular lines, reverse halo sign, or other coordinating pneumonia observations are classified as common CT manifestations unique for COVID-19 pneumonia (seen later in the disease).

The following are the key COVID-19 CT observations dependent on the period of symptom initiation as mentioned so far (Kanne et al., 2020; Rodrigues et al., 2020). The early stage starts between 0-4days after the onset of flulike symptoms. The normal CT scans in up to 50% of patients or scans with small subpleural GGO, mainly in the lower lobes are seen in (Figure 3A). Typical CT findings are infrequently observed.

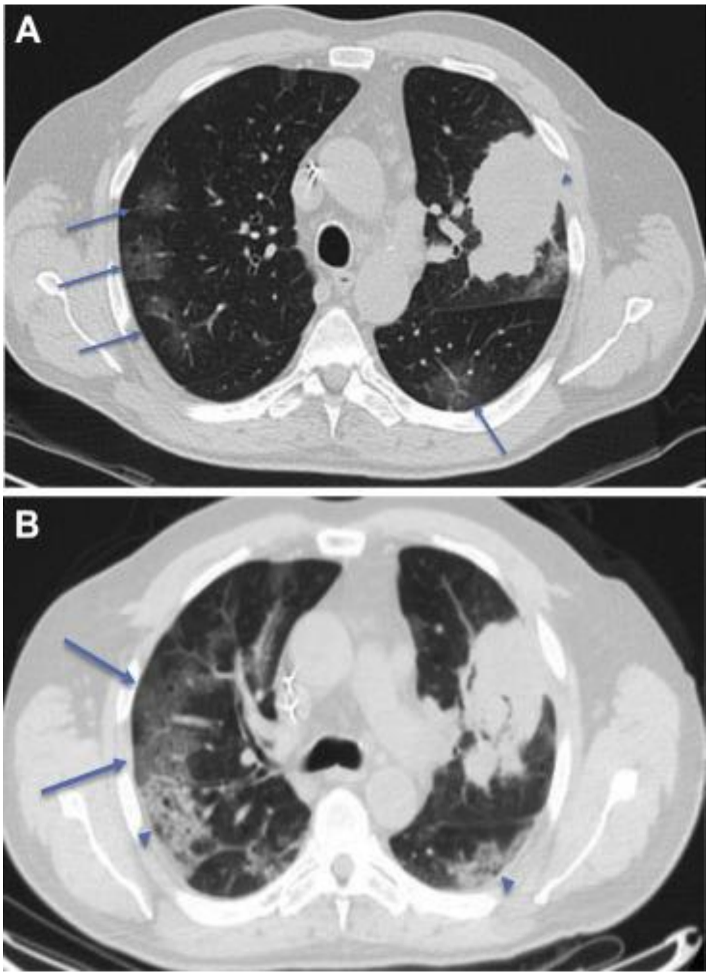

Figure 3: Early Phase of the Initial of Flulike Side Effects (Dingemans et al., 2020).

This period begins 5-8 days following the onset of symptoms, peripheral focal or multifocal GGO involves both lungs in 50% to 75% of patients, and then rapidly develops into the irrational construction and regions of convergence, the importance linked to both lungs (Figure 3B). On average, the situation worsens nine to thirteen days after the onset of side effects. As the illness progresses, illogical construction and the accumulation of air bronchograms are the most common symptoms (Figure 4A and B).

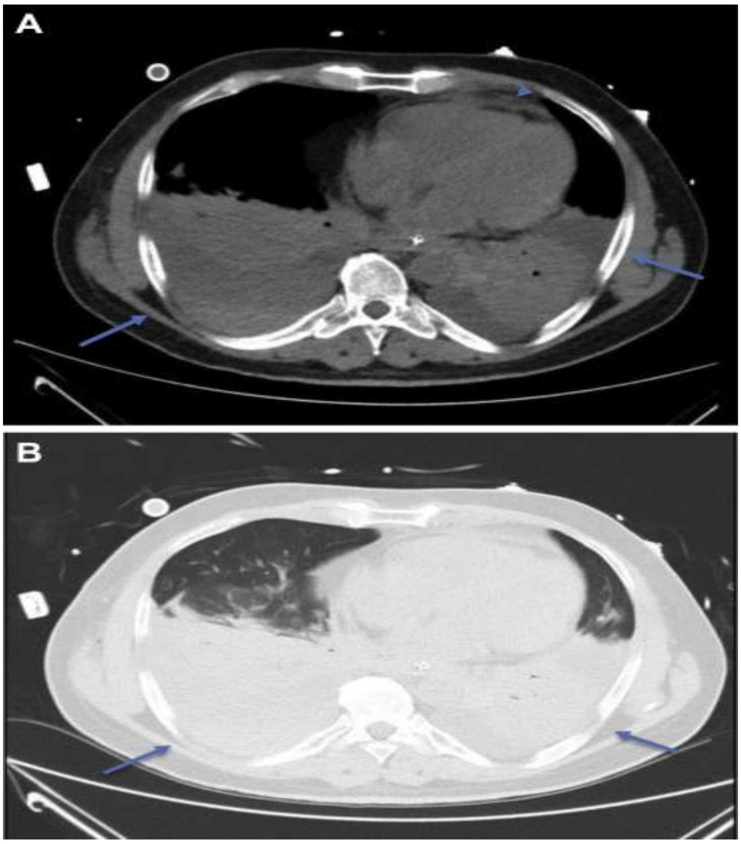

Figure 4: An Axial CT Photographs Mediastinum and Lungs (Dingemans et al., 2020).

These phases are accompanied by a gradual clearance that begins about one month after the initial diagnosis (but not before). CT image preferences for COVID-19 were stated to range from 60% to 98%, but precision was poor (25% to 53%) (Song et al., 2020). Since scanning results are not unique and may coincide with many other pathogens and respiratory failure propagating as assembling pneumonia trend from a drug overdose, elastic fibres disorder, or idiopathic causes, the American College of Radiology does not consider using a pulmonary radiograph or CT for COVID-19 assessment of patients without indications (Song et al., 2020). After all, a CT scan can allow the diagnostic also more possible in symptomatic associated with an increased presumption of COVID-19 but a negative PCR, particularly in those without respiratory complications (Dingemans et al., 2020; Guan et al., 2020).

Chapter 6

Diagnosis Strategies of COVID-19 Patients and Lung Carcinoma

6.1 Diagnostic Strategies of COVID-19

As per the WHO and the CDC, the most recent diagnostic strategy is SARS-CoV-2 nucleic acid detection. Reverse transcriptase-polymerase chain reaction (RT-PCR) is the essential diagnostic technique used to treat SARS-CoV-2, and also the most general method is used to collect a suitable specimen is a nasopharyngeal swab (Loeffelholz & Tang, 2020). SARS-CoV-2 selectively propagates in type II alveolar cells (AT2), and the height of viral shedding appears three to five days just after the appearance of the viral infection. Consequently, because of the relatively low poor prognostic impact, the immediate negative nucleic acid result does not prevent a better outcome for the coming months. Appropriate samples include above airways (pharyngeal swabs, nasal swabs, nasopharyngeal mucus), below airways (sputum, bronchoalveolar lavage fluid specimens), along with blood, feces, vomiting, and conjunctival fluids. In Sputum as well as other low respiratory tract samples, there is a large statistical rate of nucleic acids (World Health Organization, 2020). Psychiatric symptoms and radiological characteristics at which the test specimen is insufficient will rely on the evaluation and case report (Liang, 2020). Moreover, Serologic research is currently advancing. After all, due to the obvious imprecision of a variety of tests and, quite significantly, the latency from the onset of diagnosis to the production of antibodies, such tests should rather serve as a significant method for observational studies populace research, whereas reverse transcription-polymerase chain reaction (RT-PCR) appears to be the best strategy to detect acute pathogens (Dingemans et al., 2020)

6.2 Diagnostic Strategies for Patients with Lung Carcinoma

The COVID-19 screening for lung cancer was also influenced by a pandemic. To screen high-risk patients, including those with a history of smoking, low-dose chest CT is used. If a nodule is detected, it can be noted for its size and characteristics. Similarities with secondary COVID-19 pneumonia or lung cancer (such as weakness, coughing, and respiratory difficulties) find it hard to medically diagnose pneumonia and therefore can lead to the spread of viral infection among associates and healthcare professionals. Throughout a patient with diagnosed lung cancer, the main purpose of the evaluation is to collect tissue samples, through using a less invasive procedure, for histopathologic analysis. Both lung cancer sufferers planned for anti-cancer treatment should be tested for COVID-19, regardless of symptoms or communication history, in addition to assessing their condition before undermining their immune response. Unfortunately, testing kits are still not abundant (Xiang et al., 2020).

Serologic research has been proposed as just another method for SARS-CoV-2 identification. The latest study finds that seroconversion resulted in 50% of people Seven days after exposure and in 100 per cent of patients Fourteen days after exposure (Wölfel et al., 2020). It is preferable to use an image-guided biopsy to improve the diagnoses (Sydney, NSW, Australia) recommends that non-urgent surgeries be delayed or cancelled, apart from life-saving as well as irreversible damage treatments. The biopsy is the very first step of its diagnosis of lung cancer, as well as further therapies, can be prepared on a particular circumstance level by the physician (Shankar et al., 2020).

Chapter 7

Challenges Faced by COVID 19 Patients with Lung Carcinoma & their Implications

7.1 Challenges in Diagnosis and Illness Control

Respiratory doctors are amongst the front-line experts in diagnosing and treating lung cancer as well as COVID-19, a virus that has a preference for the lungs. Since much of the COVID-19 respiratory signs are close to those of lung cancer, it's important to separate the two. The decision is typically taken based on improvements in the clinical presentation, such as deteriorating baseline signs, deteriorating imaging studies, new patchy infiltrate which are different from the history of lung cancer development, and eventually, positive PCR results for infection (Bakhribah et al., 2020). Invasive tests, as well as diagnostic interventions, require creating cautious decisions regarding medical diagnostics, particularly interventional as well as invasive ones, diagnostic tests, and invasive procedures are indeed very important. Non-invasive procedures, including clinical scans and lab testing, can be used to validate the diagnosis (Bakhribah et al., 2020).

7.2 Impact of COVID-19 on Lung Cancer Prevention and Screening

The COVID-19 virus's susceptibility to the lungs and negative impacts on patients, especially smokers, should be a motivating force for healthcare services preventive campaigners, academics, and politicians to re-energize anti-tobacco campaigns to monitor tobacco use in all communities (Garassino et al., 2020). Both lung cancer screening activities must be postponed until the pandemic's height has ended and the chance of infection has decreased to the absolute minimum. There are several factors for stopping screening practices for lung cancer, particularly raising patient adherence to a needless danger of COVID-19 disease;

accidental pulmonary results in asymptomatic patients who might get COVID-19 infectious disease can raise the false positive rate and exposing patients to unnecessary treatment (Shankar et al., 2020).

7.3 The Effects of COVID-19 on Radiology

In the detection and control of both lung cancer including COVID-19, radiologists play a significant role. Radiologists have to be conscious of COVID-19 scanning outcomes to retain it when studying imaging reports regarding patients with lung cancer. If the observations that resulting from the COVID-19 infection, radiologists will be aware to never upstage the infection or indicate the progression of the disease. Due to regional infrastructure, the use of specific radiological modalities reported or cases reported of COVID-19 varies worldwide in the COVID-19 disease outbreak period. Nevertheless, in the early stages of COVID-19 pneumonia, CT scans or chest x-rays have minimal specificity for diagnosis (Rodrigues et al., 2020). Furthermore, in asymptomatic patients with a negative PCR examination, the CT scan becomes highly beneficial in diagnosing COVID-19 disease (Lin et al., 2020).

7.4 Challenges of COVID-19 Concerning Surgery

Lung cancer surgical procedures are grouped into three categories: diagnosis, preventive, and curative. Although interventional radiology is capable of managing the majority of diagnosis cases, medical procedure is often needed. To mitigate the dissemination of COVID-19 and ensure the wellbeing of all physicians and healthcare staff, regular and preventative medical treatments need not be prioritized during the COVID-19 epidemic. Leading up to any medical procedure, all patients ought to have COVID-19 evaluation or monitoring for at least 3 days, and therefore should be tested about any signs on diagnosis and checked if a secondary screening test is necessary. That should be included in the patient's signed agreement to the operation. The foregoing should also include the opportunity for patient cross-contamination as well as the treatment protocol that will be enforced. If the patient decides to reject the surgical operation, the appointment should be reported, along with the possibility of complications. The foregoing could include the opportunity for patient cross-contamination as well as the treatment protocol that will be enforced. If the patient chooses to reject the surgical operation, the appointment should be recorded, suggesting the likelihood of a pause (Bakhribah et al., 2020).

Patients with complications should indeed be controlled as per hospital guidelines, with a gap of 28 days after the start of the illness and 2 weeks from the onset of relieving symptoms and negative monitoring. It is appropriate to expose asymptomatic patients to medical procedures 14 days after their last negative examination (Baker et al., 2016). Additional minimal invasive treatments, such as outpatient chemotherapy or radiotherapy, can be preferred by the cancer committee for patients with significant danger or sustained good outcomes, or where the patient has chosen not to continue with a medical procedure (Cafarotti & Patella, 2020).

7.5 Challenges Regarding Radiotherapy

In the treatment of lung cancer, radiation treatment is highly necessary (Baker et al., 2016). This function will vary between adjuvant therapy for stage III disorder and stereotactic ablative body (SABR) radiotherapy for initial NSCLC to the preventative purpose for aggressive form distress and haemoptysis (Maher et al., 1993). For NSCLC patients with stage III cancer, a pause in radiotherapy of further than 24 days is correlated with a chance of viral infection of up to 30% (Everitt et al., 2010). Postponing radiotherapy for three to four weeks as well for an early stage of development I disease may be usually considered even if the patient was worked up with a PET-CT scan often within two months window; therefore, cancellation of radiotherapy is never recommended (Guckenberger, et al., 2020). So during a COVID-19 disease outbreak, SABR should be seen as an alternative to surgical procedure or as a key therapy for some cases of early-stage I disorder (Chang et al., 2015). To use fewer fractionations, prophylaxis cranial irradiation may be delayed for four to six weeks (Baker et al., 2016). Shorter fractions, such as single or two monthly fractions, are strongly recommended for preventative thoracic radiotherapy. Before thoracic radiotherapy, checking for COVID-19 is recommended (Rodrigues et al., 2011).

7.6 Challenges of COVID-19 on Interventional Radiology

At all levels of lung cancer treatment, interventional radiology (IR) plays an important role in the multidisciplinary management of lung cancer (Duka et al., 2017). Nevertheless, the IR service is experiencing various obstacles as a result of the emerging Corona disease outbreak COVID-19. The care of lung cancer patients should weigh the danger of late diagnosis or possibly therapeutic or preventive treatment against the apparent risk of complications under certain unusual circumstances of shortages or redistribution, regarding the health risks of COVID-19 disease. To maintain operator safety, interventional radiology services must take the recommendations and guidelines issued by the institution's infection control practices for multiple clinical practices. Ultrasound can also be used for directing treatments wherever convenient and necessary, as it allows treatments to be done at the bedside, eliminating patient travel but outside the specified unit and the possibility of nosocomial infectious diseases. Specialized ultrasound device tools, such as the wheels, must be labelled and sequestered for infected use and disinfection periods (Gregorio et al., 2020).

7.7 Various Obstacles Faced by Providers

The COVID-19 disease outbreak raised several major threats to healthcare professionals. Healthcare staff is more likely to develop the illness, as well as suffer fatigue. General patient safety measures, such as social distancing among staff as well as between patients and staff, universal masking, and others, must be enforced to shield staff from infection. To minimize the pandemic's harmful impacts, initiatives for mitigation, early warning, and prompt assistance for mental health care must be enforced (Brooks et al., 2020; Dingemans et al., 2020).

7.8 Challenges regarding Lung Carcinoma Awareness

Lung cancer is curable, and raising public consciousness about risk factors (such as active and passive smokers, several occupational agents, and indoor and outdoor environmental pollution) as well as improving one's actions are important measures in avoiding lung cancer. Many of these programs have been harmed by the COVID-19 pandemic, but information can be sustained via numerous online social media. People with lung conditions are more likely prone to COVID-19, so lung health is important (Calabrò et al., 2020).

7.9 Challenges in Tobacco Control & Smoking Cessation

Tobacco and smoking are significant risk factors for extensive lung diseases, which cause diminished lung function, cough, and respiratory difficulties. Several studies have found that people with pre-existing respiratory and cardiovascular disease have more health issues than those people who are Tobacco smokers and passive smokers. Besides that, a tobacco product induces adverse cardiorespiratory problems in the long and short term with a high risk of viral infections. To minimize cardiorespiratory diseases, as well as the incidence of COVID-19 in such subgroups of patients, stringent tobacco control and quitting smoking initiatives are required (Calabrò et al., 2020).

7.10 Challenges in Vaccination

COVID-19 vaccine can minimize the risk of severe forms of cancer. The key problem of COVID-19 vaccinations is the decline of the rate of severity in the COVID-19 cases and the maintenance of regular carcinogenic treatment. Due to limited data available and the lack of accessible vaccine doses, it is hard to determine the target population for immunization. Vaccinating cancer patients throughout therapy or with treatment shorter than three years, together with their entourage, seems theoretically significant. Patients with cancer receiving chemotherapy are presently the "high-risk" priority patients. Another "high-priority population," encompassing first and second-line patients with curatives, palliative chemotherapies, and those treated with substantial lung volumes, lymph nodes, and hematopoietic tissues by surgeries and radiation therapies recommended in one expert group. Before the beginning of the cancer therapy, the vaccination should preferably take place (Tougeron et al., 2021).

Chapter 8

Management of Lung Carcinoma Patients during COVID-19

The number of lung cancer patients is identified at an early stage, and any further delay will endanger the result, so lung cancer treatment requires a feeling of panic. Therefore, not just for physicians, but mostly for patients, treating lung cancer patients during most of the COVID-19 pandemic is a daunting challenge, as hospital visits are shortened to prevent the further spread of SARS-CoV-2. According to Yu et al. (Yu et al., 2020), cancer patients have a higher chance of contracting SARS-CoV-2 (0.79%) than non-cancer patients (0.37%), especially lung cancer sufferers (7 out of 12 patients) but those aged 60 older than age. The COVID-19 lung cancer testing was also affected by the pandemic. Low-dose chest CT is being used to test high-risk patients, such as those who have smoked in the past. If a nodule is located, its size and features can be observed. Pulmonologists, thoracic surgeons, including thoracic radiologists were among the twenty-four physicians who offered guidelines for handling lung cancer testing after the pandemic. Non-urgent cases will be delayed till after the pandemic, allowing urgent situations to undergo proper care (Mazzone et al., 2020).

Besides, the panel proposed that care for stage I non-small cell lung cancer could be delayed until a detailed review of its characteristics, such as its size, growth rate, PET scan findings, and patient preference. These are broad suggestions that should be balanced against several conditions, such as the occurrence of SARS-CoV-2 in the normal community, govt commuting rules, resource availability, and the overall effects of the COVID-19 disease outbreak (Ballout et al., 2020). COVID-19 has no established validated therapy at this time, but management consists of compassionate and symptomatic care as well as adopting prescribed preventive care and control steps. Preclinical evidence and anecdotal accounts help the evaluation of potentially successful medicines (Scavone et al., 2020). Convalescent plasma trials along with Clinical trials are still going on about Chloroquine and its analogues both with and without azithromycin, antiviral drugs like remdesivir (developed for Ebola but considered ineffective), lopinavir and ritonavir (anti-human immunodeficiency viruses), and immunotherapies to interleukin-6 are only a few of them (tocilizumab) (Coperchini et al., 2020).

8.1 Managing Patients with Different Scenarios

If the patient undergoes into chemotherapy, immunotherapy and therapeutic agents these must be adjusted to the patient's symptoms, biomarkers and complications, also taking into consideration the risk of adverse effects and COVID-19 contamination. The influx in COVID-19 cases in the surrounding communities, along with the burden on health care services, dictates which procedures should be continued on time and which should be delayed. COVID-19 incidents have overcrowded many hospitals, and operating rooms have been converted to emergency departments. Since they are in isolation or have been contaminated with SARS-CoV-2, some hospitals have lowered their staffing rate. The overriding trend and most important driving principle in the management of lung cancer and other cancers are to provide prompt adequate care against unreasonable treatment delays (Banna et al., 2020; Passaro et al., 2020).

Patients with oncogenesis-dependent NSCLC who have been identified by biomarker analysis are given personalized treatment with TKIs (Tyrosine Kinase Inhibitors). It leads to higher mortality and reaction rates, as well as a greater safety profile and fewer adverse effects (Yang et al., 2020). Asymptomatic patients who do have limited progression should be tracked each 4–8 weeks. Local disease development can be treated with radiation therapy. COVID-19 should be isolated from symptomatic development or TKI-induced pneumonitis. If a patient is diagnosed with COVID-19 while still on TKI, the COVID-19 should be treated and the TKI should be continued. Physicians must balance the advantages and dangers of steroids need for TKI-induced pneumonia (Russell et al., 2020). Since rebiopsy is a complicated technique requiring several agencies, liquid biopsy is recommended if rebiopsy is required to search for evolving mutations (Figure 5).

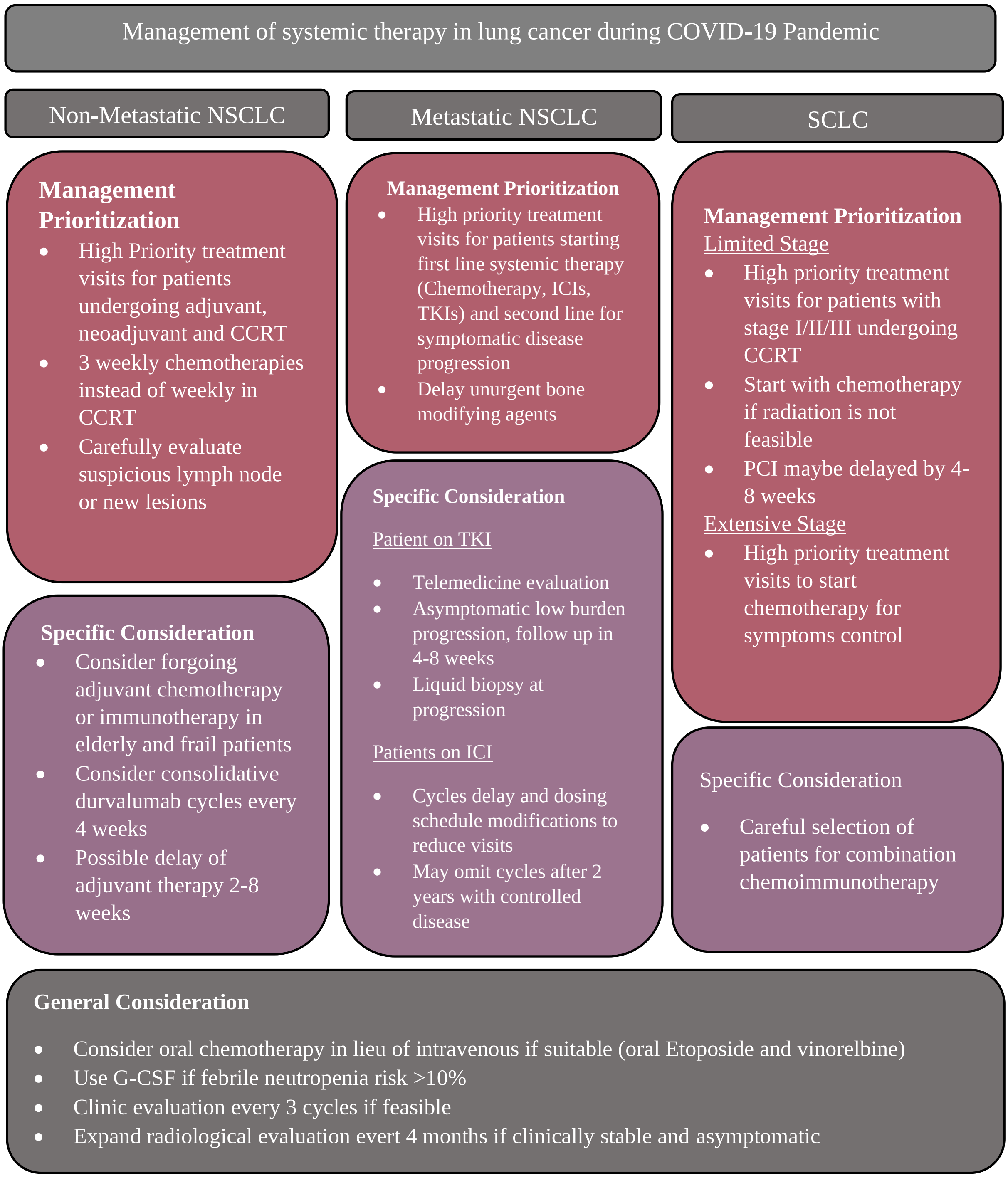

Figure 5: Flowchart for Assessing Lung Cancer Patients for Systemic Treatment (Bakhribah et al., 2020).

Immune checkpoint inhibitors (ICIs) are being used in the treatment of stage III and IV non-small cell lung cancer (NSCLC) either alone or in combination with chemotherapy (Friedlaender et al., 2020). Many concerns have been raised regarding the interaction between ICIs and COVID-19, but whether immunotherapy protects against SARS-CoV-2 by improving T cell activity, or exacerbates COVID-19 by triggering a cytokine storm, leading to higher COVID-19 survival (Coperchini et al., 2020). The TERAVOLT research finds no evidence that getting ICI harms patients with lung cancer (Garassino et al., 2020). If hospital stays are a problem, appropriate medication selection including using longer therapy times (Nivolumab every 4 weeks or permbrolizumab after 6 weeks), is an alternative. Patients with no signs of regression after two years on medication can even be recommended for discontinuation.

Chemotherapy is the treatment for patients who are seeking complementary chemoradiation, pre-operative sitting, and systemic preventative therapy. As a result, patients on chemotherapy should be closely evaluated to prevent medication delay, taking into account the possibility of immunosuppression and the need for hospitalization in vulnerable patients, as other variables can impact the result of cancer patients with COVID-19 disease that are not generally linked to chemotherapy (Lee et al., 2020). On a specific instance basis, Neoadjuvant and adjuvant chemotherapy (NACT) must be treated. For example, adjuvant chemotherapy in young patients with locally advanced cancer and NACT is used for which would enable patients to postpone the operation for three months in centers with minimal operational capability mostly during pandemics (Burki, 2020). Moreover, delaying or skipping preventive care should be addressed for people who have had long-term therapy after treatment (Hanna et al., 2020).

8.2 COVID-19 Treatments at Patient Follow-up

If possible, provide diagnostic tests at the place of therapy or near the patient's house to reduce patient travel and exposure. It is critical to make a judgment on the patients' current stage of treatment. Patients who have newly been diagnosed may need further appointments and care to begin earlier. Choosing drugs with a lower bone marrow suppression impact, using hematopoietic growth factors, and taking chemotherapy breaks can help to minimize immune suppression (for patients on maintenance therapy). After receiving CT scan/imaging monitoring and following up with a phone call, periods between treatment sessions can be prolonged or even avoided. If the patient is asymptomatic, there is no requirement for a doctor's visit for upwards of a year. Depending on the clinical condition, the CT scan time can be changed. Several techniques can be used to minimize hospital visits, such as a simulated or mobile clinic, scheduling as many patients as possible. Also, outpatient visits for routine check-up avoidance and taking chemotherapy in a controlled manner are required. Besides, patients may increase the use of oral therapy as often as possible, specifically TKIs or oral chemotherapies substances (e.g., Etoposide). Moreover, a change in the permitted dose range to a longer interval and increase the time between imaging to a safe duration in healthy patients, as with every Three cycles instead of every Two cycles are required (Bakhribah et al., 2020).

Chapter 9

Lung Cancer Patients Overall Treatment

Patients with lung cancer who are invaded by coronavirus are more likely to experience extreme COVID-19 disease, which can lead to death. However, the prognosis can vary depends on the proposed treatment used in the different stages of cancer (Guckenberger, et al., 2020).

9.1 Guiding Principles

Patients must be examined for SARS-CoV-2 infection if any of the typical symptoms are present those who physically visit the hospital should be monitored. COVID-19 infection should be checked wherever possible in patients receiving some invasive surgery or systemic chemotherapy plus immunotherapy (Dingemans et al., 2020). A demonstration of detailed guidelines and factors for all stages of lung cancer are the following.

Table 1: Prioritizing Treatment Options for NSCLC (Dingemans et al., 2020).

Scenario in Clinic	Recommendation for Therapy	Delay in the beginning (in weeks)	Delay in the beginning (in weeks)	Observations
Stages I, II, and IIIA that can be surgically removed				
Untreated stages I and II	SBRT surgery for stage I patients	Two to Eight	If the baseline CT is older than 8 weeks, repeat the scan.	

Resection of stages I and II	Remarks (adjuvant therapy for a subset of stage II disease)	Greater than 8	If asymptomatic at 4 years, extend the interval for CT scans to four to six months, and once a year after that.	Consider a CT scan, but do the follow-up from a distance.
Resectable single station in Stage IIIA	Following surgery, chemo and/or radiation are used to treat the patient.	Less than 2	Every four months have a CT scan.	
Stage III				
Stage III remains undiagnosed.	Chemotherapy and radiotherapy can be delivered at the same time, but chemotherapy may be given first for two periods.	Less than 2	Same Remarkably similar	Consider the mixture of cisplatin and pemetrexed. If you're just offering chemotherapy, G-CSF is a reasonable choice.
Chemoradiotherapy and immunotherapy were done in Stage III.		Less than 2	Immune checkpoint treatment workup as normal.	According to the report, you should wait up to 7 weeks, but the earlier the better.

Treatment for Stage II was accomplished.	Comments	Greater than 8	Every four months, get a CT scan.	Consider a CT scan, but do the follow-up from a distance.
Stage IV				
Step IV: Actionable Goals				
Without Treatment	Therapy for a clear target	Less than 2		Start on schedule, execute safety procedures such as laboratories or ECG, but instead of an in-person appointment, conduct a phone clinic. Within two months, consider undertaking a response evaluation.
On the receiving end of disease-controlling therapeutic strategies		Less than 2	When the condition is psychologically well, the illness assessment can be continued for 3 months or more if they have been on medication for a long time.	Toxicology notation, management, and any indicators of disease development are all protected in simulated hospitals.
Wild-type at stage IV				

Without Treatment	Chemotherapy only	Less than 2	Standard	Consider using growth factors instead of immunosuppressive drugs, or reducing the dosage of immunosuppressive drugs if required.
	Chemotherapy and immune therapy combination	Less than 2	Standard	Need to be very selective
	Immune therapy single agent	Less than 2	Standard	Preferred if PD-L1 score >50% consider the approved longer interval of dosing
First-line treatment	Chemotherapy			
	Chemotherapy and immunotherapy	Less than 2	If the patient is healthy, imaging can be performed every three cycles.	Try using a growth factor, striving for fewer cycles (4 if the disease is stable), and transitioning to maintenance mode.
	Immune therapy	Less than 2	If the patient is healthy, imaging can be performed every three months.	Try transitioning to maintenance as soon as possible and prescribing at a longer interval. If it's necessary, skip phases.

		Less than 2	If the patient is healthy, imaging can be performed every three cycles.	Stop at 2 years and use permitted longer dosage periods.
Apart from first-line medication	Chemotherapy	Less than 2 or two to eight	If clinically stable, expand CT scan to 3 or 4 periods.	Try having a two-to-three-cycle break from chemotherapy.
	Immunotherapy	Less than 2 or two to eight	Extend the time between outbreak tests.	Using the longer dosing periods that have been accepted.
Completed treatment				
No evidence of disease	Observation	Greater than 8	Extend the time between workups.	consult with a survival clinic
Presence of disease	Observation	Two to eight	Extend the time between workups.	per phone consultation

[Abbreviations: CT, computed tomography; ECG, electrocardiogram; G-CSF, granulocyte-colony stimulating factor; PD-L1, programmed death-ligand 1; SBRT, stereotactic body radiation therapy].

Table 2: Treatment Options for SCLC Prioritization (Dingemans et al., 2020).

Scenario in Clinic	**Recommendation for therapy**	**Delay in the beginning (in weeks)**	**Workup**	**Remarks**
Limited Stage				
Without treatment	Chemotherapy and radiation are given at the same time.	Less than 2	standard	Start with chemotherapy and apply XRT as soon as possible if radiation therapy is not available.
Following therapy	Chemotherapy and radiotherapy are offered concurrently, followed by chemotherapy	Less than 2	standard	Continue with CCRT, restrict chemotherapy cycles to four, and hold growth factors away from XRT.
Completed treatment	PCI	Two to eight	standard	
	Observation	Greater than 8	imaging could be delayed for a month	Teleclinic start flowing
Extensive Stage				
Without treatment	Chemotherapy	Less than 2	standard	should start promptly. Take into account growth conditions or dosage. reduction, consider oral etoposide for d 2 and 3
	Chemotherapy and	Less than 2	standard	Select and choose

	immunotherapy			wisely.
On treatment	chemotherapy	Less than 2	If the condition is stable, the evaluation can be extended for three periods.	
	Chemotherapy and immunotherapy	Less than 2		
Completed treatment	Observation	Two to eight	It's possible to stretch it for up to two months.	It can be extended out for up to two months.

[Abbreviations: CCRT, concurrent chemoradiation therapy; PCI, prophylactic cranial irradiation; XRT, radiation therapy].

9.2 Early-Stage Lung Cancer

Surgical intervention or radiotherapy techniques are used to treat patients with stage I/II and resectable stage III NSCLC. During the COVID-19 epidemic, the surgical principles for lung cancer remain as same. If a COVID-19 epidemic is imminent, determining whether or not to postpone resection is crucial. Surgical procedures must be planned whenever possible, according to the CDC and other specialist organizations (Dingemans et al., 2020). According to the American Society of Clinical Oncology, Physicians and patients should make individual choices based on the possible harms of avoiding required cancer-related ablation. This has been proposed that in persons with a new treatment of chronic stage lung cancer including those with suspected pulmonary nodules, the resection should be rescheduled because performing surgery during the incubation time of SARS-CoV-2 infection could result in a negative outcome (Lei et al., 2020).

The European Association of Medical Oncology, on the other hand, urges that all surgeries be prioritized in the treatment of early NSCLC. Surgical intervals can be held to a minimum of six to eight weeks (Passaro et al., 2020). If a SARS-CoV-2 result is positive, surgical resection should be deferred for at least 2 weeks. If the patient's condition is serious, the resection should be done in a specialist negative-pressure surgery room with maximum personal protection and post-operative treatment in a negative-pressure isolation chamber. When resection is postponed, patients must be reassessed for SARS-CoV-2. Neoadjuvant treatment is required for the right circumstances to minimize the chances of delaying surgery. Adjuvant EGFR tyrosine kinase inhibitor (TKI) used for resected EGFR mutation-positive and NSCLC may be suggested if local conditions make systemic chemotherapy risky (Yue et al., 2018; Zhong et al., 2018). Follow-up scans could be deferred for three to four months if patients are medically healthy following adjuvant treatment (You et al., 2020). SBRT, also known as stereotactic body radiotherapy, is a well-known non-invasive treatment for mutation-negative NSCLC in the initial stages (less than 5 cm). SBRT has a high degree of local management therapy and fast recovery with little danger (Dingemans et al., 2020).

9.3 Locally Advanced Lung Cancer

Dissection, radiation treatment, and interventional procedures may be used to combat locally advanced lung cancer. However, many patients with stage III NSCLC may be controlled with combination simultaneous chemoradiotherapy, which will probably involve platinum-based chemotherapy with radiation therapy administered as 60 Gy in 30 fractions (Bradley et al., 2020), accompanied by combination durvalumab (Antonia et al., 2018). Following both the adjuvant therapy and chemotherapy, medication after dissection must be postponed as late as possible (up to 3 months right after the resection) (Miyashita et al., 2020; Rubinstein et al., 2020; Whisenant et al., 2020).

Chapter 10

Immunotherapy in COVID-19

Constant progress has been made in understanding the biology of cancer and the genetic profile of each patient, which allows for a more accurate diagnosis and more successful treatment. Treatment strategies targeting molecular mechanisms responsible for the control of immune homeostasis and cancer immune response, especially targeted therapy inhibitors (ICIs), including such chemotherapy drugs against by the Programmed Cell Death Protein 1/Ligand 1 (PD1/L1) axes or Cytotoxic T-Lymphocyte Antigen 4 (CTLA4), have been implemented in recent times (Ocáriz-Díez et al., 2020). These compounds are important immune system negative receptors that inhibit responses to self-antigens in a biological environment, preventing autoimmune responses. Any cancers have learned to be using these substances to prevent autoimmune response and to live in the recipient, so suppressing ICs will activate certain triggers and facilitate immune-mediated tumor removal in certain circumstances.

After chemoradiation (durvalumab), ICIs are efficacious in the management of locally advanced unresectable NSCL (Antonia et al., 2018). Nivolumab, pembrolizumab, and atezolizumab were used in individuals that had previously been exposed to metastatic cancer (Borghaei et al., 2015; Herbst et al., 2016; Rittmeyer et al., 2017; Tanoue, 2016). As it is used in the treatment as both in monotherapy (pembrolizumab) (Brahmer et al., 2017) either in combination with chemotherapeutics (pembrolizumab, atezolizumab) (Gandhi et al., 2018; Socinski et al., 2018) or as the double immunotherapeutic (anti-PD1nivolumab/anti-CTLA4 ipilimumab) (Goldman et al., 2021; Horn et al., 2018).

Patients with cancer may have been immunosuppressed as a consequence of antineoplastic therapy, antioxidant drugs like hormones, and the immunosuppressive characteristics of cancer on their own. They may have an improved autoimmune disorder to disease as a side effect of immunomodulatory treatments (Blimark et al., 2015). Including central and peripheral immune resistance are impaired by programmed cell death protein 1 (PD-1). When it is ligated by programmed death-ligand 1 (PD-L1) or programmed death-ligand 2 (PD-L2), a continuing or beginning immune reaction is blocked. PD-1 is known as the immune "rheostat" because it specifies the threshold, intensity, and length of an immune reaction. The chemotherapeutic activity has been observed as monoclonal antibodies block PD-1. Anti–PD-1 or PD-L1 monoclonal antibodies are also accepted as a common quality of practice for several cancers, such as first-line and second-line NSCLC therapy, as well as first-line SCLC medication (Remon et al., 2020).

10.1 Therapy for Viral Infection

Cytotoxic CD8 T-cells up-regulate membrane PD-1 while on an immediate viral infection. At this point, blocking PD-1 allows viral clearing to be enhanced (Ahn et al., 2018; David et al., 2019). This can be based on the location of the infection followed by a more serious inflammatory response of the surrounding tissues. The extended virus-specific T-cell population contracting after antiviral therapy, and T-cell recollection is established. Through viral pathogens of the lower respiratory tract, one form of the T-cell memory cell, known as tissue-resident memory T-cells, actively populates cancerous cells, including such lung cells (Shin, 2018). At this level, PD-1 and its receptors PD-L1/2 may be able to avoid additional cell damage, while blocking the PD-1/PD-L1 axis may lead to immunopathology. Additionally, in an acute disease process, PD-L1 transcription can be differentially regulated. When compared to PD-1, PD-L1 has a much broader expression. In addition to cells of the hematopoietic lineage will rise PD-L1 Endothelial and parenchymal cells (Keir et al., 2006).

During an acute viral illness in accordance with CD8 and CD4 T-cell production PD-L1 is opened by cytokines, particularly interferon. T-cells may be hampered by the release of PD-L1 by pathogen cells. Late-stage PD-L1 production could reduce cellular injury by regulating PD-1-expressing pathogen T-cell in many other types of the acute disease process (Keir et al., 2006). As a result, an immune reaction should preferably act in such a manner that virus removal happens with the least amount of cell death. Whether or not something happens is possibly a pathogen, and nothing is recognized about COVID-19 thus far. It's difficult to tell how checkpoints blockade would impact SARS-CoV-2 contamination based on the minimal evidence available right now. Patients with COVID-19 who've been taking a checkpoint inhibitor should get their data collected as soon as possible (Garassino et al., 2020; Whisenant et al., 2020).

Chapter 11

Conclusion

The fast emergence of the COVID-19 disease outbreak needs deep evaluation by oncologists of immediate decisions to manage lung cancer. Several oncologists also modified the changes to medication therapy for lung cancer to allow adequate healthcare delivery under the agreed requirements and new recommendations. According to the WHO and CDC recommendations, doctors must inform patients to help discourage more dissemination of COVID-19 following the determination of a therapeutic route for lung cancer. These patients must also be recommended for continuity of scheduled chemotherapy, immunotherapy, or radiation in the lack of any signs indicating COVID-19. Patients who are committed to caring should better dedicate themselves, all patients, and caregivers to self-isolation and healthy procedures. Ultimately, COVID-19 can be handled. Pandemics are prone to resolve, though. A variety of foreign COVID research groups were formed to be trained, and active engagement is welcomed.

Chapter 12

Future aspects

Current treatment strategies to treat lung cancer in COVID-19 positive patients have been successful, although the association of immunotherapy with COVID-19 treatment is uncertain at this time. It is important to highlight how we can effectively handle Covid-19 patients who have already been diagnosed with lung cancer. Furthermore, more studies are needed to be conducted regarding the different treatment strategies to reduce average mortality rates in such patients. Indeed, it is crucial to commence the cancer treatment immediately and strive to minimize the delay of its progression. In this case, the COVID-19 patient needs to be recovered as soon as possible to prevent complications. This can be achieved by the conjoint effort of all the healthcare professionals. Apart from this, the safety profile and efficacy of COVID-19 vaccines which are currently available need to be assessed further, especially in the case of lung carcinoma patients.

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