

# COVID-19 and Its Effects on Patients with Terminal Cancer

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**Abstract:** ***Background:** Outbreak of COVID-19 has affected both healthy individuals as well as immunocompromised patients. The relation between COVID-19 and cancer, mainly radiological findings and impact of COVID 19 among end stage cancer patients was reviewed in this article. **Method:** Search in the online databases such as PubMed, Google Scholar, ScienceDirect was done to find related studies according to search strategies. Various articles were identified, after the title and abstract review, few articles were retained which were considered as more relevant. A full-text evaluation resulted in 40 studies to be included for review. **Conclusion:** The novel coronavirus i. e. SARS-COV 2 or COVID-19 is considered as a worldwide threat. The emergence of COVID-19 infected cancer research directly, as COVID-19 infected cancer patients are more vulnerable to various complications. In this review paper, the effect of COVID-19 on cancer patients was discussed.*

**Keywords:** COVID 19, Cancer, Pandemic, SARS-COV2, radiological findings, Immunity.

## 1. Introduction

The responsible pathogen for the outbreak of COVID-19 is a severe acute respiratory coronavirus syndrome (SARS-COV2) which was first seen in Wuhan city, China in late December 2019 (1). SARS-COV2 is highly infectious and extremely contagious which can spread fast globally (2, 3). The complete role and severity of SARS-COV2 remain indefinite. In this review article, we focus on determining the relationships between SARS-COV2 and cancer patients.

Coronaviruses (COVs) in the coronaviridae family belongs to the genus coronavirus. COVs is a positive-stranded enveloped RNA virus (4). SARS-COV2 have many similarities with SARS that is they have both a crown or halo-like appearance & glycoprotein envelope (5). SARS-COV2 has 4 structural proteins, envelope, spike, nucleocapsid and membrane. Cancer refers to the uncontrolled growth of abnormal cells in a part of the body. Patients with cancer and who are infected with COVID 19 have an increased chance of mortality and morbidity rate compared to non-immunocompromised individuals (6-9).

### 1.1 Structure of SARS-COV2

It consists of four structural proteins, nucleocapsid, membrane, envelope spike. They contain S1 and S2 functional subunits which are responsible for ACE 2 receptor detection present on the host cells.

### 1.2 Virology Pathogenesis

The spike proteins mediate host cells invasion by SARS-COV2 through binding of the host cells protein receptor i. e. ACE 2 (Angiotensin Converting Enzyme 2) (10, 11). An analysis carried out demonstrated that this cell invasion requires the synthesis of S-Proteins assisted by serine protease TMPRSS211 present in the host cell. The viral genome encodes RNA dependent RNA polymerase (RdRp), papain-

like protease and corona viral principal protease (3CL Pro). The genome is released into the cell as positive sense of Single-Stranded RNA (SS-RNA). Thereafter it uses ribosomes for viral polyprotein production and then split into an effector viral protease proteins 3CL Pro & PL pro (12). The complex component of the genome is RBD (receptor binding domain) in S protein. There are 6 RBD amino acids which are considered to be important for ACE2 binding (13). SARS-COV2 appears to hold an RBD that connects cats, ferrets, humans and other high receptor homologated animals with high affinity with ACE 2 (14).

### 1.3 Epidemiology of SARS-COV 2

In late December 2019 a life-threatening pneumonia outbreak was started in Wuhan, China. The International Committee on Taxonomy of Virus (ICTV) identified the virus as SARS-COV 2 (15). To control the epidemic stage, the Chinese administration ordered a quarantine to monitor the outbreak and determine how effective a quarantine is against the virus (15). However, the number of cases increased, spreading to other countries, thereby WHO declared as a global pandemic on March 11, 2020. More confirmed cases were seen in China, North America, Europe. The natural host of the virus is considered to be a bat that is *Rhinolophus affine* (16). Some research suggested that pangolin (*Manis Javanica*) could be the intermediate host. It is still unknown how the virus has been spread from bat to humans (17, 18).

### 1.4 COVID 19 Symptoms

Symptoms might be mild, moderate or severe based on the immunity of the infected individuals. Severe symptoms include ARDS, Sepsis, influenza, septic shock. In case of mild to moderate illness, symptoms include mild fever, sore throat, dry cough, fatigue, respiratory irritation, malaise. In some asymptomatic cases, dyspnea was seen (19). In moderate cases, pneumonia-like symptoms such as cough and children's tachypnea were seen. Extreme Pneumonia fever is

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caused by serious respiratory illnesses hypoxia or depression (SpO<sub>2</sub> <90% in the room). Cyanosis can be seen in children. Sepsis is a life-threatening condition which can lead to organ failure (20, 21). During the incubation phase, human to human transmission occurs. In some cases, no symptoms are seen and they are referred to as super spreaders. Transmission route is mainly through touching inanimate things mediated via the eye, nose, mouth. Respiratory droplets can be present in the air for a longer time direct inhalation can lead to the transmission (5, 22, 23).

## 2. Effect of COVID 19 on Cancer Patients

Earliest studies conducted in Wuhan, China depicted heightened outcome or reactions of COVID-19 hence suggested more care to be taken while handling cancer patients in the early 2020s (24). Preliminary study containing 1524 COVID-19 cases from Wuhan Outbreak showed increased or to be precise, doubled the likelihood of welcoming COVID-19 in comparison with non-cancer patients (An Odd Ratio [OR] OF 2.31; and 95% CI [Confidence Interval] of 1.89 to 3.02 (25). Following the outbreak and series of unfortunate deaths, studies at Wuhan pointed towards the increasing mortality of cancer patients. Admissions to intensive care units (ICUs) became more common for such patients (5.4-CI 1.8 to 16.2) (25). Hospitals had dealt with higher intubations in a broader range of age groups. Mortality rate measured were estimated to have fallen between 11% to 28%, whereas the general population of Wuhan in the initial stages experienced a mortality rate of 1.4%. According to Study conducted by Bitterman *et. al* showed that the chances of about 4 times the hospitalization and 10 times the death are higher among patients with haematological malignancy who are receiving multiple doses of chemotherapy when compared to a healthy population of COVID patients (26). Another study stated as there is a poor prognosis seen with a patient with malignant disease, they also stated that cancer patients with COVID-19 should use decreased drug dose or avoid immunosuppression drugs & also vital COVID-19 screening should be carried out. Patients receiving antineoplastic drugs treatment are highly prone to COVID-19 similar to older (>60 years) patients (27, 28).

Data received from Italy showed about 20% of patients among 3000 cases who died had malignant issues. A study from Wuhan University among 1524 patients showed that the patients above 60 years of age with NSCLC had a higher risk of COVID-19 diseases (7 patients) and about 3 patients had breast cancer & 4 patients had oesophageal cancer. These patients showed severe complications and also ventilators were required (9, 29).

The deaths among cancer patients were mainly seen due to acute respiratory syndrome, pulmonary embolism, septic shock, acute myocardial infarction. The main laboratory findings among the patients were low blood count, low serum albumin level, high lactate dehydrogenase with sensitive C reactive protein, high serum globulin, leucopenia, and erythrocyte sedimentation rate were also high (30).

## 3. Radiological Significance

RT-PCR as a diagnostic test tool has proven gold-standard for the detection of COVID-19 infection. In the early days of COVID-19, the scarcity of RT-PCR test kits pushed medical professionals towards other alternatives like radiology for assistance. Radiology as a department has played an important role in medicine for more than 100 years. Revolutionary changes in the use of X-Rays in medicine for diagnosis has proven clinically significant. CT scans with their ability to provide axial or transverse high-resolution images have made a contribution in diagnosing and characterizing diseases to fine details. Chest computed tomography (CT) is a high sensitivity tool for diagnosis of lung diseases. With almost 90% sensitivity and 78% accuracy (OR 2.39 [95% CI, 1.16-4.91] (31). To conclude, studies have shown that CT scan of the chest can be used as a critical diagnostic tool, especially in cases where RT-PCR results are negative.

### 3.1 Radiological Findings

Ground glass opacity, Patchy consolidation, Reticular appearances, Interlobular septal thickening and fibrous strips were the radiological findings, more lung cancer patients were detected with pneumonia & decreased lung volume [28, 29]. In a study comparing the effect of COVID-19 with pre-existing cancer patients and non-cancer patients of all the imaging observations, pleural effusion was notably more prevalent in the lung cancer group (71.43%, with a P value of 0.004), while metastatic nodules were more frequently observed in the breast cancer group (21.43%, with a P value of 0.042) compared to other findings within these respective groups (32). It was also noted that patients exhibiting typical CT scan findings indicative of COVID-19 were observed to face a nearly three-fold higher risk of mortality in comparison to those with a normal CT scan (with an odds ratio of 3.47 and a 95% confidence interval ranging from 1.14 to 8.98). Consolidation on CT scans increased the risk of mortality by 1.9 times compared to a normal scan. This risk surged to 4.5 times when consolidation was the predominant observation (OR 4.5; 95% CI 1.3-16.2). Additionally, patients with pleural effusion (OR 2.94; 95% CI 1.69-5.12), centrilobular nodule (OR 2.89; 95% CI 1.25-6.65), and architectural distortion (OR 3.76; 95% CI 1.5-9.4) exhibited a poorer prognosis compared to those with a normal chest CT scan.

About 70% of COVID-19 malignant patients had stage IV cancer with severe complications (33). The required scientific and clinical data contribute to correct perception of COVID-19 risk onsets in malignant cases. It thus helps oncologists tailor the clinical treatment of COVID-19 to the advantages of these patients. Therefore, critical guidelines and recommendations for the management of patients with cancer depending on the age of the patient, stage of cancer, affected organs during the outbreak is crucial (33).

The current diagnosis method used for detection of COVID-19 is a real-time polymerase chain reaction (RT-PCR). Serological tests include ELISA (Enzyme-linked immunosorbent assay) for the detection of antibodies mainly Nucleocapsid (N) and Spike (S) antibodies which bind to the viral protein. CDC recommends a method called as

microneutralization, when a positive result is detected through ELISA. Microneutralization is a method which is used to detect antibodies that may neutralize the virus. It is considered as a gold standard method for detection of SARS COVID-2 using a serum sample but this method requires a minimum of 5 days to give a result (20, 34).

Other PCR tests include COVID-19 IgM/IgG rapid kit test, colorimetric assay based on gold nanoparticles, RT-LAMP, western blot assay N195 proteins. The viable solutions which was used are social distancing, promoting medical treatment and surveillance, patient isolation.

For Vaccine Development, antibodies that are developed against viral protein by the immune system of the host can be used. The procedure includes purification of plasma containing antibodies from the patient who is recovered from COVID-19 then targeting these antibodies on the viral proteins to neutralize it and develop passive immunity against the disease. As TMPRSS2 is involved in the process called priming, inhibitors of TMPRSS 2 example like mostat mesylate can be used to prevent the entry of the virus into the host cell. ACE 2 receptor blockers can also be used (34-36).

One of the drugs used was Remdesivir which target viral RNA polymerase production. Chloroquine and Hydroxychloroquine can also be used to control the symptoms. These two drugs promote the production of cytokines thereby suppress Lysosomal functionality and autophagy in the host cells. Hydroxychloroquine, when combined with drugs such as Azithromycin, has more effect on virus clearance than using it alone (14, 17, 37).

#### 4. Conclusion

This review shows the chance of mortality and morbidity is higher in cancer patients infected with COVID-19 when compared to other COVID-19 patients. Studies has found out that patients with blood cancers are at higher risk of prolonged infection and death from COVID 19 than patients with solid tumors. Especially for patients with lung cancer, it is prudent to test for SARS-CoV-2 PCR as soon as possible for a clear diagnosis and to thoroughly evaluate risk factors and symptoms of SARS-CoV-2 infection in all patients who have received or are undergoing immune checkpoint inhibition therapy. It is still advised that these individuals receive the SARS-CoV-2 immunisation. Further research on treatment and prevention needs to be done.

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#### References

- [1] Zhang Yanping. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020. China; 2020.
- [2] 2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*.2020 Feb 15; 395 (10223): 497-506.
- [3] 3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *New England Journal of Medicine*.2020 Feb 20; 382 (8): 727-33.
- [4] 4. Marco Cascella, Michael Rajnik, Abdul Aleem, Scott C. Dulebohn, Raffaella Di Napoli. Features, Evaluation, and Treatment of Coronavirus (COVID-19) [Internet]. StatPearls [Internet]. Treasure Island (FL), editor. StatPearls Publishing; [cited 2023 Aug 18]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK554776/>
- [5] 5. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Vol.63, *Science China Life Sciences*. Science in China Press; 2020. p.457-60.
- [6] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*.2020 May 1; 8 (5): 475-81.
- [7] Zhang J jin, Dong X, Cao Y yuan, Yuan Y dong, Yang Y bin, Yan Y qin, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy: European Journal of Allergy and Clinical Immunology*.2020 Jul 1; 75 (7): 1730-41.
- [8] Guan W jie, Ni Z yi, Hu Y, Liang W hua, Ou C quan, He J xing, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *New England Journal of Medicine*.2020 Apr 30; 382 (18): 1708-20.
- [9] Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. Vol.323, *JAMA-Journal of the American Medical Association*. American Medical Association; 2020. p.1775-6.
- [10] Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation [Internet].2019. Available from: <https://www.gisaid>.
- [11] Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*.2020 Apr 16; 181 (2): 271-280. e8.
- [12] Báez-Santos YM, St. John SE, Mesecar AD. The SARS-coronavirus papain-like protease: Structure, function and inhibition by designed antiviral compounds. Vol.115, *Antiviral Research*. Elsevier B. V.; 2015. p.21-38.
- [13] Zhao Y, Wei Y, Shen S, Zhang M, Chen F. Appealing for efficient, well organized clinical trials on COVID-19. *Ann Transl Med*.2020 May; 8 (10): 632-632.
- [14] Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an

- Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J Virol.*2020 Mar 17; 94 (7).
- [15] King AMQ, Lefkowitz EJ, Mushegian AR, Adams MJ, Dutilh BE, Gorbalenya AE, et al. Changes to taxonomy and the International Code of Virus Classification and Nomenclature ratified by the International Committee on Taxonomy of Viruses (2018). *Arch Virol.*2018 Sep 1; 163 (9): 2601-31.
- [16] Hou C, Chen J, Zhou Y, Hua L, Yuan J, He S, et al. The effectiveness of quarantine of Wuhan city against the Corona Virus Disease 2019 (COVID-19): A well-mixed SEIR model analysis. *J Med Virol.*2020 Jul 1; 92 (7): 841-8.
- [17] Zhou P, Yang X Lou, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.*2020 Mar 12; 579 (7798): 270-3.
- [18] Lam TTY, Jia N, Zhang YW, Shum MHH, Jiang JF, Zhu HC, et al. Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins. *Nature.*2020 Jul 9; 583 (7815): 282-5.
- [19] Xiao K, Zhai J, Feng Y, Zhou N, Zhang X, Zou JJ, et al. Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. *Nature.*2020 Jul 9; 583 (7815): 286-9.
- [20] Centers for Disease Control and Prevention RVBD of VD. Real-Time RT-PCR Panel for Detection 2019-Novel Coronavirus.2019-nCoV rRT-PCR Panel.2020;
- [21] Al Johani S, Hajeer AH. MERS-CoV diagnosis: An update. *J Infect Public Health.*2016 May 1; 9 (3): 216-9.
- [22] Liu C, Zhou Q, Li Y, Garner L V., Watkins SP, Carter LJ, et al. Research and Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases. *ACS Cent Sci.*2020 Mar 25; 6 (3): 315-31.
- [23] Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis.*2020 Apr 1; 20 (4): 425-34.
- [24] Fernandes Q, Inchakalody VP, Merhi M, Mestiri S, Taib N, Moustafa Abo El-Ella D, et al. Emerging COVID-19 variants and their impact on SARS-CoV-2 diagnosis, therapeutics and vaccines. Vol.54, *Annals of Medicine.* Taylor and Francis Ltd.; 2022. p.524-40.
- [25] Aboueshia M, Hussein MH, Attia AS, Swinford A, Miller P, Omar M, et al. Cancer and COVID-19: Analysis of patient outcomes. *Future Oncology.*2021 Sep 1; 17 (26): 3499-510.
- [26] Bitterman R, Eliakim-Raz N, Vinograd I, Zalmanovici Trestioreanu A, Leibovici L, Paul M. Influenza vaccines in immunosuppressed adults with cancer. Vol.2018, *Cochrane Database of Systematic Reviews.* John Wiley and Sons Ltd; 2018.
- [27] Sidaway P. COVID-19 and cancer: what we know so far. Vol.17, *Nature Reviews Clinical Oncology.* Nature Research; 2020. p.336.
- [28] Moujaess E, Kourie HR, Ghosn M. Cancer patients and research during COVID-19 pandemic: A systematic review of current evidence. Vol.150, *Critical Reviews in Oncology/Hematology.* Elsevier Ireland Ltd; 2020.
- [29] Vuagnat P, Frelaut M, Ramtohl T, Basse C, Diakite S, Noret A, et al. COVID-19 in breast cancer patients: A cohort at the Institut Curie hospitals in the Paris area. *Breast Cancer Research.*2020 May 28; 22 (1).
- [30] Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Annals of Oncology.*2020 Jul 1; 31 (7): 894-901.
- [31] Kovács A, Palásti P, Veréb D, Bozsik B, Palkó A, Zsigmond &, et al. The sensitivity and specificity of chest CT in the diagnosis of COVID-19. Available from: <https://doi.org/10.1007/s00330-020-07347-x>
- [32] Khorasanizadeh F, Kaviani S, Salamroudi S, Seyyedsalehi MS, Gity M, Zendehtdel K. Role of chest CT scan in patients with preexisting cancer and COVID-19 pneumonia. *BMC Med Imaging.*2023 Dec 1; 23 (1).
- [33] Bitar N, Kattan J, Kourie HR, Mukherji D, Saghir N El. The Lebanese Society of Medical Oncology (LSMO) statement on the care of patients with cancer during the COVID-19 pandemic. Vol.16, *Future Oncology.* Future Medicine Ltd.; 2020. p.615-7.
- [34] Woo PCY, Huang Y, Lau SKP, Yuen KY. Coronavirus genomics and bioinformatics analysis. Vol.2, *Viruses.* MDPI AG; 2010. p.1805-20.
- [35] Casadevall A, Pirofski L anne. The Ebola Epidemic Crystallizes the Potential of Passive Antibody Therapy for Infectious Diseases. Vol.11, *PLoS Pathogens.* Public Library of Science; 2015.
- [36] Matsuyama S, Nagata N, Shirato K, Kawase M, Takeda M, Taguchi F. Efficient Activation of the Severe Acute Respiratory Syndrome Coronavirus Spike Protein by the Transmembrane Protease TMPRSS2. *J Virol.*2010 Dec 15; 84 (24): 12658-64.
- [37] Schmidt R, Beltzig LC, Sawatsky B, Dolnik O, Dietzel E, Krähling V, et al. Generation of therapeutic antisera for emerging viral infections. *NPJ Vaccines.*2018 Dec 1; 3 (1).