



## Lung cancer management challenges amidst COVID-19 pandemic: hope lives here

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“As lung cancer patients are more vulnerable to unfavorable outcomes, there is an obvious need for immediate treatment and any delay could compromise survival. Thus, managing lung cancer during the COVID-19 crisis is a challenging task and all necessary measures should be taken to protect both the patient and the staff, especially from asymptomatic carriers.”

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Lung cancer is the most common cancer type among males and the mortality is high, despite recent advances in cancer management. These patients are at a significantly higher risk of getting infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) amidst the current pandemic [1]. In most countries, the majority of hospital resources are being diverted for the management of COVID-19, leaving less space for cancer care. Overburdened healthcare systems are facing a shortage of protective equipment, diagnostic testing kits, ventilators and intensive care units (ICUs). Additionally, there are further restrictions to routine clinical care in order to limit the transmission of SARS-CoV-2 infection. All of these factors combined make the current pandemic one of the biggest healthcare crises in history.

Successful lung cancer management requires frequent hospital visits and admission for investigations, radiotherapy, chemotherapy etc. over the course of many weeks, thus risking high exposure of already immunocompromised patients to SARS-CoV-2 infection.

The majority of lung cancer patients are diagnosed at advanced stages and any further delay will compromise the outcomes, so there is a need of urgency in the lung cancer management field. Lung cancer patients are also prone to other community acquired and nosocomial infections, more commonly than other cancer types [2]. This makes management of lung cancer patients during the COVID-19 pandemic a challenging task not only for oncologists, but also for patients, as hospital visits are restricted to check the spread of SARS-CoV-2.

In a study by Yu *et al.* [3], it is reported that cancer patients have a higher risk of getting infected with SARS-CoV-2 (0.79%), compared with non-cancer patients (0.37%), especially lung cancer patients (7 out of 12 patients) and those aged 60 years or older.

As lung cancer patients are more vulnerable to unfavorable outcomes, there is an obvious need for immediate treatment and any delay could compromise survival. Thus, managing lung cancer during the COVID-19 crisis is a challenging task and all necessary measures should be taken to protect both the patient and the staff, especially from asymptomatic carriers.

Currently, there are guidelines regarding the continuation of cancer treatment or delaying it, but the onus is on the oncologist after detailed discussion with the patient.

### Challenges in lung cancer diagnosis

The similarities in pneumonia secondary to COVID-19 or lung cancer (such as fatigue, cough and difficulty in breathing) make it difficult to differentiate them clinically and can result in the spread of the viral infection among contacts and health staff. All lung cancer patients scheduled for anticancer treatment must be tested for COVID-19, irrespective of symptoms or contact history, to determine the status before compromising their immune system. Unfortunately, testing kits are not readily available [4].

It is advisable to use image-guided biopsy to establish the diagnosis and avoid aerosol-generating procedures like bronchoscopic biopsy, bronchial lavage cytology and mediastinal staging with endobronchial ultrasound.

The Royal Australian and New Zealand College of Radiologists (Sydney, NSW, Australia) recommends deferring or cancelling the nonurgent procedures except procedures to save life and permanent disability [5]. For lung cancer treatment, biopsy is the first step and it should be decided by the doctor, on a case-by-case basis to plan further interventions.

### Challenges in lung cancer treatment: surgery

Lung cancer surgeries can still be performed depending on the hospital resources, risk of exposure to SARS-CoV-2 and risk of delaying cancer surgery, which can be anything from few days to weeks.

In hospital settings with fewer COVID-19 patients, all confirmed and suspected lung nodules with tumor size greater than 2 cm or node positive cases should undergo surgical intervention immediately as any delay could result in rapid progression. While for confirmed or suspected cases of lung cancer with tumor size less than 2 cm, treatment can be delayed and other cancer therapies can be considered [6].

In hospital settings with many COVID-19 patients, there is limited availability of ICUs and ventilators. Surgery should be preferred for lung cancer cases with complications like pneumonia, hemothorax and empyema as these conditions have a negative impact on survival in lung cancer patients. However, in this present crisis, lung cancer surgeries should be deferred if possible and should only be performed in cases where adjunctive treatment is not available and hospital resources are able to support such surgeries. In this situation, lung cancer patients can be managed at other cancer centers or can be treated with other modalities like neoadjuvant chemotherapy or radiotherapy [7]. Targeted therapy should be considered in patients where mutation analysis is favorable to support such therapy.

### Challenges in lung cancer treatment: radiotherapy

As lung cancer is a rapidly proliferating disease, radiotherapy or chemo-radiotherapy plays an important role in the management. All lung cancer patients scheduled for radiotherapy should be treated separately to prevent the spread of infection. Extra precautions should be taken for lung cancer patients and proper cleaning of the area should be done before and after treating lung cancer patients with COVID-19 [6].

As per recent data, coronavirus can remain viable on plastic surfaces for up to 72 hours, making radiotherapy equipment a potential transmission nidus [7]. Immobilization devices need to be disinfected, wrapped and sealed in a plastic bag after each daily use. Treatment tables and positioning devices need to be disinfected after every patient use.

Decontamination of rooms should be properly done along with thorough cleaning of the CT scan room, wearing personal protective equipment if previously occupied by patients with suspected or known COVID-19 infection. Room ventilation is an important consideration for the prevention of airborne transmission in both treatment and imaging areas.

### Challenges in lung cancer treatment: chemotherapy, targeted therapy & immunotherapy

According to the American Society of Clinical Oncology (VA, USA), “*To date, there is no supporting evidence to delay, withhold, or change chemotherapy, targeted therapy or immunotherapy in cancer patients. Therefore, routinely withholding critical anticancer or immunosuppressive therapy is not recommended.*”

Zhang et al. [8] reported a case of 57-year-old male lung cancer patient who presented with fever and other symptoms of COVID-19 while receiving palliative radiotherapy and was found positive for the disease. This patient continued to receive the planned targeted therapy after cure of COVID-19 because his overall situation

permitted the same, but there is always a conflicting situation regarding continuing chemotherapy, targeted therapy and immunotherapy.

If a lung cancer patient on targeted therapy develops COVID-19, the treating team would need to look at the potential drug interactions between the targeted drug(s) that the patient was taking and the medication(s) needed to treat COVID-19. Increased risk of hepatic and/or renal dysfunction, are distinct possibilities; if so, may mandate either a reduction in dose/frequency or temporary discontinuation of the ongoing-targeted drug(s). Theoretically, a short duration of discontinuation/dose modification is unlikely to have any adverse impact on the disease status (especially if the patient is in clinical remission) but the risk of tumor progression may increase if this interruption is sustained for several days. Targeted therapies with known cardiovascular toxicities (especially VEGF inhibitors) may need to be temporarily withheld until the patient has recovered fully from COVID-19, especially since there is a concern that myocardial dysfunction may be an important contributing factor to mortality from COVID-19 [9].

Immunotherapy scheduled cycles may be modified or delayed to reduce clinical visits. For instance, a 4- or 6-weekly dosing could be used instead of a 2- or 3-weekly for selected agents when appropriate.

### Challenges in supportive care in lung cancer

The primary role of palliative and supportive care is symptom management by addressing the physical, emotional, social and spiritual needs of patients in a life-threatening illness. Advanced stages of lung cancer are rarely curative in nature, hence there is an increased need for palliative and supportive care. Symptoms that require palliation include pain, breathlessness, anxiety and depression. The management of these symptoms will not only increase survival but also improves the quality of life of lung cancer patients.

Elderly lung cancer patients are vulnerable group for COVID-19. Acute onset breathlessness in lung cancer patients at this time of COVID-19 pandemic will always lead to a diagnostic dilemma whether it is due to disease progression or due to COVID-19 infection. The social and psychological stigma associated with COVID-19 is the major cause of suffering in this group of patients. This is associated with disproportionate anxiety and depression. So, anxiety and depression needs to be addressed simultaneously with other symptoms like pain and cough [10].

### Challenges in lung cancer screening

Lung cancer unfortunately does not become clinically apparent until it reaches an advanced stage; more than 75% of lung cancers are only diagnosed once the disease is advanced or metastatic. Screening is an effective method to detect cancer at an early stage. While there are regular screening recommendations for breast and cervical cancer, it is not the same in case for lung cancer. Low dose computed tomography has been recommended for lung cancer screening, as this is proven to be an effective modality with mortality reduction benefit. Most countries or organizations have not framed any guidelines for lung cancer screening due to cost-effectiveness and morbidity issues related to low dose computed tomography [11]. In this current situation, all organizations/institutions have recommended to postpone routine lung cancer screening for high risk smokers.

### Challenges in lung cancer awareness

Lung cancer is preventable and awareness regarding risk factors (i.e. active and passive smoking, a variety of occupational agents and indoor and outdoor air pollution) along with behavior modifications are key strategies in lung cancer prevention [12]. The COVID-19 pandemic has adversely affected all these activities, but awareness can be continued using the various platforms for online education. Lung health is of utmost importance as people with lung diseases are more prone to develop severe or critical form of COVID-19.

### Challenges in tobacco control & smoking cessation

Tobacco and smoking are important risk factors of obstructive pulmonary diseases, resulting in reduced lung capacity, coughing and difficulty in breathing. Tobacco, smoking and secondhand smoke are also associated with increased risk of cardiovascular disease and many studies established the fact that patients with pre-existing respiratory and cardiovascular disease have more severe events, ICU admission and deaths compared with other conditions. Furthermore, waterpipe, a tobacco product, leads to short- and long-term harmful cardiovascular and respiratory disorders, associated with increased risk of infectious diseases [13].

Various studies in China have demonstrated that COVID-19 patients who were current and former smokers have a higher incidence of ICU admission. These findings were also reported in the Middle East Respiratory Syndrome Coronavirus outbreak [14]. ACE2 expression in the lung increases with tobacco consumption and age; it

has been suggested that over expression is linked with higher susceptibility to COVID-19, which explains why old age, pre-existing respiratory and hypertensive disorders are associated with higher mortality [15].

Thus, strict implementation of tobacco control and smoking cessation measures are necessary to reduce respiratory and cardiovascular diseases and reduce the severity of COVID-19 in these subsets of patients.

### Lung cancer patients precautions & choices

Lung cancer patients must be educated regarding close contact and droplet transmission along with COVID-19 symptoms (i.e. fever, dry cough, respiratory distress and gastrointestinal symptoms). Patients should immediately report to hospital in case of any symptoms to rule out COVID-19.

According to French guidelines, lung cancer patients can continue their treatment while lung cancer patients with COVID-19 can continue their cancer treatment after recovery from COVID-19. Hospitals can prioritize the management or treatment of lung cancer patients based on disease progression, age, general condition, aggressive nature of cancer type and requirement of palliative care. In the case of advanced or metastatic disease, treatment should be prioritized with no delay [16].

All cancer care hospitals should develop a triage in a separate isolated area for all patients coming to hospital. Teleconsultation/video-consultation can be arranged to avoid follow-up visits in the hospital, but this can only help the patients to receive advice on some pertaining issues, to minimize fear and insecurities related to treatment break, delay and to psychologically relieve them. There are many myths associated with COVID-19, that are causing panic among patients; all these myths with relevant facts are summarized in an editorial from Shankar *et al.* [17].

### Conclusion

It is well established that delayed lung cancer surgery may lead to disease progression and result in tumors that are no longer resectable, leading to worse outcomes, including overall survival. The same goes for neo-adjuvant or adjuvant chemotherapy regimens administered with suboptimal timing. It should be emphasized that these scenarios involve patients in whom the disease is potentially curable by appropriately administered cancer treatment. Therefore, a sincere attempt should be made to avoid delays in any of these fundamental procedures. For patients with locally advanced and metastatic disease, treatment delays could be associated with disease progression and reduced overall survival as well as a poorer quality of life. However, this needs to be balanced with increased risk of infections (including SARS-CoV-2) resulting from administration of chemotherapy. Targeted therapies are generally safe while the potential interaction between immunotherapy and COVID-19 remains unknown at present. Therefore, such patients in the absence of any symptoms suggestive of COVID-19 should be considered for continuation of planned chemotherapy, immunotherapy or radiation. The inability to deliver palliative care to patients unable to move from their homes and the management of treatment side effects are other significant concerns from a forced quarantine.

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