Emphasize and Administrative Recommendations for Lung Cancer Patients in COVID-19

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Abstract: The recent COVID-19 pandemic has impacted world health in tangible as well as yet unforeseen ways. One particularly worrisome population for infection with viral pneumonia is patients with lung cancer.

Although clinical data regarding the specific health effects of COVID-19 on patients with lung cancer are limited, case studies are proving to be valuable in understanding the pulmonary pathology of the viral disease.
With insufficient clinical awareness, a missed diagnosis of viral pneumonia may occur due to the fever and respiratory symptoms caused by lung cancer and its secondary diseases. Scientific protection and individual management of lung cancer patients are particularly important during corona virus epidemic prevention and control.

I. INTRODUCTION

Lung Cancer and COVID-19 risk

In a study published in *The Lancet Oncology*, which spanned 575 hospitals across China, researchers collected and analysed data from 1,590 patients having confirmed COVID-19, among which 18 had a history of cancer. Of these patients, 5 (28%) had lung cancer, which was the most common type of cancer. Those with cancer and COVID-19 were older, with a mean age of 63.1 years vs. 48.7 years among patients without cancer.
Interestingly, researchers noted that patients with cancer were at higher risk of severe events (ie, admission to the ICU requiring intensive ventilation and/or death) than those without cancer. Specifically, patients who received chemotherapy or surgery in the past month were at greater risk of clinically severe events compared with those who did not receive such treatment. The researchers also noted that the incidence of cancer in the sample population was higher than that of the overall Chinese population. In all, patients with cancer were found to be at greater risk of COVID-19 than those without cancer, and patients with cancer had poorer outcomes from COVID-19.

II. TREATMENT STRATEGIES

The researchers thus proposed three major treatment strategies for patients with cancer during the COVID-19 pandemic as well as other potential novel viral onslaughts:

First, an intentional postponing of adjuvant chemotherapy or elective surgery for stable cancer should be considered in endemic areas. Second, stronger personal protection provisions should be made for patients with cancer or cancer survivors. Third, more intensive surveillance or treatment should be considered when patients with cancer are infected with SARS-CoV-2, especially in older patients or those with other comorbidities.

III. LIMITATIONS

Although findings from this retrospective study were "excellent," according to the authors of a related commentary published in *The Lancet Oncology*, some limitations were noted.
First, the data in the Concluded by Liang and colleagues showed a higher percentage of patients with cancer in the COVID-19 cohort than in the overall population. However, this observation was not sufficient to conclude that patients with cancer had a higher risk of COVID-19. The incidence of COVID-19 in patients with cancer would be more informative in assessing whether or not patients with cancer have an increased risk of COVID-19.
Second, they reviewed the cancer history of the 18 individuals discussed in Liang and colleagues' Comment. They are concerned that such a small sample size with a large amount of heterogeneity, presenting as various cancer types with different biological behaviours, highly variable disease courses (from 0–16 years), and diverse treatment strategies, might be filled with contingency and thus not ideally representative of the whole population with cancer. Notably, half of the patients with cancer had a disease course of more than 4 years, indicating that a substantial proportion of these patients might be clinically cured. Therefore, any conclusions that generalise to all patients with cancer should be interpreted with caution.
Third, 13 (72%) of 18 patients with cancer had a history of surgical resection; the prolonged effects induced by surgery including immunosuppression should not be neglected. Comparison of patients with COVID-19 and surgical history with and without cancer would be of interest.
Nevertheless, authors of a Chinese-language review article, published in the *Chinese Journal of Lung Cancer*, seemed to support the idea of targeted, prioritized treatment strategies

for patients with cancer—particularly lung cancer—amid the COVID-19 pandemic:

IV. PRIORITIES FOR LUNG CANCER PATIENTS

4.1 Outpatient visit priorities

High Priority

New diagnosis or suspicion of invasive lung cancer with either:

- Disease-related symptoms (dyspnoea, pain, haemoptysis, etc.)
- Suspicion of clinical stage II/IIIA/IIIB or metastatic NSCLC or SCLC

Visits for treatment administration

Medium Priority

- New diagnosis or suspicion of localised lung cancer of clinical stage I
- Post-operative patients with no complications
- Follow-up for patients at high risk of relapse
- Established patients with new problems or symptoms from treatment: convert as many visits as possible to telemedicine visits

Low Priority

- Survivorship visits
- Follow-up for patients at low/intermediate risk of relapse
- Patients visits for psychological support (convert to telemedicine)

4.2 Priorities for Lung Disease: Imaging

High Priority

- Patients with significant respiratory symptoms and/or other clinically relevant chest, cancer- or treatment-related symptoms. In patients with new respiratory symptoms such as dyspnoea, cough with or without fever, a CT-scan is recommended
- Standard staging work-up for suspected lung cancer of unknown stage or stage II/III/IV
- Biopsies for suspicious nodules or mass for suspected lung cancer of stage or stage III/IV
- Evaluation of active treatment response in the first 6 months of treatment or if suspicion of progression at any timepoint
- Pre-planned imaging evaluation per clinical trial protocol

Medium Priority

- Follow-up imaging for high/intermediate risk of relapse within one year of completion of radical treatment
- Standard staging work-up for early lung cancer (stage I)
- Biopsies for suspicious nodules or mass for suspected invasive cancer of unknown stage or stage I/II
- Established patients with new problems or symptoms from treatment
- Evaluation of active treatment response beyond 6 months of treatment if stable/controlled situation
- Follow-up of nodules of incidental finding with either:
  - Solid nodule 50-500 mm^3
  - Pleural-based solid nodule 5-10 mm
  - Partially solid nodule with a non-solid component of ≥8 mm
- Known VDT (Volume Doubling Time) 400-600 days

Low Priority

- Follow-up imaging for high/intermediate risk of relapse more than a year after completion of radical treatment
- Follow-up imaging after radical treatment in a low risk of relapse scenario
- Follow-up of nodules of incidental finding with either:
  - Solid nodule <50 mm^3
  - Pleural-based solid nodule <5 mm
  - Partially solid nodule with a non-solid component of <8 mm
  - Non-solid nodule <8 mm
  - Benign morphology
  - Known VDT >600 days
- Lung cancer screening can be deferred until the COVID-19 pandemic resolves – It is reasonable for patients in the general population to defer screening low-dose CT, a deferral that is not likely to have an impact on overall survival

4.3 Priorities for Lung Disease: Surgical Oncology

High Priority

- Drainage +/- pleurodesis of pleural effusion, pericardial effusion, tamponade risk
- Evacuation of empyema-abscess
- T2N0 tumours naïve from treatment or after induction chemotherapy
- Resectable T3/T4 tumours naïve from treatment or after induction chemotherapy
- Resectable N-1/N2 disease naïve from treatment or after induction chemotherapy
- Diagnostic procedure such as mediastinoscopy/thoracoscopy/pleural

biopsy/endoscopy/transthoracic investigations for diagnostic/staging work-up

Medium Priority

- Discordant biopsies likely to be malignant
- Resectable NSCLC with T1AN0 (alternative if no surgical capacity available, is stereotactic radiotherapy; surgery is preferred)
- Diagnostic work-up and/or resection of nodules of incidental finding with either:
  - Solid nodule >500 mm^3
  - Pleural-based solid nodule >10 mm
  - Solid component >50 $0mm^3$ in partially solid nodule
  - Known VDT <400 days
  - New solid component in pre-existing non-solid nodule
- alternative if surgery indicated and no surgical capacity available is stereotactic radiotherapy

Low Priority

- Discordant biopsies likely to be benign
- Operable pure GGO nodule (T1a)
- Diagnostic work-up and/or resection of all other nodules of incidental finding including also:
  - Solid nodule >500 mm^3 *and known VDT >600 days*
- alternative if surgery indicated and no surgical capacity available is stereotactic radiotherapy

4.4 Priorities for Lung Cancer: Medical Oncology – Early Stage Lung cancer

High Priority

- Concomitant chemoradiotherapy for SCLC limited disease stage I/II
- Neoadjuvant chemotherapy (enabling deferral of surgery by 3 months) in clinical stage II
- Delivery of adjuvant chemotherapy in T3/4 or N2 disease for young (<65 years old) and fit patients
- G-CSF use if febrile neutropaenia risk evaluated to be >10-15%

Medium Priority

- Adjuvant chemotherapy in T2b-T3N0 or N1 disease should be discussed with patients, considering clinical features and prognosis
- Medical follow-up between 2 cycles should be performed only if necessary and by telephone
- Blood check between 2 cycles should be performed only if necessary and at home if possible

Low Priority

- Adjuvant chemotherapy in stage T1A-T2bN0 with negative prognostic features (lymphovascular infiltration, histological subtype…). The risk versus potential benefit should be individually discussed with patients
- Adjuvant chemotherapy for patients with significant comorbidities, or elderly patients >70y, should be discussed and possibility omitted

4.5 Priorities for Lung Cancer: Medical Oncology – Locally advanced Lung Cancer

High Priority

- Concomitant chemoradiotherapy for SCLC limited disease stage III
- Concomitant or sequential chemoradiotherapy for inoperable NSCLC Stage III
- Starting consolidation durvalumab (within 42 days)
- Neoadjuvant chemotherapy in clinical stage III
- G-CSF use if febrile neutropaenia risk evaluated to be >10-15%

Medium Priority

- Medical follow-up between 2 cycles should be performed only if necessary and by telephone
- Blood check between 2 cycles should be performed only if necessary and at home if possible

4.6 Priorities for Lung Cancer: Medical Oncology – Metastatic Lung Cancer

High Priority

- 1^{st}-line treatment including chemotherapy, chemotherapy plus IO, IO alone or TKIs to improve prognosis, cancer-related symptoms and QoL
- Start 2^{nd}-line chemotherapy or IO in symptomatic and progressive disease patients
- Start 2^{nd}-line TKI in progressive disease patients
- G-CSF use has to be considered if despite optimal dose modification, risk of febrile neutropaenia is >10%
- Anti-PD-(L)1 scheduled cycles may be modified/delayed to reduce clinical visits (for instance, using 4-weekly or 6-weekly dosing instead of 2- or 3-weekly for selected agents when appropriate (where allowed from National Regulatory Agency)

Medium Priority

- Start 2^{nd} and beyond line chemotherapy or IO in asymptomatic patients, in absence of threatening disease (volume/location)
- Consider, when feasible, oral chemotherapy treatment instead of intravenous (etoposide, vinorelbine) to reduce hospital visits

- Medical follow-up between 2 cycles should be performed only if necessary and by telephone
- Blood check between 2 cycles should be performed only if necessary and at home if possible
- For patients ongoing with IO from more than 12/18 months, delaying the next cycle, omitting some scheduled cycle, or generally enlarging intervals should be considered

Low Priority

- Discontinuation of IO after 2 years of treatment should be considered, keeping in mind the lack of prospective evidence
- For patients ongoing with IO having stopped due to toxicity, resuming might be delayed in absence of disease progression
- Postpone antiresorptive therapy (zoledronic acid, denosumab) that is not needed urgently

4.7 Priorities for Lung Cancer: Radiation Oncology

High Priority

- Radiotherapy for inoperable stage II-III cancers, with contra-indications for chemotherapy
- Concomitant (preferred) or sequential chemoradiotherapy for inoperable NSCLC Stage II/III
- Concomitant (preferred) or sequential chemoradiotherapy for SCLC limited disease
- Superior vena cava obstruction, significant haemoptysis, spinal cord compression, significant bone pain or any life-threatening condition amenable to palliative radiotherapy

Medium Priority

- SABR-SBRT for stage I cancers
- Adjuvant PORT for R1 resection, if indicated in NSCLC could be considered at the at the end of adjuvant chemotherapy or delayed up to 3 months from surgery
- PCI in limited stage SCLC after chemotherapy

Low Priority

- Adjuvant PORT N2 R0, if indicated in NSCLC should be discussed and if retained considered at the at the end of adjuvant chemotherapy or delayed up to 3 months from surgery
- PCI in extensive stage SCLC after chemotherapy may be replaced by MRI active surveillance
- Non-life-threatening conditions such as mild bone or chest pain should be considered for more aggressive analgesics and use of palliative radiotherapy should be individualised depending on individual benefit/risk ratio

V. CHALLENGES AND UNANSWERED QUESTIONS

One overriding difficulty when assessing the impact of COVID-19 and other novel respiratory viruses on the precarious state of lung cancers is a lack of research.

We expect that in the months to come, more detailed studies will be forthcoming on the impact of COVID-19 infection in cancer patients, including the risk of infection, the clinical impact of COVID-19 and concurrent cancer, the effect on different types of cancer, and the ability to deliver appropriate and even curative cancer treatments in the setting of infection.

For now, many questions remain unanswered: Should cancer treatments such as chemotherapy or radiotherapy be delayed or modified? Should cancer patients undergo a differential screening process for COVID-19 infection, compared with the general population? How can we reduce the rate of nosocomial infections?

We will need to understand the heterogeneity in effectiveness of what we hope are soon-to-be approved COVID-19 vaccines and antiviral agents in cancer patients, and that COVID-19 infection will become just one additional factor to take into consideration in the comprehensive management of oncology patient.

List of abbreviations: CT: computed tomography; G-CSF: granulocyte colony-stimulating factor; GGO: ground-glass opacity; IO: immune-oncology; NSCLC: non-small cell lung cancer; QoL: quality of life; PD-1: programmed cell death protein 1; PD-L1: programmed death-ligand 1; SABR: stereotactic ablative radiotherapy; SBRT: stereotactic body radiotherapy; SCLC: small cell lung cancer; TKI: tyrosine kinase inhibitor; VDT: volume doubling time.

VI. REFERENCES

[1]. WHO: World Health Organization, 11 March 2020, WHO Director-General's opening remarks at the media briefing on COVID-19, Geneva

[2]. Liang W, Guan W ,Chen R (2020),Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China, *LancetOncol.* 2020; 21: 335-337

[3]. Ksiazek TG ,Erdman D ,Goldsmith CS ,A novel coronavirus associated with severe acute respiratory syndrome ,*N Engl J Med.* 2003; 348: 1953-1966

[4]. Samson P ,Patel A ,Garrett T ,Effects of delayed surgical resection on short-term and long-term outcomes in clinical stage I non-small cell lung cancer, *Ann Thorac Surg.* 2015; 99: 1906-1912

[5]. Dai M ,Liu D Liu M (published online April 28.),Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak, *Cancer Discov.* 2020;

[6]. Miyashita H ,Mikami T ,Chopra N(published online April 21.) ,Do patients with cancer have a poorer prognosis of COVID-19? An experience in New York City, *Ann Oncol.* 2020;