Radiotherapy for Lung Cancer during COVID pandemic – A Narrative Review of Practical Recommendations

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Abstract

Background: The coronavirus disease pandemic produced changes in the treatment approach of lung cancer patients. They represent a vulnerable population due to the negative impact of delays in diagnosis and treatment and also because of the impaired immune system. Radiation Therapy plays a crucial role in both curative and palliative settings, so finding the best approach for these patients in this context was attempted by many professionals. The aim of this study was to make a synthesis of the current published literature on this topic and summarize the recommendations.

Material and methods: We searched the PubMed database for articles published between 20th December 2019 and 30th August 2020. We used 14 key words related to COVID 19 and Lung Cancer. The articles were selected by two senior clinicians who excluded overlapping information and prioritized original research reports and professional organization's official recommendations.

Results: There were 562 papers corresponding to the search criteria, of which 64 were analyzed. Treatment decision must be tailored according to the status of SARS CoV-2 positivity, the aim of the treatment (curative VS palliative), pathological type and clinical stage, disease complications, symptoms, prognostic, performance status, and alternative treatments. Hypofractionation is preferred whenever possible in order to minimize risk for patients and staff. Safety measures have to be implemented, with extra cautions if SARS CoV-2 positive patients have to be treated. Cone beam CT can be used early identification of lung infiltrates and special attention is recommended to differentiate Radiation pneumonitis from COVID-19 pneumonia.

Conclusion: For SARS CoV-2 positive lung cancer patients the treatment should be postponed, until they are tested negative. For patients which are SARS CoV-2 negative treated with curative intent, hypofractionated schedules are preferred. Palliative treatments should be given according to the life threatening risk.

Keywords: COVID-19, SARS CoV-2, Corona Virus, Lung Cancer, Radiotherapy, Radiation Oncology, Hypofractionation

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Introduction

The changes caused by the spread of Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) have a significant impact on cancer care (1), including radiation oncology practice (2-4). The new challenges were reflected by the increasing number of publications, which are helping the members of the professional community to share their experience and learn from each other (5). Among the Oncology publications, there was an initial focus on the procedures and policies implemented to help protect the patients and personnel, followed by attempts to define the optimal management of cancer during the pandemic (6).

There is emerging data on cancer patients, including lung cancer, reporting a higher incidence of severe and fatal infections with SARS CoV-2 compared with age-adjusted patients without cancer. According to registries like COVID-19 and Cancer Consortium (CCC-19) Thoracic cancer international coVID 19 collaboration (TERAVOLT), and institutional reports, the fatality rate in lung cancer patients ranged from 25% to 55% (7-11). However, most patients recovered, including 25% of those that required intubation. Patient-specific

factors, like smoking status and chronic obstructive pulmonary disease, were the main determinants of the outcome (9).

The decision that has to be made for each case takes in account the risk of infection with SARS-CoV-2 (and its potential complications), and the risks associated to postponing or interrupting the treatment of lung cancer, which has a higher mortality.

Objective challenges related to transportation, hospital admission or medical procedures, and also subjective reasons like the hesitation of leaving home during COVID-19 pandemic lockdowns, caused delayed diagnosis, and subsequent upstaging, changing the treatment indication and worsening the prognosis (12).

The prediction of a long co-existence with SARS CoV-2 virus requires striking a balance between whom to treat and whom to delay the treatment.

The aim of the current article is to provide an insight on the practical recommendations for Radiation Oncologists regarding risk analysis, prioritization and timing of workup and therapeutic procedures in lung cancer patients infected with SARS CoV-2. Since there is lack of high quality scientific evidence, gathering data from multiple sources can improve the ability of taking the

best clinical decision in each patient's specific context.

Materials and Methods

Papers listed on the PubMed database between 20th December 2019 and 30th August 2020 were searched using 14 key words related to COVID-19 and Lung Cancer. Complete PubMed search string can be found in the supplementary materials. All articles were verified for their content by two senior clinicians. Preclinical studies and articles reporting the same results were not included in the analysis. The final review was carried out only for articles in English, which were considered to report new, trustable and clinically applicable findings regarding diagnosis and treatment particularities in lung cancer patients who were diagnosed with COVID-19. We prioritized in our analysis the original research data and recommendations of professional societies, groups, and organizations.

Results

Total number of articles identified was 562, of which we selected 64, using the above-mentioned criteria.

We grouped the material into three sections:

1. Radiotherapy for lung cancer patients in the curative setting
2. Radiotherapy for lung cancer patients in the palliative setting
3. Radiotherapy-related imaging aspects

1. Radiotherapy for lung cancer patients in the curative setting

Based upon the consensus ESTRO-ASTRO recommendations by Guckenberger *et al.* (13) and the Oncologic Group for the Study of Lung Cancer and the Spanish Society of Radiation Oncology (GOECP/SEOR) recommendations by Couñago *et al.* (14) we identified three strategies that can be applied, alone or combined, depending on the case: selecting priority cases for early management, fractionation alterations, and delay or interruption of treatment. The first one applies to all patients, the second to SARS CoV-2 negative cases, and the last one in SARS CoV-2 positive patients.

1.1. Selecting priority cases for early management

In order to balance the risk of exposing patients and healthcare staff to the SARS CoV-2 virus, with the risk of failing to treat a potentially fatal cancer, especially in the context of limited resources, relative priority of different lung cancer cases must be set. The decision should be based on following factors: potential for cure, relative benefit of Radiotherapy (RT) vs. other treatment options, active SARS-COV-2 infection (or its absence), life expectancy and performance status.

Accordingly, locally advanced Non Small Lung Cancer (NSCLC) > limited stage Small Cell Lung Cancer (SCLC) > early stage NSCLC might be the priority order of patients from most important to least important.

1.2. Fractionation alterations in SARS CoV-2 negative patients

The alternative dose fractionation schedules reduce the risks associated with multiple hospital visits (12, 15) and subsequently would increase radiotherapy service capacity for patients with stage I-III operable lung cancer, who might be unable to have surgery during the pandemic. A shorter course of radiotherapy is less likely to be obstructed by unplanned staff shortage and at the same time reduces exposure to staff members. It also maximizes the use of a single Personal Protective Equipment kit and optimizes resource utilization and costs.

In addition to the consensus recommendations cited above, guidelines for reduced fractionation during the pandemic by Finn *et al.* can be considered (16).

Peripheral lesions in the "safe" zone

Stereotactic Body Radiotherapy (SBRT) with 30-34 Gray (Gy) in single fraction (fr) should be considered in patients with tumours ≤ 2 cm in size, > 1 cm from the chest wall and outside the no-fly zone as per National Comprehensive Cancer Network (NCCN) guidelines (17). Two phase II trials (Radiation Therapy Oncology Group (RTOG) 0915, Roswell Park) (18-20) showed that local control, progression free survival and overall survival, as well as late toxicity and quality of life, were comparable between single-fraction and multi-fraction SBRT regimens for this group of tumors. Such extreme hypofractionation should be considered for cases otherwise typically treated with 54 Gy/3 fr, rather than 55 Gy/5

fr and for tumours that move <1 cm after appropriate motion management on 4D-CT imaging.

Lesions adjacent to the chest wall

For early NSCLC tumors ≤ 2.5 cm from chest wall, 48 Gy/4 fr and 54 Gy/3 fr SBRT regimens can be considered safely taking into consideration the limited possible chest wall toxicity (21-22).

The rate of grade 3 chest wall toxicity with SBRT from a large meta-analysis (combining several different dose and fractionations) is 1.2% (23).

Moderately Central Tumours

Defined as a lesion within 2 cm of the bronchial tree, trachea, major vessels, oesophagus, heart, pericardium or brachial plexus, or a Planning Target Volume (PTV) abutting mediastinal pleura or pericardium, excluding ultra-central disease – an SBRT regimen of 50 Gy/ 5 fr (24) is favoured over 60 Gy/ 8 fr (25) for these lesions in these pandemic times.

Central/Ultra-central tumors

An ultra-central lesion is where the PTV abuts either the main bronchi or trachea. In spite of being early stage, these NSCLC tumors are not suitable for SBRT based on organs at risk constraints. The dose of 50 to 60 Gy/ 15 fr radiotherapy with/ without sequential chemotherapy may be considered in current scenario. These dose fractionations are based on a prospective Phase III study by Iyengar P *et al.* (26), and a retrospective study by Cho *et al.* (27).

The first study randomized 60 patients of stage II-III NSCLC patients between 60 Gy/

30 fr and 60 Gy/ 15 fr. Interim results reported less toxicity in the 15-fractions arm.

Stage III NSCLC

The current standard of care for unresectable Stage III NSCLC (Concurrent platinum based chemotherapy and External Beam Radiotherapy (EBRT) 60-66 Gy/ 30-33 fr followed by consolidation Durvalumab according to the patient's PD-L1 status), is still valid. However, severe resource constraint may lead to choosing sequential Chemotherapy (limited to 2 cycles) followed by hypofractionated radiotherapy. The rationale is based on reducing the potential immunosuppressive effects of concurrent CT-RT, which would subsequently minimize the risk of complications caused by COVID-19.

The impact of the COVID-19 pandemic on surgery departments, including thoracic surgery, will likely increase the number of patients with potentially resectable stage III NSCLC who receive non-surgical treatment. For hypofractionation in Stage III NSCLC, the widely used protocols are: 55 Gy/20 fr based on the commonly used UK regime (28), 60 Gy/15 fr as reported by the Canadian Sunny Brook Cancer Centre (29) and 65 Gy/20 fr as studied by the I-START trial (30).

However, apart from the UK regimen mentioned above, other regimens have not been established by phase III Randomised Control Trials (RCT).

Early Stage SCLC

SBRT is recommended in pandemic times for early stage SCLC, as supported by

ASTRO 2020 guidelines (31) and the 2020 NCCN guidelines (32).

Limited Stage SCLC with good performance status

Though the current standard of care is twice-daily radiotherapy (45 Gy/ 30 fr) delivered concurrently with cycle 1 or 2 chemotherapy (33, 34), this protocol implies increased exposure to the hospital environment. Therefore, hypo-fractionated regimes with once daily fractionation are preferable, though only scant evidence is available to support these in limited stage SCLC. Regimens like 40 Gy/ 15 daily fractions and 50-55 Gy/ 20 daily fractions are used in UK centers (35).

Grønberg *et al.* reported similar survival and toxicity outcomes with 42 Gy in 15 daily fractions versus 45 Gy in 30 fractions, given twice daily in a randomized phase II trial. Guliani *et al.* (36) reported similar toxicity profiles for 40 Gy/15 daily fractions and 45 Gy/ 30 fr given twice daily.

Although Prophylactic Cranial Irradiation (PCI) for limited stage SCLC remains the standard recommendation even during the pandemic, it could be delayed if brain Magnetic Resonance Imaging (MRI) is used to closely monitor the patient (37).

Extensive Stage SCLC

Consolidation CT-RT has been shown to improve survival in extensive stage SCLC patients who had significant response to chemotherapy (38), but in the current scenario it is safe to consider omitting consolidation CT-RT in cases where complete response of lung disease to

chemotherapy has been recorded. Similarly, PCI in extensive stage SCLC can be replaced with brain MRI monitoring (37).

1.3. Delay or interruption of treatment in SARS CoV-2 positive patients

If a lung cancer patient is tested positive for SARS-COV-2, before starting the RT, there is uniform consensus among experts to postpone initiation of RT until the patient becomes asymptomatic and the test for SARS-COV-2 becomes negative.

If a patient undergoing radiotherapy develops COVID-19 disease, the decision to interrupt RT depends on various tumour, patient and COVID-19 related factors. The tumor related factors are the extent of the disease, the presence or absence of tumor-related symptoms (obstruction, haemoptysis, or pain), and the risk of tumor progression. Patient related factors are patient's respiratory status and general condition. COVID-19 related factors are infection-severity, presence or absence of pneumonia, and COVID-19 related symptoms.

There is strong consensus to interrupt RT till recovery from COVID-19 in cases with low risk of tumor progression like post-operative cases or PCI cases. However, for cases like Stage I NSCLC, Stage III NSCLC, Limited Stage SCLC, where treatment gap would considerably reduce effectiveness of radiotherapy - opinions to interrupt RT are split among experts.

If decision is made to continue radiotherapy in a SARS-COV-2 positive patient, strict safety measures to protect

health care personnel as well as other non-infected patients must be implemented according to recommendations of national and international organizations. The main safety measures include avoiding physical contact between infected and non-infected patients in the department. This may include different rooms for COVID-19 patients, and/or treating these patients at different times, and strict cleaning and disinfection protocols (39, 40).

2. Recommendations in the palliative setting:

A significant proportion of lung cancer patients require palliative radiotherapy for symptoms caused by advanced or metastatic disease, especially in the context of delayed diagnosis and/or treatment (41).

The indication and the dose-fractionation of palliative radiotherapy should be discussed with the multidisciplinary team, taking in account patient factors, logistic factors and availability of alternative therapy or best supportive care that can be provided at home. The patient also needs to be informed about the prognosis, treatment's goal, and the associated risks.

The Memorial Sloan Kettering Cancer Center (MSKCC) guideline recommends selection of patients requiring palliative radiation based on diagnosis, symptoms and life expectancy of the patient. They classified the patients into three groups, according to priority and emergency of the treatment.

- The first group includes neurological complications, high volume haemoptysis

and airway obstruction. In these cases, immediate palliative radiation is recommended.

- The second group includes two categories of patients: those having symptomatic disease, where radiation is standard of care, (excluding the above-mentioned emergencies) and those with asymptomatic disease, for which RT is recommended to prevent imminent complications. For this group, RT can be delayed.

- The third group, of lowest priority, includes patients requiring palliation, but for which radiotherapy represents one of the options, alternative therapies being available. The guideline also suggests medical therapies or best supportive care to patients with life expectancy of days to weeks (42).

Similar to radical radiotherapy, almost all the publications have recommended use of short course or abbreviated palliative radiotherapy schedules with omission or delaying such treatment for selected patients. There was strong consensus from the ESTRO-ASTRO report favouring hypofraction in palliative settings for NSCLC in contrast to the adjuvant and radical radiotherapy (including PCI for NSCLC and limited stage SCLC), where there was a weak agreement (13).

One article published from MSKCC in March 2020 recommended teleconsultation for initial evaluation of symptoms, performance status and imaging results, followed by clinical examination for selected patients by a single care giver (Radiation Oncologist or Advanced Practice Provider) especially when there are neurological symptoms re-

lated to spinal cord compression or brain metastasis (42).

Telemedicine facility was implemented quickly during the pandemic and was found to be associated with improvements in management of symptoms and comfort index. Adequate counselling via telemedicine approach increased patient and family satisfaction in palliative settings, as it was previously reported in the literature.

Telemedicine has also potential barriers, because it requires technological experience and also because both patient and physician may feel uncomfortable with indirect interaction. However, it can be a reasonably good communication tool, especially during pandemic, as suggested by the Netherlands group (43).

In the early phase of pandemic, for the palliative setting, the ESTRO-ASTRO statement reported a strong consensus (96%) on not postponing treatment more than 4-6 weeks for NSCLC patients. However, for SARS-CoV-2 positive patients there was strong consensus to postpone palliative radiotherapy till patients become asymptomatic and test for COVID-19 becomes negative. In case patients become positive for SARS-CoV-2 during treatment, interruption of radiotherapy was recommended (13).

2.1 Haemostatic radiotherapy

The most effective preferred dose-fractionation for haemostatic radiotherapy was 20 Gy in 5 fractions or 8 Gy single fraction as recommended by most of the

articles (42, 44). Both fractionations are well established for their efficacy of nearly 90% in controlling tumor bleed and are not found to be inferior to longer fractionation as suggested by Sapienza group (45).

2.2 Brain metastases

For single or oligometastatic disease in brain with favorable prognosis, stereotactic radiosurgery is recommended, when appropriate. MSKCC recommends treatment for all or the dominant lesion(s) that are most likely to increase morbidity. Twenty Gy in 5 fractions was found to be the most popular whole brain radiotherapy fractionation in this situation with 30 Gy in 10 fractions reserved for very carefully selected patients expecting longer survival (42).

2.3. Superior vena cava syndrome and malignant airway obstruction

The commonly recommended dose fractionation for Superior vena cava obstruction caused by locally advanced disease was 20 Gy in 5 fractions. Alternatively, 17 Gy in 2 fractions one week apart can be delivered, as both of these fractions are associated with similar results to standard fractionation. The two fractions regime is particularly useful for in-patients who can be discharged after one fraction and readmitted before next one, thus reducing the hospital stay. However, the radiation oncologist needs to be cautious about the spinal cord toxicity while using 2 fractions course, especially during re-irradiation. (42, 46-47)

In the early phase of pandemic, there was strong consensus (89%) to deliver 30 Gy in 10 fractions over 2 weeks for NSCLC causing symptoms related to mediastinal or hilar disease progression, severe cough and moderate dyspnoea in the report by Guckenberger *et al.* However, in the late phase of pandemic the authors recommended shortening of treatment up to 8-10 Gy in single fraction, due to lack of radiotherapy resources (13).

For malignant airway obstruction, cases should be discussed in multi-disciplinary tumor board on individual basis before selecting radiotherapy as choice of palliation. In patients with SARS-CoV-2 infection, there is limited data on effect of radiation exposure on lung, which could lead to acute respiratory distress syndrome requiring mechanical ventilation (12).

2.4. Spinal cord compression

For patients with spinal cord compression, 8 Gy single fraction remain to be the choice of palliative radiation dose in the pandemic situation due its similar efficacy in symptom control compared to longer fractionation schedules. (48, 17)

2.5. Bone metastases

Similar dose fractionation has been recommended for uncomplicated painful bone metastases also (12). Selected solitary bone metastases can be treated with SBRT which is found to be equally effective in controlling pain without significant toxicity (49).

However, bone metastases with impending fracture should be treated with elective surgery to reduce the incidence of pathological fracture and prolonged hospital stay thereafter. The MSKCC guideline also recommends follow up assessments via telemedicine with nursing or physician visit on a rotational basis for medical emergencies. All such visits shall be conducted maintaining all necessary protocols to avoid cross infection and spread of SARS-CoV-2 infection (42).

3. Radiotherapy-related imaging aspects

a. Cone beam computer tomography (CBCT) information during radiotherapy

Chest computer tomography (CT) plays a major role in the identification of COVID-19 pneumonia, with radiologic hallmarks including bilateral, peripheral ground-glass opacities and consolidation. Imaging features of this viral pneumonia are diverse, typically ranging from normal appearance to diffuse changes in the lungs; patients with multiple comorbidities are more likely to have bilateral and diffuse disease. Overall, there is a slight predilection for the right lower lobe. The extent of disease on CT scan increases gradually from the subclinical period throughout the first 3 weeks then decreases thereafter, but radiographic changes may continue to evolve beyond 26 days of symptoms.

During the RT treatment, the CBCT needed for image-guided RT can be useful to assess the lung tissue. An Italian group

recommended that daily CBCT can be effective for early detection of COVID-19 lung disease in asymptomatic or mildly symptomatic patients, helping to prevent the diffusion of this contagious disease to the care providers and of other patients in the department (50). The radiotherapy technicians working at CT simulation and linear accelerator should be trained to recognize suspicious images and refer the patients to the diagnostic department for standard CT acquisition or infectious disease monitoring, contributing to the early diagnosis (51). Youssef et al. from Brooklyn (52) reported an institutional protocol using a Halcyon's KV CBCT for the prospective review of thoracic CBCT scans in patients undergoing RT, in an effort to detect pulmonary changes. Both the initial simulation CT and on-board CTs acquired as part of daily image guidance should be reviewed for new or increasing infiltrates, particularly in patients with new symptoms, according to Samson *et.al* (53).

Owing to the observation that radiologic changes may precede physical symptoms, and considering a false negative rate ranging from 10% to 30%, this daily routine gives an additional tool to monitor patients and might be helpful especially for the frailest ones.

b. Overlapping of Radiation Pneumonitis and Covid-19 signs and symptoms

Radiation pneumonitis (RP) is a well described toxicity of thoracic radiation that has significant morbidity that has an

incidence ranging up to 40% as reported by Rodrigue group. The overlapping clinical and radiological features of RP and COVID-19 require risk stratification, as has been reported by Shaverdin *et al.* (54). This report illustrates the overlapping symptoms and imaging features of RP and COVID-19 and the need for diagnostic caution in the management of these findings. They recommend the following steps in the management of patients with a differential diagnosis that includes RP:

- Review of imaging findings to characterize the nature and distribution of pulmonary changes in relation to the radiation treatment field.

- Prioritization of COVID-19 testing before starting high-dose corticosteroids to prevent potential exacerbation of COVID-19 in these high-risk patients.

- Close monitoring of pulmonary symptoms, particularly among patients who initially test negative for SARS-CoV-2 virus infection, to assess for superimposed conditions including radiation pneumonitis.

In cancer patients with a history of thoracic radiotherapy treatment and a suspicion of COVID-19 disease, an extra effort should be made to differentiate COVID-19 interstitial disease from RP (55).

A summary of recommendations can be found in Table 1.

Table 1. Recommendations for Radiotherapy during COVID-19 pandemic

	Stage/ Location/Specific situation	Recommendations
NSCLC	Peripheral lesions in the "safe" zone	34 Gy/ single #
	Lesions adjacent to the chest wall	48 Gy/4#; 54 Gy/3#
	Moderately Central Tumours	50 Gy/5#
	Central/Ultra-central tumors	50-60 Gy/15#
	Stage III	55 Gy/20# & sequential chemotherapy
SCLC	Early stage	SBRT
	Limited Stage with good performance status	• 40 Gy/15 daily # or 50-55 Gy/20 daily # • Brain MRI monitoring instead of PCI
	Extensive Stage	• Omit consolidation CT-RT if complete response of lung disease to chemotherapy • Brain MRI monitoring instead of PCI
General	Priority of cases	locally advanced NSCLC > limited stage SCLC > early stage NSCLC
	If the patient gets infected before start of RT	Postpone RT initiation until the patient is asymptomatic and the test for COVID-19 becomes negative.

	If the patient gets infected during a course of RT	Interrupt RT till recovery from COVID if low risk of tumor progression.

Abbreviations: NSCLC- Non- small cell lung cancer; SCLC- Small cell lung cancer; Gy- Gray; #- Fraction; SBRT- Stereotactic Body Radiotherapy; PCI- Prophylactic cranial irradiation; CT-RT- Chemoradiotherapy; RT- Radiotherapy; COVID- Corona virus disease

Discussion

The first question regarding radiotherapy for lung cancer patients during COVID-19 pandemic is: to treat or not to treat - and if yes, when: now or later?

The ESTRO/ASTRO Consensus Statement had a significant contribution for Lung Cancer Radiotherapy recommendations, including at least twelve recommendation in early stage/ locally advanced NSCLC, Post Operative Radiotherapy (PORT) in NSCLC, limited stage SCLC, PCI in SCLC and palliative NSCLC (13).

One topic on which different opinions were expressed, was the postponement or interruption of treatment until the patient becomes SARS-CoV-2 negative

In response to the recommendation of the ESTRO/ASTRO Consensus Statement, Magrini *et al.* suggested that this practice would significantly impair the possibility of cure for a relevant number of SARS-CoV-2 positive cases. It was considered particularly worrisome for stage III disease, because of high incidence and severity. The long term survival for these cases is 15%-20%, and the death rate from SARS-CoV-2 infection is estimated between 2% and 8%. Delaying or denying the treatment might be their main cause of death, especially when the radiotherapy is interrupted after more than

half of the treatment fractions. The same team considered that the best approach is to manage both COVID-19 and Lung cancer at the same time (56).

For the patients exhibiting COVID-19 symptoms after admission, a Chinese group recommended isolation in single occupancy for 14 days and observation, decision which was considered as debatable by the same Italian group, as interruptions are recognized as detrimental for curative treatments (57).

The authors of ESTRO/ASTRO Consensus Statement admitted that the practice recommendation has to be meticulously individualized in a given setting. They emphasized that there is limited safety data about the potential interaction and added risk for Lung Cancer patients from SARS-CoV-2 infection, the thoracic radiotherapy and the combination of the two (58).

After deciding the necessity and the timing of the treatment, the second question needs to be answered: How to treat the patient - the same as before pandemic or in a different manner?

Since shorter treatments are expected to reduce facility's patient load, and subsequently the risk of SARS-CoV-2 infection, provisional guidelines were published, recommending implementation of evidence-based hypofractionation (59, 60).

However, in the context of larger doses per fraction, the dose constraints for the organ at risk need to be correctly evaluated and respected, and toxicity should be documented and reported (16).

There has been increasing enthusiasm for using single fraction SBRT that includes not only retrospective but also multiple prospective studies including some randomized trials. Although consensus guidelines strongly recommend single fraction SBRT for peripheral early stage NSCLC, single fraction SBRT has not been clearly proven as a reasonable alternative to multi fraction SBRT for other primary or oligometastatic targets. However, single fraction SBRT may expand beyond the pandemic if the advantages will outweigh other schedules, in metastatic setting.

Another particular aspect that has to be taken in account is that access to adequate nodal staging procedures through endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and respiratory function testing probably being suboptimal during the pandemic (16).

Regarding the palliative radiotherapy, delaying or replacing it with alternative therapy were not uniformly accepted among radiation oncologists. In a COVID-19 Rapid letter, the authors disagree to the fact that curative intent shall receive more priority than palliative treatment as the end points of the treatment in these two settings are not the same (survival for curative treatment versus quality of life for palliative care) but equally important from patient's perspective.

Thus, Francesco *et al* pointed out that medical therapy like analgesics for pain is not an alternative to palliative radiotherapy but is usually administered concomitantly for optimum pain control. Dose escalation of medical analgesic therapy in absence of radiotherapy may increase adverse effects, affecting the quality of life (61).

Another thing worth mentioning is that the experts' recommendations cannot be followed in all settings, and that the clinicians' decision is highly influenced by the workload and the available technology. All countries are facing the double challenge of controlling the spread of COVID-19 and at the same time providing cancer care, but low- and low- to middle-income countries (LMICs) are even more vulnerable, because their response cannot take the same path as the advanced-economy counterparts. Their health care systems are overstretched on one side by the growing burden of cancer and on the other side by the material and human resources limitations. In the socioeconomic context of densely populated cities, with many people living in poverty, the nonpharmaceutical interventions like social distancing and strict hygiene measures are hard to respect. These aspects have been experienced by our country and are valid for many other Asian countries. On the brighter side, Digital Contact Tracing slowed COVID-19 in East Asia, Telemedicine was implemented by many centres for Cancer Care, and cooperation was established at regional and national levels.

Limitations of the paper consist in the subjective selection criteria and the possible omission of relevant data. All recommendations must be cautiously adapted to each clinical scenario.

Conclusions

Status of SARS-COV-2 positivity, the degree of emergency, curability, life expectation, performance status and other available treatments are taken in account when recommending the treatment delivery and the moment of starting it.

In case of curative intent, for SARS-CoV-2 negative patients, various hypofractionation schedules can be used to minimise

the exposure. For SARS-CoV-2 positive patients, if the treatment cannot be delayed, safety measures should be taken to reduce risk of contagion for staff members and other patients. Interruption of treatment should be avoided whenever possible.

In case of palliative intent, SARS-CoV-2 negative patients should receive the treatment according to the degree of emergency. For most of the SARS-CoV-2 positive patients, treatment should be delayed if possible until the patient is tested negative.

Treatment decision needs to be individualized and practitioners should use their clinical judgement for balancing benefit and the risks.

Abbreviations:

ASTRO – American Society for Radiation Oncology

CBCT – Cone beam computer tomography

COVID-19 – Coronavirus disease

CT – computer tomography

CT-RT – Chemoradiotherapy

EBRT – External Beam Radiotherapy

EBUSTBNA – endobronchial ultrasound-guided transbronchial needle aspiration

ESTRO – European Society for Radiotherapy and Oncology

fr – fraction

GOECP – Oncologic Group for the Study of Lung Cancer

Gy – Gray

LMICs – low- to middle-income countries

MRI – Magnetic Resonance Imaging

MSKCC – Memorial Sloan Kettering Cancer Center

NCCN – National Comprehensive Cancer Network

NSCLC – Non Small Lung Cancer

PCI – Prophylactic cranial irradiation

PD-L1 – Programmed Death-Ligand 1

PORT – Post Operative Radiotherapy

PTV – Planning Target Volume
 RP – Radiation pneumonitis
 RTOG – Radiation Therapy Oncology Group
 SARS-CoV-2 – Severe acute respiratory syndrome corona virus 2
 SBRT – Stereotactic Body Radiotherapy
 SCLC – Small Cell Lung Cancer
 SEOR – Spanish Society of Radiation Oncology

Statements:

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