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Perspectives in surgical and anaesthetic management of lung cancer in the era of coronavirus disease 2019 (COVID-19)

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Abstract

Early in 2020, coronavirus disease 2019 (COVID-19) quickly spread globally, giving rise to a pandemic. In this critical scenario, patients with lung cancer need to continue to receive optimal care and at the same be shielded from infection with the potentially severe acute respiratory syndrome coronavirus 2. Upgrades to the prevention and control of infection have become paramount in order to lower the risk of hospital contagion. Aerosol-generating procedures such as endotracheal intubation or endoscopic procedures may expose health care workers to a high risk of infection. Moreover, thoracic anaesthesia usually requires highly complex airway management procedures because of the need for one-lung isolation and one-lung ventilation. Therefore, in the current pandemic, providing a fast-track algorithm for scientifically standardized diagnostic criteria and treatment recommendations for patients with lung cancer is urgent. Suggestions for improving existing contagion control guidelines are needed, even in the case of non-symptomatic patients who possibly are responsible for virus spread. A COVID-19-specific intraoperative management strategy designed to reduce risk of infection in both health care workers and patients is also required.

Keywords: Coronavirus disease 2019 • 2019-nCoV • SARS • Coronavirus • Lung cancer • Thoracic anaesthesia • Infection prevention and control

INTRODUCTION

In December 2019, coronavirus disease 2019 (COVID-19) emerged and disseminated rapidly throughout China and many other countries worldwide [1]. Lockdown measures including limitations on people's movements and cancellation of non-essential activities designed to reduce the spread of COVID-19 have been introduced globally. Elective surgery should be limited in order to reduce patient traffic and to avoid virus spread [2]. In Italy, hospitals limited operations to those for class A diseases (diseases that require hospitalization within 30 days for clinical conditions that can potentially worsen rapidly to the point of becoming an emergency or, in any case, seriously affect the prognosis of the patient).

Lung cancer remains the most common cause of cancer deaths worldwide, representing a relevant health care burden [3]. If it is essential to continue to guarantee adequate care to patients with lung cancer, it is also important to protect this frail population from infection.

Therefore, in the current pandemic situation, several aspects of the surgical treatment of lung cancer, patient selection and

perioperative management should be highlighted and reconsidered. Delaying surgical treatment even for early-stage lung cancer could be inappropriate because no one knows how long the pandemic will last.

Even though no prospective or well-designed studies can provide answers to these questions, the following observations, which are based on the experiences of extremely skilled, high-volume thoracic surgical departments whose management teams are continuously working on and updating their procedures, can serve as useful guidelines.

Lung cancer surgical centres

During the COVID-19 pandemic, it is relevant to consider carefully the lung cancer surgical centre to which patients are referred, taking into account the different levels of complexity of lung cancer management in terms of diagnostic processes and surgical indications. It is important to know whether the surgical centre deals with stage IIIA patients and whether its surgeons perform extended lung resections, including bronchovascular reconstructions; carinal sleeve resections; heart, great vessel,

chest wall and spine reconstructions; and post-chemotherapy resections. It has been reported that high-volume hospitals have higher lung resection rates and operate on patients who are older and have more comorbidities. Nevertheless, these patients have better surgical outcomes than younger patients with fewer comorbidities, most notably in the early postoperative period. Higher-volume hospitals have more specialized infrastructures, are more likely to have dedicated thoracic surgeons on site and can be expected to have staff with advanced skills in the management of all patients with lung cancer, including anaesthetists. Higher hospital volumes may increase the relevant experience and maintain the skills of surgeons who perform complex lung cancer resections [4].

During the pandemic, it is paramount to avoid sending patients to surgical centres where locally advanced lung tumours are not regularly treated or that lack management by multidisciplinary teams (oncologists, radiotherapists and surgeons).

Moreover, the medical institution should adopt a COVID-19 dedicated therapeutic pathway for patients whose test results are positive for severe acute respiratory syndrome coronavirus (SARS-CoV-2). They should be separated from non-infected patients or from patients who are suspected of being infected [COVID-dedicated wards, intensive care units (ICUs), radiological areas and operating rooms separated from COVID-free areas]. Alternatively, some hospitals should be committed to treating COVID-19 patients exclusively (hub hospitals), whereas other medical centres can continue to treat ordinary non-infected cases (COVID-19-free spoke hospitals) [5].

The following suggestions and perspectives are provided by a European high-volume referral centre where locally advanced lung cancer patients are treated surgically in a COVID-19 hospital that guarantees a COVID-free therapeutic pathway.

Diagnosis of lung lesions

During the pandemic, the process of diagnosing and treating patients affected by lung space-occupying lesions has to be performed carefully in order to appropriately select patients suitable for surgery. If fluorodeoxyglucose positron emission tomography (PET) plays an essential role in normal clinical practice in selecting the actual neoplastic cases, it is even more important during this worldwide crisis that it be the main diagnostic tool for excluding benign lesions and identifying malignant neoplasms.

Moreover, bronchoscopy should be avoided when possible [6] as should any redundant staging procedure that could potentially lead to infection of other patients or medical staff. However, bronchoscopy is necessary to determine the surgical strategy when a bronchial or carinal reconstruction is planned.

Hence, we need a fast-track algorithm for diagnostic and therapeutic strategies (Fig. 1A–C) to be used in patients with stage IA–IIIA lung cancer, to guide the use of computed tomography (CT) and fluorodeoxyglucose PET scans and the pretest risk of malignancy and cytological/histological diagnostic procedures (Fig. 2A). A practical diagnostic algorithm for approaching the solitary pulmonary nodule, stratifying clinical risk factors in a standardized manner and combining this information with radiological signs would point the physician towards a benign or malignant cause and recommend invasive tests for the nodules likely to be malignant. Several sources or references are routinely used to calculate the probability of malignancy, taking into consideration the following factors: age, smoking habit, haemoptysis,

history of malignancy, nodule diameter, location, edge characteristics, growth rate, cavity wall thickness, calcification, contrast enhancement on CT scan >15 HU and PET scan results. A convenient and reliable way of performing this assessment is by using a calculator available online at www.chestx-ray.com, taking into account the likelihood ratios.

When the probability that the lesion is benign is >70% [3, 7], elective surgery should be postponed for 3 months. If the probability that the lesion is malignant is high, a cytological/histological diagnostic procedure should be considered. If the lesion is diagnosed as a lung cancer, the patient should undergo surgery. Conversely, if a diagnosis of lung cancer is not reached, follow-up studies should be performed within 1 month.

GROUND-GLASS OPACITY

SARS-CoV-2 interstitial pneumonia is characterized by multifocal bilateral glass-like opacities [8]. These radiological features need special attention because, when there is an early-stage or a resolution-phase infection, a differential diagnosis with lepidic lung adenocarcinoma should be considered (Fig. 2B and C). Obviously, clinical history and radiological features should be considered simultaneously to reach a diagnostic conclusion.

A pure ground-glass opacity (GGO) can be radiologically clear or have a solid component, easily detected on a CT scan. Generally, GGOs produce negative findings on PET scans, so a fluorodeoxyglucose PET scan has a limited role in the GGO characterization process. A needle biopsy is a poor diagnostic tool for GGOs; there is no decrease in life expectancy when it is performed [9, 10].

According to published reports, a follow-up period could be necessary to rule out changes in both pure and solid-component GGOs [11]. For a mixed GGO, there is no unanimous consensus for surgical indication or follow-up.

Thus, in light of the unknown evolution of a pure GGO or a predominantly solid-component GGO lesion (solid component <50%), we recommend a 3-month follow-up period during the COVID-19 outbreak. Conversely, a predominantly solid-component GGO (>50%) should be considered for surgical resection without further characterization (Fig. 1A), always considering the risk-benefit ratio for each patient.

Lung cancer surgical treatment

In the wake of the COVID-19 pandemic, navigating cancer is challenging. However, some fixed surgical indications should be clear to avoid delayed treatment potentially causing tumour progression and even endangering the patient's life.

High suspicion of lung cancer and a histological diagnosis of lung cancer. All patients with a high probability of lung cancer or a recently received lung cancer diagnosis should undergo surgical resection. To minimize inter-regional movement, patients should be encouraged to go to the nearest thoracic surgery centre; only those patients affected by locally advanced lung cancer should be referred to high-volume, highly skilled thoracic surgery centres for fast-track diagnostic and therapeutic procedures.

All patients receiving multimodal treatment, including surgery, should be considered for lung resection. Patients with lung

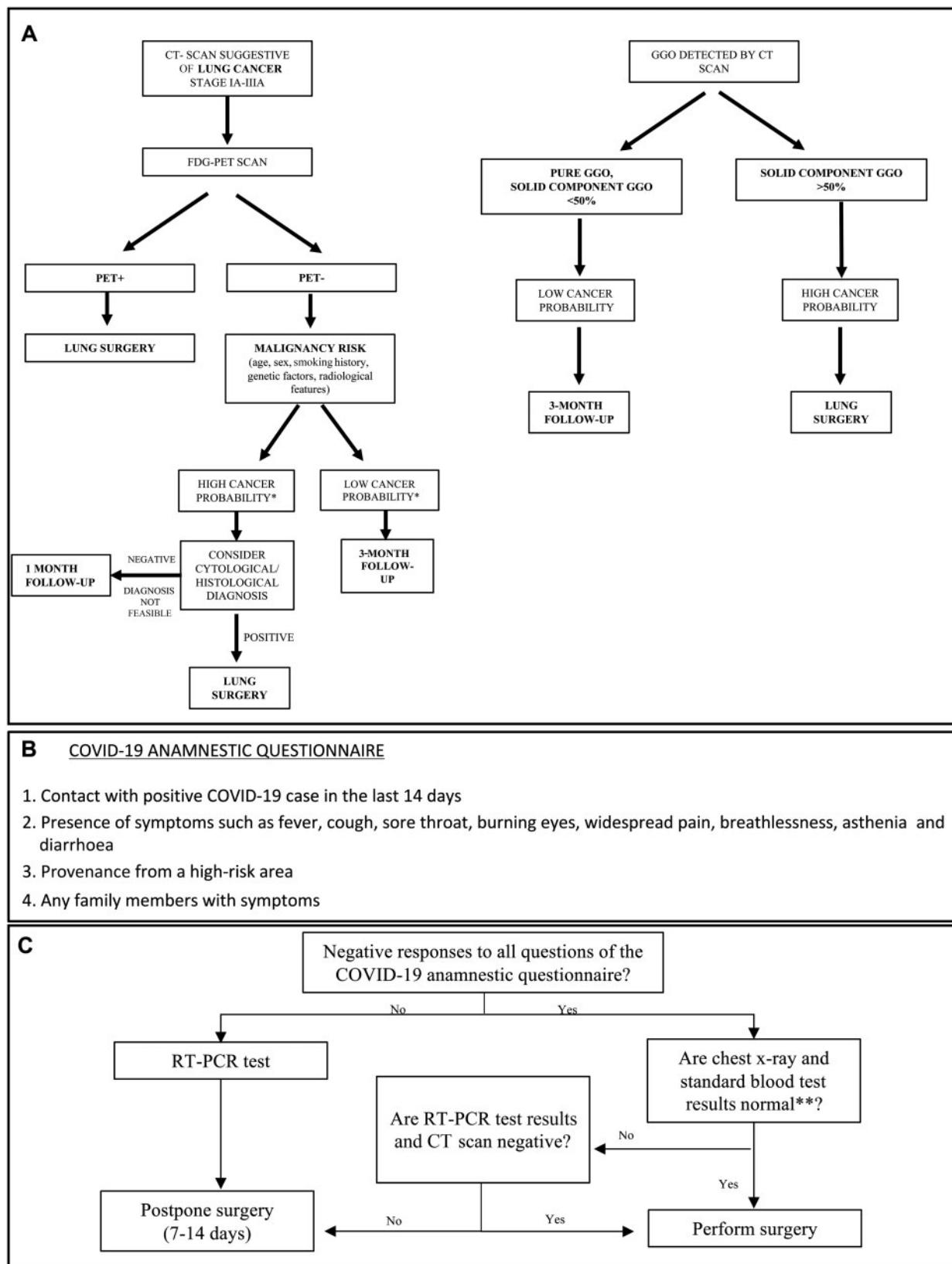


Figure 1: (A) Diagnostic and therapeutic algorithm for lung cancer and GGOs during COVID-19 pandemic. (B) COVID-19 anamnestic questionnaire. (C) Screening algorithm for COVID-19 patients before hospitalization and surgery. *The risk of malignancy is calculated considering age, sex, smoking history, genetic factors, radiological features on the CT scan according to a pretest risk of malignancy from www.chestx-ray.com. **Standard blood tests should include red blood cell count, white blood cell count and lactate dehydrogenase and C-reactive protein levels. COVID-19: coronavirus disease 2019; CT: computed tomography; FDG-PET: fluorodeoxyglucose positron emission tomography; GGO: ground-glass opacity; RT-PCR: reverse transcriptase-polymerase chain reaction.

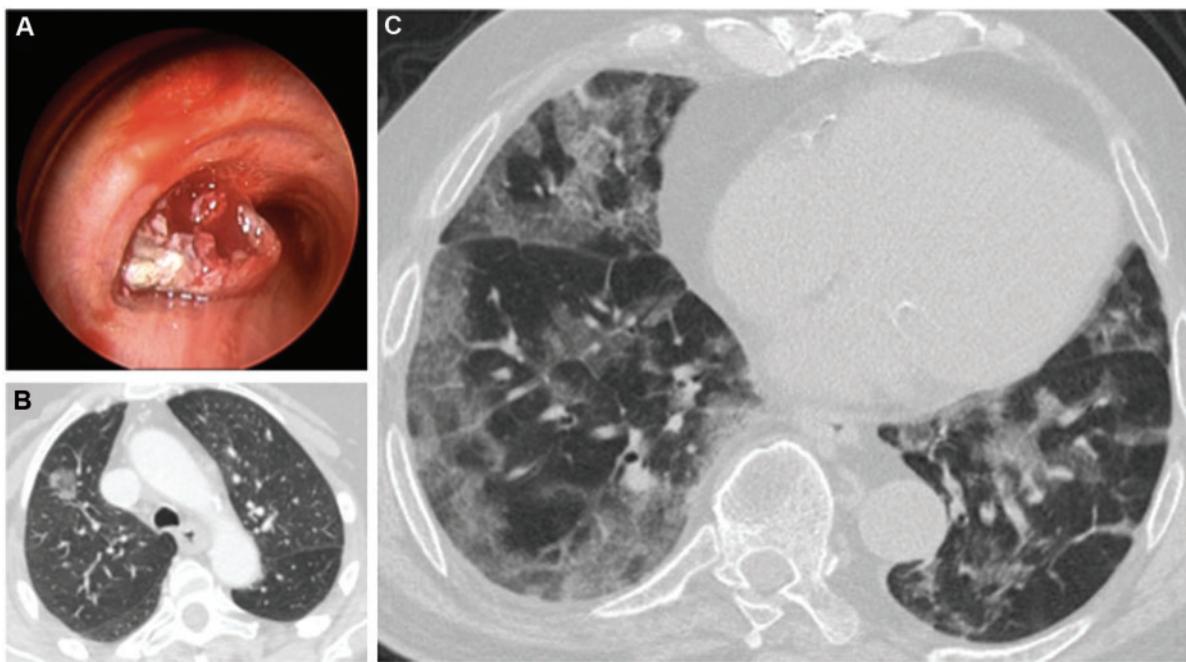


Figure 2: (A) Endoscopic view of a bleeding endobronchial lung cancer causing haemoptysis. (B) Ground-glass opacity of a right upper lobe with a solid component suggestive of lung cancer. (C) Bilateral ground-glass opacities of the lower lobes suggestive of coronavirus disease 2019.

cancer who are being treated with induction chemo- or radiotherapy while waiting for surgical treatment should be considered for a fast-track surgical procedure.

Conversely, surgery for patients who need adjuvant chemotherapy could be delayed. Studies have shown that starting chemotherapy at 57–127 days after surgery did not increase mortality (hazard ratio 1.037) [12].

The Thoracic Surgery Outcomes Research Network (an American multi-institutional cooperative of experts) [13] recently published a Covid-19 guide for triage of operations for thoracic malignancies, suggesting that patients with solid or predominantly solid (>50%) GGOs or lung cancer/presumed lung cancer ≥2 cm should not defer surgery. However, they recommend that patients with small lesions (GGOs with solid component <50% or lung cancer <2 cm) should postpone surgery for 3 months. According to our experience as a European surgical centre unexpectedly struck by the COVID-19 surge, because we do not know the impact, timeline and duration of surge, it is not appropriate to delay surgery 'a priori' as long as hospital resources are still intact during the pandemic. For this reason, we recommend using PET to identify lesions that should be operated on right away. In PET-negative lesions with a high probability to be cancer, all the diagnostic procedures to reach a certain preoperative diagnosis of lung cancer (bronchoscopy, endobronchial ultrasound or CT guided needle biopsy) should be considered to carefully select patients who should have the surgical procedures.

Palliative surgical treatment for lung cancer. Patients with stage IV lung cancer who require palliative treatment should be identified and referred without delay. Breathlessness due to pleural effusion (M1 stage) may be relieved by fluid removal via needle aspiration or a narrow-bore indwelling catheter [3, 14]. Patients affected by recurrent pleural effusions should be offered talc pleurodesis for longer-term benefit. Although talc slurry is a

viable choice for patients who are not suitable for thoracoscopy, video-assisted thoracic surgery procedures with talc poudrage are strongly indicated for patients with stage IV lung cancer even during the COVID-19 outbreak because of the significant quality-of-life improvement and the favourable benefit/risk ratio.

Life-threatening lung cancer. Centrally or endobronchially located lung cancer could represent a life-threatening condition causing haemoptysis or respiratory failure (Fig. 2A). Urgent assessment for and treatment with operative procedures should be considered during the COVID-19 pandemic.

Rigid bronchoscopy, mechanical dilatation or neodymium-yttrium-aluminium-garnet laser to remove obstructions and airway stenting are suggested to maintain/re-establish airway patency, thereby providing immediate relief for the patient and allowing him or her to undergo chemo- or radiotherapy.

Preoperative patient clinical assessment and selection

Preoperative clinical assessment should be performed by evaluating performance status and lung function [15]. During the COVID-19 pandemic, spirometry could increase the risk of contagion for patients and medical staff. Initial guidance from several respiratory societies [16] suggests avoiding airway challenge testing, which actively induces cough. Therefore, analysis of blood gases and spot-check oximetry could be sufficient for preoperative assessment, thereby limiting spirometry to patients with previous respiratory failure, to unfit patients or to patients for whom extended surgical resection is planned. These societies also recommend wiping down equipment and surrounding areas after each patient, cleaning the department at the end of each day and providing patients with tissues to cough into and disposing of the tissues in an appropriate clinical waste bin.

SUGGESTIONS FOR AIRWAY MANAGEMENT IN THORACIC SURGERY DURING COVID-19 PANDEMIC

Double lumen tube (DLT) use for lung isolation
Check DLT position by auscultation
Avoid bronchoscope use if possible

Preoxygenate for 3 min with 100% oxygen to avoid manual ventilation
If manual ventilation is required, apply a small tidal volume

Rapid sequence intubation technique
Ensure complete neuromuscular blockade

High efficiency particulate air filter (HEPA)
Placed between the expiratory and inspiratory limbs of the breathing circuit, between the mask and the breathing circuit, between the double catheter mount and breathing circuit and excluded from the DLT branch

Use video laryngoscopy if available
Preferably with disposable blades

Avoid air leaks
Immediate inflation of DLT cuffs; avoidance of circuit disconnections; alveolar recruitment manoeuvres and pulmonary re-expansion tests performed by circle breathing

Figure 3: Visual summary of suggested procedures during airway management in thoracic anaesthesia. COVID-19: coronavirus disease 2019; DLT: double lumen tube; HEPA: high-efficiency particulate air filter.

To screen and carefully select patients undergoing spirometry and then elective lung surgery, it can be helpful to administer a telephone COVID-19 anamnestic questionnaire, following a patient's screening algorithm before hospitalization (Fig. 1B and C).

Intraoperative anaesthetic management

Aerosol-generating procedures (tracheal intubation, bronchoscopy, tracheotomy, non-invasive ventilation, cardiopulmonary resuscitation, manual ventilation) [17] put health care workers at high risk of contagion and need reinforced airborne precautions. Using adequate personal protective equipment (PPE) and taking appropriate precautions help lower the risk of infection from aerosol-generating procedures [18]. Despite the fact that several recommendations for intraoperative management have been determined for patients known to be or suspected of being infected with COVID-19, no specific standardized protective measures are recommended for patients with no suspicion of infection. Specific suggestions should be implemented in order to prevent hospital acquired infections because of possible viral transmission from asymptomatic or minimally symptomatic patients. An experienced anaesthesiologist should use level 3 protection airborne precautions [19, 20] including mask respirators (e.g. N95, FFP2 or equivalent standard) [21] when performing endotracheal intubation. Particulate respirators, designed to

block 95–99% of aerosol particles and recommended during management of COVID-19 patients, should be routinely used during thoracic anaesthesia. In fact, because high-complexity airway management is often required with thoracic anaesthesia and because lung isolation could be necessary, additional precautions are mandatory. Despite the fact that the use of respirator masks is critical when treating COVID-19 patients and that PPE could become scarce during the pandemic, advanced airway management during thoracic anaesthesia needs mandatory reinforcement of airborne precautions. To limit PPE consumption and to reduce the number of health care workers exposed, unnecessary operating room staff should be eliminated.

In this setting, the double lumen tube should be preferred, because it is easier and faster to position than the bronchial blocker [22]. The position of the double lumen tube can be checked by auscultation and by observation of the movements of the chest wall, which differs from a bronchial blocker, which requires the use of a bronchoscope for proper positioning. During the COVID-19 pandemic, the use of a bronchoscope should be avoided and reserved for predicting difficult airway management situations (awake fibre-optic intubation with single lumen endotracheal tube and bronchial blocker) or for tube misplacement that cannot be managed with minimal double lumen tube advancement or withdrawal. They also recommended avoiding procedures that could cause aerosolization and potential virus spreading [19]. A visual summary of the suggested precautions during thoracic anaesthesia is shown in Fig. 3.

Postoperative management

It is beneficial to avoid unnecessary aerosol therapy during the postoperative hospital stay in order to limit the spread of the virus. The patient's discharge from the hospital can be managed by providing an indwelling chest tube connected to a Heimlich valve in order to contain contaminated air or pleural effusion from the lung. During the pandemic, postoperative follow-up can be managed through a telemedicine service or by the general practitioner remaining in contact with the surgeon.

CONCLUSION

Due to the disruption caused by the COVID-19 pandemic, a huge number of elective surgical procedures will be cancelled or postponed, risking inappropriately treated lung cancer and an increase in the time-related mortality rate [23]. Governments should develop recovery plans and implement strategies to rapidly restore surgical activity in situations in which elective procedures were severely curtailed.

In their communication of 14 May 2020, the World Health Organization warns that the new coronavirus may be here to stay and that it is impossible to predict when the pandemic might be controlled [24].

Thus, during the COVID-19 pandemic, patient selection guidelines for lung surgery need to be revisited. Differential diagnosis from benign diseases (including a possible SARS-CoV-2 infection) is mandatory. The present perioperative suggestions may help to accurately select patients undergoing lung cancer surgery, guaranteeing a rapid diagnostic and therapeutic process. Intraoperative precautions and adequate PPE should also be

applied to the management of all patients to prevent cross infections.

When we embraced the foregoing recommendations, our high-volume thoracic surgery centre reported a 30% decrease in surgical procedures in a month (6 March–7 April), from ~120 patients to 85, mostly due to the allocation of resources from the institutional administration. During the observation period, 88 patients were evaluated, 85 patients (96.6%) were operated on, 1 patient (1.1%) was deferred because of the presence of fever and contact with confirmed cases of COVID-19 at the time of questionnaire and 2 patients (2.2%) voluntarily waived surgery. The ICU admission rate was 3.5% (3 patients). Thus, it is important to highlight the sustainability of early-stage lung cancer surgery when the ICU admission rate is low.

To date, no cases of SARS-CoV-2 infection were recorded among the medical staff or the patients who were operated on during their hospital stay. This favourable outcome may have been determined by the appropriate screening of patients and the improved precautions adopted.

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