Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Review article: Biomedical intelligence | Published 07 February 2022 | doi:10.4414/SMW.2022.w30109
Cite this as: Swiss Med Wkly. 2022;152:w30109

Surgical management of lung cancer during the COVID-19 pandemic – a narrative review and single-centre report

Raphael S. Werner[a], Andreas Lörtscher[b], Michaela B. Kirschner[a], Olivia Lauk[a], Katarzyna Furrer[a], Claudio Caviezel[a], Didier Schneiter[a], Ilhan Inci[a], Sven Hillinger[a], Alessandra Curioni-Fontecedro[c], Isabelle Opitz[a]

[a] Department of Thoracic Surgery, University Hospital Zurich, Switzerland
[b] Faculty of Medicine, University of Zurich, Switzerland
[c] Department of Medical Oncology and Haematology, University Hospital Zurich, Switzerland

Summary

The coronavirus disease 2019 (COVID-19) pandemic has had a severe impact on oncological and thoracic surgical practice worldwide. In many hospitals, the care of COVID-19 patients required a reduction of elective surgery, to avoid viral transmission within the hospital, and to save and preserve personnel and material resources. Cancer patients are more susceptible to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and are at an increased risk of a severe course of disease. In many patients with lung cancer, this risk is further increased owing to comorbidities, older age and a pre-existing lung disease. Surgical resection is an important part of the treatment in patients with early stage or locally advanced non-small cell lung cancer, but the treatment of these patients during the COVID-19 pandemic becomes a challenging balance between the risk of patient exposure to SARS-CoV-2 and the need to provide timely and adequate cancer treatment despite limited hospital capacities. This manuscript aims to provide an overview of the surgical treatment of lung cancer patients during the COVID-19 pandemic including the triage and prioritisation as well as the surgical approach, and our own experience with cancer surgery during the first pandemic wave. We furthermore aim to highlight the risk and potential consequences of delayed lung cancer treatment due to the deferral of surgery, screening appointments and follow-up visits. With much attention being diverted to COVID-19, it is important to retain awareness of cancer patients, maintain oncological surgery and avoid treatment delay during the pandemic.

Correspondence:
Prof. Dr. med. Isabelle Opitz
Director of Department of Thoracic Surgery
University Hospital Zurich
Rämistrasse 100
CH-8091 Zürich
isabelle.schmitt-opitz[at]usz.ch

Introduction

The coronavirus disease 2019 (COVID-19) is a potentially life-threatening infection of the respiratory tract, caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2) [1]. As of 11 March 2020, the World Health Organisation (WHO) declared the COVID-19 outbreak a pandemic. With its reproductive ratio of 1.4 to 2.5 additional transmissions following every infection, an exponential increase in transmitted cases was seen early on [2]. Ever since the outbreak of the pandemic, the aim was to identify vulnerable patients based on clinical, epidemiological, laboratory or radiological characteristics in order to protect the high-risk population [3, 4]. The case fatality rate, defined as the fraction of deaths among COVID-19-positive patients, was found to be significantly increased in older patients, as well as in patients with chronic concomitant disease such as cardiovascular disease, chronic respiratory disease, diabetes or cancer [5–7]. The latter form a large population who are generally more susceptible to infections due to their immunosuppressed state as a result of systemic treatment or surgery [8]. The most common cause of cancer-related death worldwide is lung cancer, annually resulting in more than 36 million disability-adjusted life years worldwide [9]. In Switzerland, the lifetime risk for developing lung cancer is 7% and more than 4000 people are diagnosed with lung cancer each year [10]. In early, locally advanced and in oligometastatic non-small cell lung cancer, anatomical surgical resection plays a central role in the treatment [11, 12]. The COVID-19 pandemic, however, substantially impacts upon general and thoracic surgical practice, requiring a reduction of surgical volumes by cancellation or postponement of many elective interventions, in order to avoid viral transmission within the hospital, and in order to save and preserve personnel and material resources required for the care of COVID-19 patients [13]. Consequently, a deferral of elective surgery and radiotherapy, as well as a reduction in the use of systemic treatment for cancer patients is seen in many countries [14]. Although for certain patients with early stage lung cancer, delayed surgery is unlikely to have a negative effect on the outcome, most other patients may require an urgent resection despite complicating circumstances. In the time of COVID-19, the triage and treatment of lung cancer patients therefore involves a delicate balancing act between preserving hospital resources, minimising inter-

ventions in a vulnerable group of patients and avoiding treatment delay [15].

In this article, we aim to review the current data and discuss our own results concerning surgical treatment of patients with non-small cell lung cancer (NSCLC) during the COVID-19 pandemic, in order to provide practical guidance in the management of these patients. An online database search (PubMed) was performed to identify publications that address the prevalence and outcomes of SARS-CoV-2 infections in patients with lung cancer.

Lung cancer patients at risk

Patients with cancer are not only more susceptible to SARS-CoV-2 infection [16, 17], but are also at an increased risk of severe events or death, with reported case fatality rates as high as 28.6% among hospitalised patients [16–18]. In a Swiss cohort, an even higher in-hospital mortality rate of 43% was reported in 15 hospitalised patients with active cancer and COVID-19 [19]. Cancer patients are more likely to present in a relatively immunocompromised state, either due to the underlying malignancy itself or as a result of anticancer treatment [20]. The risk for clinically severe events was further increased if the patients had undergone surgery or chemotherapy within four weeks or less before the infection [17, 18]. The Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) registry assessed outcomes of a selected group of patients with thoracic malignancies (76% NSCLC) and COVID-19 and reported a high mortality rate of 33% [21]. Despite the high number of hospitalisations (76%) and the good overall performance status within the cohort, only 9% of all hospitalised patients had been admitted to an intensive care unit [21]. This may partly be explained by the geographical locations included in the registry with many European regions that were heavily affected during the first pandemic wave [21].

Since most NSCLC cases occur in elderly patients with a smoking history, many of these patients are frail not only because of the tumour, but also due to their age and due to potential comorbidities [22]. Among patients with thoracic malignancy and SARS-CoV-2 infection, a smoking history itself appears to be independently associated with an increased risk of death [21]. The higher expression of angiotensin converting enzyme II , the receptor used by SARS-CoV-2 to enter the host cell, in small airway epithelia of smokers and patients with chronic obstructive pulmonary disease (COPD) suggests an increased susceptibility to an infection in these patients [23, 24]. However, epidemiological data from the general population without thoracic malignancy do not support this hypothesis of an association between smoking and severe COVID-19 [3, 25–27]. In patients with thoracic cancer, pre-existing symptoms from the malignancy or from comorbidities such as dyspnoea, cough and fatigue may furthermore mimic and mask a SARS-CoV-2 infection, resulting in a delayed medical consultation.

Despite the substantial amount of information related to COVID-19 and cancer treatment, reports concerning the outcome after lung cancer surgery during the pandemic are scarce. Seitlinger et al. report 9 cases of COVID-19 and one COVID-19 related death among 731 patients undergoing surgical procedures for thoracic malignancies [28]. The procedures were performed in six high-volume thoracic surgery departments located in heavily affected regions in Italy, France, Germany and Canada. In consideration of the low incidence and low mortality, the authors conclude that oncological thoracic surgery can be safely maintained during the COVID-19 pandemic in order to avoid a delay in cancer treatment [28]. However, although the incidence of COVID-19 infections appears to be low after thoracic surgery, case series from China suggest that lethality may be high in these patients with reduced functional reserve. Two case series of patients with confirmed SARS-CoV-2 infection following anatomical lung resection report two deaths among six infected patients with NSCLC and one death among two infected patients with NSCLC, respectively [29, 30]. In a recent retrospective analysis of patients diagnosed with COVID-19 after thoracic surgery, two deaths occurred among seven patients with NSCLC, resulting in a lethality rate of 28.5% [31]. In accordance with these findings, the United Kingdom Lung Cancer Coalition (UKLCC) estimates an increased mortality of 40–50% if a lung cancer patient contracted COVID-19 after surgery [32]. The current studies reporting the incidence of COVID-19 and the associated mortality among patients with NSCLC are summarised in table 1.

Special attention should be paid to the subgroup of cancer patients receiving neoadjuvant or adjuvant immune checkpoint inhibitors. Since immunotherapy aims at restoring

Table 1:
Lung cancer patients at risk.

Author	NSCLC cases with COVID-19	Hospitalised	Key findings
Yu et al. [16]	n/a	7/1524 (0.5%)	2 COVID-19-related deaths among 7 hospitalised NSCLC patients (28.6%)
Garassino et al. [21] (TERAVOLT)	151	111	33% mortality rate among all thoracic malignancies with COVID-19
			Low admission rate to ICU
			Most patients with stage IV disease
			Most patients under systemic treatment
Seitlinger et al. [28]	9/731 (1.2%)	4 (0.5%)	1 COVID-19-related death among 4 hospitalised thoracic cancer patients (25.0%)
			Thoracic surgery during COVID-19 pandemic is safe and feasible
Cai et al. [29]	6	n/a	6 postoperative COVID-19 cases after lung resection for NSCLC
			2 COVID-19-related deaths among 6 NSCLC patients (33.3%)
Huang et al. [30]	2	n/a	2 postoperative COVID-19 cases after lung resection for NSCLC
			1 COVID-related death among 2 NSCLC patients (50.0%)
Peng et al. [31]	7	5	7 postoperative COVID-19 cases after lung resection for NSCLC
			2 COVID-19-related deaths among 7 hospitalised NSCLC patients (28.6%)

ICU: intensive care unit; n/a: not applicable; NSCLC: non-small cell lung cancer

cellular immunocompetence, patients under immune checkpoint inhibition could be more immunocompetent than patients receiving conventional chemotherapy [33]. Concerns of overlapping pneumological toxicity from anti-PD-1/PD-L1 (PD-1: programmed cell death protein-1; PD-L1: PD ligand-1) agents and COVID-19 pneumonia, as well as concerns of a hyperactivated immune response potentially resulting in a cytokine release syndrome, raise the question of whether immunotherapy should be administered in the middle of a regional COVID-19 outbreak [33]. Similarly to reports of paradoxical immunological responses with influenza infections [34], single case reports also describe a fatal course with rapid clinical worsening after SARS-CoV-2 infections [35]. Even though there is no clear evidence supporting an interaction of SARS-CoV-2 and systemic treatment, a short-term suspension of anticancer treatment may be reasonable in infected patients who have had long-term cancer control [22]. In the TERAVOLT cohort, the majority (74%) of patients who contracted SARS-CoV-2 were receiving systemic treatment, with chemotherapy alone and immune checkpoint inhibitors alone being the most common therapy. However, the type of systemic treatment and especially immunotherapy did not worsen the outcome of these patients [21].

Triage of lung cancer patients for surgery

In the time of COVID-19, vast hospital resources are used for diagnostic tests and the treatment of infected patients. In many hospitals, elective surgery was therefore temporarily suspended during the first pandemic wave [15]. The scarcity of hospital resources results in ethical questions that go beyond the scope of this review. However, a transparent management plan may facilitate decision-making and the triage of lung cancer patients, and provide a modifiable framework for local strategy planning. The major goal in this pandemic is to find a balance between the risk of patient exposure to SARS-CoV-2 and the need to provide adequate and timely cancer treatment despite limited hospital capacities [20]. Since thoracic surgery plays an essential role in the management of NSCLC and many other thoracic malignancies, many experts agree that oncological surgical activity should be maintained throughout the pandemic whenever logistically feasible to avoid delayed cancer treatment [20, 28, 36, 37]. When hospital resources are predominantly routed for the care of COVID-19 patients, the consensus statement of the Thoracic Surgery Outcomes Research Network (ThORN) recommends prioritisation of cancer treatment according to the phase of the COVID-19 pandemic, as well as according to prognostic factors including tumour grade and stage, symptoms of cancer or cancer treatment-associated complications [15]. In the semi-urgent setting of pandemic phase I, resections of NSCLC with predominantly solid appearance, NSCLC greater than 2 cm, centrally located NSCLC and node-positive NSCLC, as well as staging interventions (mediastinoscopy, bronchoscopy and endobronchial ultrasound) should not be deferred as long as hospital resources are intact. An exception should be considered only for indolent lesions such as predominantly ground-glass nodules, single solid nodules <2 cm or histologically confirmed and peripherally located typical carcinoid tumours. In these cases, a treatment deferral of up to 3 months may be justifiable [15, 38]. During the urgent phase II with limited capacities, surgery for lung cancer may be reserved only for tumour-associated complications or surgical complications such as haemorrhage, empyema and other infections [15]. During the critical phase III with exhausted resources, surgery is performed only in emergency situations such as threatened airways, septic and/or unstable patients [15]. In addition to the triage of surgeries, alternative treatment options such as neoadjuvant therapy, stereotactic body radiation therapy, cryotherapy or transfer to another hospital with sufficient resources may be valuable when surgical capacity is exhausted, despite the possible minor efficiency of these alternative therapies in early stage cancer [15]. In locally advanced lung cancer, the administration of neoadjuvant chemotherapy may enable a timely start of anticancer treatment despite exhausted surgical capacities [39]. In the same group of patients, an early resection and adjuvant chemotherapy may be preferred if hospital resources are intact, but the risk of exposure during frequent trips to the hospital for chemotherapy cycles should be minimised [20]. In general, a patient-centred approach is essential and such decisions should always be discussed with the patient and within the multidisciplinary tumour board [15, 40]. Patients whose treatment is delayed should be followed up and, if applicable, follow-up imaging (e.g., computed tomography) should be performed [15]. Once the surgical capacities are increasing again, delayed procedures should be re-scheduled according to case priority [15]. All in all, it remains in the hands of the oncologists, pneumologists and thoracic surgeons to insist on the performance of adequate diagnostic and therapeutic steps in times when resources are limited.

Surgical approach in lung cancer patients during the COVID-19 pandemic

In a retrospective analysis of 11 patients who contracted SARS-CoV-2 after thoracic surgery, fatality was significantly associated with a resection of five or more segments [31]. In view of the increased risk in this cohort, some authors conclude that the benefit of a sublobar resection with faster convalescence after surgery may outweigh the risk of cancer recurrence during the COVID-19 pandemic, especially considering the possibility of a subsequent anatomical resection after the pandemic [41]. Particularly patients with limited preoperative functional reserve who would be considered marginal candidates for lobectomy may benefit from a sublobar resection [38]. Intraoperatively, it is important to minimise the risk of aerosolisation and viral transmission to the medical team. A minimally invasive approach by video-assisted thoracic surgery or robotic-assisted thoracic surgery should therefore be used whenever possible and FFP-2 respirator masks should be worn by all staff members regardless of the patient's COVID-19 status [36, 42].

During the COVID-19 pandemic, it becomes more important than ever before to implement pathways for enhanced recovery after surgery (ERAS). Given the limited capacities on wards and intensive care units, such protocols have the potential to improve the outcome after surgery, promote a timely postoperative discharge, reduce complications and thereby increase the resources required for the treatment of COVID-19 patients. The above mentioned

minimally invasive approach has been shown to enable a reduction in the hospital length of stay, as well as a reduction in postoperative complications and pain [43–45]. Further key recommendations for thoracic surgery published by the ERAS society include smoking cessation, prehabilitation, preoperative carbohydrate loading, intra- and postoperative (regional) anaesthesia, opioid-sparing analgesia, and early postoperative mobilisation [46].

The long incubation period and thus the absence of clinical symptoms during the first days after infection further challenge the decision-making process before lung cancer surgery. Low viral RNA counts shortly after exposure may not be identified by polymerase chain reaction (PCR)-based surveillance tests, resulting in patients undergoing surgery despite incubating SARS-CoV-2 infection [47]. Asymptomatic "super spreader" patients not only pose the greatest risk for a nosocomial transmission of the virus, but are also a threat to medical personnel [41]. Routine preoperative PCR testing is therefore crucial in patients scheduled for lung cancer surgery. In lung cancer patients with a positive SARS-CoV-2 test, the operation should be delayed for 2–3 weeks [20]. Furthermore, meticulous clinical surveillance and triage is essential because of the high fatality rate of COVID-19 following surgical resection [41]. Since COVID-19 symptoms such as shortness of breath, cough, fever and fatigue overlap with those of a usual clinical course after lung surgery, COVID-19 diagnosis may be further delayed [31, 36]. This circumstance requires the treating surgeons, pulmonologists and general practitioners to pay close attention to clinical signs for a potential SARS-CoV-2 infection and – if in doubt – to take a nasopharyngeal swab for testing [31]. Lymphopenia is commonly seen in patients with COVID-19 and may help to distinguish between a common postoperative course and a COVID-19 pneumonia [48, 49]. In general, COVID-19 should remain a differential diagnosis in surgical patients with signs of pneumonia, even if preoperative tests had been negative [15]. This is especially important in heavily affected regions with a high number of laboratory-confirmed cases and increasing risk of in-hospital transmission.

The risk of cancer treatment delay and its consequences

In non-pandemic times, the disciplines involved in cancer treatment have created operating procedures and pathways to minimise the interval from diagnosis to the initiation of treatment [50]. In NSCLC, patients, a timely start of the treatment has been shown to result in better survival rates [14, 51, 52]. This effect was particularly seen in early stage (stage I and II) NSCLC, where treatment initiation 7 days after pathological diagnosis was associated with a 10% increase in the 5-year survival rate [51]. It is already ambitious to complete the staging and perform preoperative tests within 7 days under normal conditions, but it is basically impossible with severely reduced hospital resources. A treatment delay of over 8 weeks was found to be an independent risk factor for disease progression in an analysis of the United States National Database, indicating that no cancer surgery should be deferred by more than 2 months [36]. According to the European Society for Medical Oncology (ESMO), NSCLC resections should remain a priority throughout the pandemic and surgical delays should not exceed 6–8 weeks [37].

The first wave of the COVID-19 pandemic has already had a detrimental effect on the management of patients with cancer. A notable decrease of cancer diagnoses was reported from the Netherlands and among deferred surgeries in Europe and North America, almost 40% were cancer surgeries [20, 28, 53]. These findings match our own experience with a reduced number of NSCLC admissions during the pandemic wave. In 2020, the Comprehensive Cancer Center Zurich reports a significant decrease in NSCLC diagnoses of all tumour stages and all treatment modalities when compared with numbers of NSCLC diagnoses in the past years (table 2). Due to the overlapping symptoms of COVID-19 and lung cancer, early detection of lung cancer is further complicated and the distraction effect generates much opportunity for misdiagnosis [32]. With much attention being diverted to COVID-19 patients and the deferral of surgeries, screening and follow-up appointments, lung cancer may therefore be one of the cancer types most affected by treatment delay during the pandemic [32]. According to the UK lung cancer coalition report, cancer centres experienced a 75% decrease in urgent lung cancer referrals and current data reveal a substantial rise in late-stage lung cancer cases [32]. Similarly, a delay in presentation and an increase in advanced stages was also noted in Korea [54]. In Italy, a significant decrease in early stage NSCLC and in lobectomies for NSCLC was seen after the first pandemic wave, when compared with the same period in 2019 [55]. A COVID-19-associated delayed diagnosis and treatment initiation in NSCLC may therefore reduce rates of survival in otherwise curable stages. Depending on histology and volume doubling time, a stage IA1 tumour can transform into a stage IB within a few months and thereby reduce the 5-year survival from 92% to 68% [28, 56, 57]. In the case of a single hilar lymph node involvement, a further reduction to a 5-year survival of 53% would be expected [57]. Despite the distracting and demanding situation, lung cancer awareness remains highly important and efforts should be made to expedite the diagnosis of lung cancer, maintain surgical activity and avoid treatment delay.

Table 2:
Annual distribution of non-small cell lung cancer (NSCLC) cases reported by the comprehensive cancer centre Zurich.

	2018	2019	2020
Overall	262	256	198
IA	67	51	48
IB	12	19	12
IIA	8	3	2
IIB	27	30	16
IIIA	43	37	27
IIIB	13	15	12
IIIC	3	3	5
IVA	41	37	21
IVB	48	61	55

NSCLC stages are reported according to the Union for International Cancer Control (UICC) staging classification (8th edition).

Single-centre experience from the University Hospital Zurich

Methods

In order to complement this review with current data from Switzerland, we aimed to assess the risk of postoperative SARS-CoV-2 infection in our own patient cohort. Patients undergoing anatomical and non-anatomical surgical resection for NSCLC shortly before or within the first pandemic wave (between December 2019 and June 2020) at the Department of Thoracic Surgery of the University Hospital Zurich were identified in order to assess the risk of postoperative SARS-CoV-2 infection. Patients with benign thoracic lesions or thoracic malignancies other than NSCLC were excluded from the analysis. The diagnosis of NSCLC was histopathologically confirmed in all cases. A survey was conducted to assess the presence of COVID-19-like symptoms in a total of 55 identified and eligible subjects . The survey assessed the presence of typical COVID-19 symptoms such as fever, new onset of cough, shortness of breath, fatigue and loss of taste and/or smell. In addition, the survey evaluated whether PCR-based SARS-CoV-2 testing had been performed postoperatively, whether a SARS-CoV-2 infection occurred during the follow-up period and whether the recommended infection precaution measures had been followed. The follow up ranged between 4 and 10 months. The project was considered pure quality assurance by the local ethics committee and was therefore not subject to approval. Statistical analysis was performed in IBM SPSS Statistics Version 27 (SPSS Inc, Chicago, IL). Continuous variables are reported as mean ± standard deviation for normally distributed data and median with 95% confidence interval (CI) for non-normal distributions.

Results

Fifty survey responses from NSCLC patients who underwent surgical resection were captured (table 3). Seventy-four percent of all patients presented with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 at the time of the operation. Surgical resections included 30 lobectomies (including 4 sleeve-lobectomies), 9 segment-resections, 8 wedge-resections, 2 pneumonectomies and one sleeve-bilobectomy. Concomitant procedures were performed in 18% of all cases and included 3 chest wall resections and 3 partial pleurectomies. The procedures were most commonly performed by video-assisted thoracoscopic surgery (VATS, 42%), followed by open access in 30% and robotic-assisted thoracic surgery (RATS) in 28% of all cases. Thirty-day and 90-day mortality were 0%. Postoperative complications occurred in 17 cases and included 6 cases of prolonged air leak (>10 days), 3 cases of new onset atrial fibrillation, 2 cases of recurrent laryngeal nerve palsy, one chylothorax, one pulmonary embolism, one postoperative bleeding and one postoperative neurological deficit due to spinal cord ischaemia. The patient cohort represented all stages of NSCLC, including 20 Union for International Cancer Control (UICC, 8th edition) stage I cases, 13 stage II cases, 11 stage III cases and 4 oligometastatic (stage IV) patients.

During the postoperative course, 6 patients (12%) experienced COVID-like symptoms including fever, coughing or shortness of breath (table 4). All symptomatic subjects and 19 asymptomatic patients underwent PCR-based SARS-CoV-2 testing. None of the patients were tested positive by the end of October 2020. All patients reported that they followed the precautions recommended by the Swiss Federal Office of Public Health, including the regular use of hand sanitisers and social distancing, as well as wearing face masks in public transport and in public spaces where a distance of 1.5 metres cannot be maintained. In our study population, the impact of SARS-CoV-2 on patients undergoing surgical resection for NSCLC was therefore mild and the recommended hygiene and social distancing rules appear to provide sufficient protection in this group of patients. In addition, the consequent deferral of non-urgent procedures and the expansion of intensive care capacities has allowed the timely surgical treatment of patients with thoracic malignancies to be maintained throughout the pandemic waves to date at our centre.

Table 3:
Baseline characteristics.

Baseline characteristics		**n = 50**
Male		28 (56%)
ECOG performance status	0	37 (74%)
	1	10 (20%)
	2	2 (4%)
	3	1 (2%)
Operation	Wedge resection	8 (16%)
	Segement resection	9 (18%)
	Lobectomy	26 (52%)
	Sleeve lobectomy	4 (8%)
	Sleeve bilobectomy	1 (2%)
	Pneumonectomy	2 (4%)
Lymphadenectomy		44 (88%)
Concomitant procedures	Chest wall resection	3 (6%)
	Partial pleurectomy	3 (6%)
	Other	3 (6%)
Access	VATS	21 (42%)
	RATS	14 (28%)
	Thoracotomy	14 (28%)
	Other	1 (2%)
Histology	Adenocarcinoma	27 (54%)
	Squamous cell carcinoma	10 (20%)
	Adeno-squamous carcinoma	3 (6%)
	Pulmonary carcinoid	9 (18%)
	Large-cell carcinoma	1 (2%)
UICC stage	0 (Tis)	1 (2%)
	IA1	5 (10%)
	IA2	8 (16%)
	IA3	3 (6%)
	IB	3 (6%)
	IIA	5 (10%)
	IIB	10 (20%)
	IIIA	7 (14%)
	IIIB	4 (8%)
	IVA	4 (8%)

ECOG: Eastern Cooperative Oncology Group; VATS: video-assisted thoracoscopic surgery; RATS: robotic-assisted thoracic surgery; UICC: Union for International Cancer Control

Table 4:
COVID-19 status.

COVID-19 status		n = 50
COVID-19 Symptoms	Fever	2 (4%)
	Cough	3 (6%)
	Shortness of breath	1 (2%)
	Loss of smell /taste	0 (0%)
	Fatigue	0 (0%)
Postoperative COVID-19 test performed		25 (50%)
Positive tests		0 (0%)

Data based on 50 returned surveys. All COVID-19 tests were polymerase chain reaction (PCR)-based.

Conclusion

Patients with NSCLC are at an increased risk for contracting a SARS-CoV-2 infection and experiencing a severe course of the disease. However, the existing evidence and our own reported experience suggest that the postoperative incidence of COVID-19 in patients undergoing surgical resection for NSCLC is relatively low and anatomical resections can be performed safely. In order to protect healthcare providers, surgical access should be minimally invasive whenever possible and an ERAS protocol should be followed to enable an early discharge. Although these results are reassuring, data on treatment delay and a subsequent increase in advanced stages are worrisome. Lung cancer awareness and the maintenance of adequate oncological surgery should therefore be emphasised throughout the COVID-19 pandemic.

Potential competing interests
All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al.; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Feb;382(8):727–33. http://dx.doi.org/10.1056/NEJMoa2001017. PubMed. 1533-4406
2. Phan LT, Nguyen TV, Luong QC, Nguyen TV, Nguyen HT, Le HQ, et al. Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. N Engl J Med. 2020 Feb;382(9):872–4. http://dx.doi.org/10.1056/NEJMc2001272. PubMed. 1533-4406
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al.; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr;382(18):1708–20. http://dx.doi.org/10.1056/NEJMoa2002032. PubMed. 1533-4406
4. Huang H, Zhang M, Chen C, Zhang H, Wei Y, Tian J, et al. Clinical characteristics of COVID-19 in patients with preexisting ILD: A retrospective study in a single center in Wuhan, China. J Med Virol. 2020 Nov;92(11):2742–50. http://dx.doi.org/10.1002/jmv.26174. PubMed. 1096-9071
5. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020 Apr;323(13):1239–42. http://dx.doi.org/10.1001/jama.2020.2648. PubMed. 1538-3598
6. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA. 2020 May;323(18):1775–6. http://dx.doi.org/10.1001/jama.2020.4683. PubMed. 1538-3598
7. Passaro A, Peters S, Mok TS, Attili I, Mitsudomi T, de Marinis F. Testing for COVID-19 in lung cancer patients. Ann Oncol. 2020 Jul;31(7):832–4. http://dx.doi.org/10.1016/j.annonc.2020.04.002. PubMed. 1569-8041
8. Kamboj M, Sepkowitz KA. Nosocomial infections in patients with cancer. Lancet Oncol. 2009 Jun;10(6):589–97. http://dx.doi.org/10.1016/S1470-2045(09)70069-5. PubMed. 1474-5488
9. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015 Jan-Feb;65(1):5–29. http://dx.doi.org/10.3322/caac.21254. PubMed. 1542-4863
10. Heusser R, Baumann A, Noseda G. Krebs in der Schweiz. Zahlen, Weiterentwickung der Krebsregistrierung und Folgen. Onkologe. 2017;23(8):588–96. http://dx.doi.org/10.1007/s00761-017-0252-4. 0947-8965
11. Postmus PE, Kerr KM, Oudkerk M, Senan S, Waller DA, Vansteenkiste J, et al.; ESMO Guidelines Committee. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017 Jul;28 suppl_4:iv1–21. http://dx.doi.org/10.1093/annonc/mdx222. PubMed. 1569-8041
12. Opitz I, Patella M, Payrard L, Perentes JY, Inderbitzi R, Gelpke H, et al. Prognostic factors of oligometastatic non-small-cell lung cancer following radical therapy: a multicentre analysis. Eur J Cardiothorac Surg. 2020 Jun;57(6):1166–72. http://dx.doi.org/10.1093/ejcts/ezz384. PubMed. 1873-734X
13. Iacobucci G. Covid-19: all non-urgent elective surgery is suspended for at least three months in England. BMJ. 2020 Mar;368:m1106. http://dx.doi.org/10.1136/bmj.m1106. PubMed. 1756-1833
14. Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ. 2020 Nov;371:m4087. http://dx.doi.org/10.1136/bmj.m4087. PubMed. 1756-1833
15. Antonoff M, Backhus L, Boffa DJ, Broderick SR, Brown LM, Carrott P, et al.; Thoracic Surgery Outcomes Research Network, Inc. COVID-19 guidance for triage of operations for thoracic malignancies: A consensus statement from Thoracic Surgery Outcomes Research Network. J Thorac Cardiovasc Surg. 2020 Aug;160(2):601–5. http://dx.doi.org/10.1016/j.jtcvs.2020.03.061. PubMed. 1097-685X
16. Yu J, Ouyang W, Chua ML, Xie C. SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China. JAMA Oncol. 2020 Jul;6(7):1108–10. http://dx.doi.org/10.1001/jamaoncol.2020.0980. PubMed. 2374-2445
17. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020 Mar;21(3):335–7. http://dx.doi.org/10.1016/S1470-2045(20)30096-6. PubMed. 1474-5488
18. 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. Ann Oncol. 2020 Jul;31(7):894–901. http://dx.doi.org/10.1016/j.annonc.2020.03.296. PubMed. 1569-8041
19. Pellaud C, Grandmaison G, Pham Huu Thien HP, Baumberger M, Carrel G, Ksouri H, et al. Characteristics, comorbidities, 30-day outcome and in-hospital mortality of patients hospitalised with COVID-19 in a Swiss area - a retrospective cohort study. Swiss Med Wkly. 2020 Jul;150:w20314. http://dx.doi.org/10.4414/smw.2020.20314. PubMed. 1424-3997
20. Dingemans AC, Soo RA, Jazieh AR, Rice SJ, Kim YT, Teo LL, et al. Treatment Guidance for Patients With Lung Cancer During the Coronavirus 2019 Pandemic. J Thorac Oncol. 2020 Jul;15(7):1119–36. http://dx.doi.org/10.1016/j.jtho.2020.05.001. PubMed. 1556-1380
21. Garassino MC, Whisenant JG, Huang LC, Trama A, Torri V, Agustoni F, et al.; TERAVOLT investigators. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Lancet Oncol. 2020 Jul;21(7):914–22. http://dx.doi.org/10.1016/S1470-2045(20)30314-4. PubMed. 1474-5488
22. Russano M, Citarella F, Vincenzi B, Tonini G, Santini D. Coronavirus Disease 2019 or Lung Cancer: What Should We Treat? J Thorac Oncol. 2020 Jul;15(7):e105–6. http://dx.doi.org/10.1016/j.jtho.2020.04.001. PubMed. 1556-1380
23. Cai H. Sex difference and smoking predisposition in patients with COVID-19. Lancet Respir Med. 2020 Apr;8(4):e20. http://dx.doi.org/10.1016/S2213-2600(20)30117-X. PubMed. 2213-2619
24. Leung JM, Yang CX, Tam A, Shaipanich T, Hackett TL, Singhera GK, et al. ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19. Eur Respir J. 2020 May;55(5):55. http://dx.doi.org/10.1183/13993003.00688-2020. PubMed. 1399-3003
25. Rossato M, Russo L, Mazzocut S, Di Vincenzo A, Fioretto P, Vettor R. Current smoking is not associated with COVID-19. Eur Respir J. 2020 Jun;55(6):55. http://dx.doi.org/10.1183/13993003.01290-2020. PubMed. 1399-3003
26. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al.; China Medical Treatment Expert Group for COVID-19. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analy-

sis. Eur Respir J. 2020 May;55(5):55. http://dx.doi.org/10.1183/13993003.00547-2020. PubMed. 1399-3003
27. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). Eur J Intern Med. 2020 May;75:107–8. http://dx.doi.org/10.1016/j.ejim.2020.03.014. PubMed. 1879-0828
28. Seitlinger J, Wollbrett C, Mazzella A, Schmid S, Guerrera F, Nkomo DB, et al. Safety and feasibility of thoracic malignancy surgery during the COVID-19 pandemic. Ann Thorac Surg. 2020. PubMed. 0003-4975
29. Cai Y, Hao Z, Gao Y, Ping W, Wang Q, Peng S, et al. Coronavirus Disease 2019 in the Perioperative Period of Lung Resection: A Brief Report From a Single Thoracic Surgery Department in Wuhan, People's Republic of China. J Thorac Oncol. 2020 Jun;15(6):1065–72. http://dx.doi.org/10.1016/j.jtho.2020.04.003. PubMed. 1556-1380
30. Huang J, Wang A, Kang G, Li D, Hu W. Clinical course of patients infected with severe acute respiratory syndrome coronavirus 2 soon after thoracoscopic lung surgery. J Thorac Cardiovasc Surg. 2020 Aug;160(2):e91–3. http://dx.doi.org/10.1016/j.jtcvs.2020.04.026. PubMed. 1097-685X
31. Peng S, Huang L, Zhao B, Zhou S, Braithwaite I, Zhang N, et al. Clinical course of coronavirus disease 2019 in 11 patients after thoracic surgery and challenges in diagnosis. J Thorac Cardiovasc Surg. 2020 Aug;160(2):585–592.e2. http://dx.doi.org/10.1016/j.jtcvs.2020.04.005. PubMed. 1097-685X
32. Gourd E. Lung cancer control in the UK hit badly by COVID-19 pandemic. Lancet Oncol. 2020 Dec;21(12):1559. http://dx.doi.org/10.1016/S1470-2045(20)30691-4. PubMed. 1474-5488
33. Bersanelli M. Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors. Immunotherapy. 2020 Apr;12(5):269–73. http://dx.doi.org/10.2217/imt-2020-0067. PubMed. 1750-7448
34. Bersanelli M, Scala S, Affanni P, Veronesi L, Colucci ME, Banna GL, et al. Immunological insights on influenza infection and vaccination during immune checkpoint blockade in cancer patients. Immunotherapy. 2020 Feb;12(2):105–10. http://dx.doi.org/10.2217/imt-2019-0200. PubMed. 1750-7448
35. Bonomi L, Ghilardi L, Arnoldi E, Tondini CA, Bettini AC. A Rapid Fatal Evolution of Coronavirus Disease-19 in a Patient With Advanced Lung Cancer With a Long-Time Response to Nivolumab. J Thorac Oncol. 2020 Jun;15(6):e83–5. http://dx.doi.org/10.1016/j.jtho.2020.03.021. PubMed. 1556-1380
36. Merritt RE, Kneuertz PJ. Considerations for the Surgical Management of Early Stage Lung Cancer During the COVID-19 Pandemic. Clin Lung Cancer. 2020. PubMed. 1525-7304
37. Passaro A, Addeo A, Von Garnier C, Blackhall F, Planchard D, Felip E, et al. ESMO Management and treatment adapted recommendations in the COVID-19 era: lung cancer. ESMO Open. 2020 Jun;5 Suppl 3:5. http://dx.doi.org/10.1136/esmoopen-2020-000820. PubMed. 2059-7029
38. Muñoz-Largacha JA, Wei B. Commentary: lung surgery in the time of COVID-19. J Thorac Cardiovasc Surg. 2020 Aug;160(2):e97–8. http://dx.doi.org/10.1016/j.jtcvs.2020.04.088. PubMed. 1097-685X
39. Banna G, Curioni-Fontecedro A, Friedlaender A, Addeo A. How we treat patients with lung cancer during the SARS-CoV-2 pandemic: *primum non nocere* . ESMO Open. 2020 Apr;5(2):e000765. PubMed. 2059-7029
40. Rosca A, Krones T, Biller-Andorno N. Shared decision making: patients have a right to be informed about possible treatment options and their risks and benefits. Swiss Med Wkly. 2020 Jul;150:w20268. http://dx.doi.org/10.4414/smw.2020.20268. PubMed. 1424-3997
41. Scarci M, Raveglia F. Commentary: The double responsibility of the thoracic surgeon at the time of the pandemic: A perspective from the North of Italy. J Thorac Cardiovasc Surg. 2020 Aug;160(2):595–6. http://dx.doi.org/10.1016/j.jtcvs.2020.04.003. PubMed. 1097-685X
42. Seco M, Wood J, Wilson MK. COVIDSafe thoracic surgery: minimizing intraoperative exposure to aerosols. JTCVS Tech. 2020 Sep;3:412–4. http://dx.doi.org/10.1016/j.xjtc.2020.05.017. PubMed. 2666-2507
43. Falcoz PE, Puyraveau M, Thomas PA, Decaluwe H, Hürtgen M, Petersen RH, et al.; ESTS Database Committee and ESTS Minimally Invasive Interest Group. Video-assisted thoracoscopic surgery versus open lobectomy for primary non-small-cell lung cancer: a propensity-matched analysis of outcome from the European Society of Thoracic Surgeon database. Eur J Cardiothorac Surg. 2016 Feb;49(2):602–9. http://dx.doi.org/10.1093/ejcts/ezv154. PubMed. 1873-734X
44. Bendixen M, Jørgensen OD, Kronborg C, Andersen C, Licht PB. Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer: a randomised controlled trial. Lancet Oncol. 2016 Jun;17(6):836–44. http://dx.doi.org/10.1016/S1470-2045(16)00173-X. PubMed. 1474-5488
45. Cao C, Manganas C, Ang SC, Peeceeyen S, Yan TD. Video-assisted thoracic surgery versus open thoracotomy for non-small cell lung cancer: a meta-analysis of propensity score-matched patients. Interact Cardiovasc Thorac Surg. 2013 Mar;16(3):244–9. http://dx.doi.org/10.1093/icvts/ivs472. PubMed. 1569-9285
47. Mina MJ, Parker R, Larremore DB. Rethinking Covid-19 Test Sensitivity - A Strategy for Containment. N Engl J Med. 2020 Nov;383(22):e120. http://dx.doi.org/10.1056/NEJMp2025631. PubMed. 1533-4406
48. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020 Feb;395(10223):514–23. http://dx.doi.org/10.1016/S0140-6736(20)30154-9. PubMed. 1474-547X
49. Çınar HN, İnce Ö, Çelik B, Saltabaş F, Özbek M. Clinical course of COVID-19 pneumonia in a patient undergoing pneumonectomy and pathology findings during the incubation period. Swiss Med Wkly. 2020 Jun;150:w20302. PubMed. 1424-3997
50. Brocken P, Kiers BA, Looijen-Salamon MG, Dekhuijzen PN, Smits-van der Graaf C, Peters-Bax L, et al. Timeliness of lung cancer diagnosis and treatment in a rapid outpatient diagnostic program with combined 18FDG-PET and contrast enhanced CT scanning. Lung Cancer. 2012 Mar;75(3):336–41. http://dx.doi.org/10.1016/j.lungcan.2011.08.017. PubMed. 1872-8332
51. Tsai CH, Kung PT, Kuo WY, Tsai WC. Effect of time interval from diagnosis to treatment for non-small cell lung cancer on survival: a national cohort study in Taiwan. BMJ Open. 2020 Apr;10(4):e034351. http://dx.doi.org/10.1136/bmjopen-2019-034351. PubMed. 2044-6055
52. Christensen ED, Harvald T, Jendresen M, Aggestrup S, Petterson G. The impact of delayed diagnosis of lung cancer on the stage at the time of operation. Eur J Cardiothorac Surg. 1997 Dec;12(6):880–4. http://dx.doi.org/10.1016/S1010-7940(97)00275-3. PubMed. 1010-7940
53. Dinmohamed AG, Visser O, Verhoeven RH, Louwman MW, van Nederveen FH, Willems SM, et al. Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands. Lancet Oncol. 2020 Jun;21(6):750–1. http://dx.doi.org/10.1016/S1470-2045(20)30265-5. PubMed. 1474-5488
54. Park JY, Lee YJ, Kim T, Lee CY, Kim HI, Kim JH, et al. Collateral effects of the coronavirus disease 2019 pandemic on lung cancer diagnosis in Korea. BMC Cancer. 2020 Oct;20(1):1040. http://dx.doi.org/10.1186/s12885-020-07544-3. PubMed. 1471-2407
55. Bertolaccini L, Sedda G, Spaggiari L. Paying Another Tribute to the COVID-19 Pandemic: The Decrease of Early Lung Cancers. Ann Thorac Surg. 2020. PubMed. 0003-4975
56. Mackintosh JA, Marshall HM, Yang IA, Bowman RV, Fong KM. A retrospective study of volume doubling time in surgically resected non-small cell lung cancer. Respirology. 2014 Jul;19(5):755–62. http://dx.doi.org/10.1111/resp.12311. PubMed. 1440-1843
57. Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, et al.; International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee, Advisory Boards, and Participating Institutions . The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol. 2016 Jan;11(1):39–51. http://dx.doi.org/10.1016/j.jtho.2015.09.009. PubMed. 1556-1380