

Safety and Feasibility of Thoracic Malignancy Surgery During the COVID-19 Pandemic



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Background. The coronavirus disease 2019 (COVID-19) pandemic has decreased surgical activity, particularly in the field of oncology, because of the suspicion of a higher risk of COVID-19–related severe events. This study aimed to investigate the feasibility and safety of thoracic cancer surgery in the most severely affected European and Canadian regions during the COVID-19 pandemic.

Methods. The study investigators prospectively collected data on surgical procedures for malignant thoracic diseases from January 1 to April 30, 2020. The study included patients from 6 high-volume thoracic surgery departments: Nancy and Strasbourg (France), Freiburg (Germany), Milan and Turin (Italy), and Montreal (Canada). The centers involved in this research are all located in the most severely affected regions of those countries. An assessment of COVID-19–related symptoms, polymerase chain reaction (PCR)–confirmed COVID-19 infection, rates of hospital and intensive care unit admissions, and death was performed for each

patient. Every deceased patient was tested for COVID-19 by PCR.

Results. In the study period, 731 patients who underwent 734 surgical procedures were included. In the whole cohort, 9 cases (1.2%) of COVID-19 were confirmed by PCR, including 5 in-hospital contaminants. Four patients (0.5%) needed readmission for oxygen requirements. In this subgroup, 2 patients (0.3%) needed intensive care unit and mechanical ventilatory support. The total number of deaths in the whole cohort was 22 (3%). A single death was related to COVID-19 (0.14%).

Conclusions. Maintaining surgical oncologic activity in the era of the COVID-19 pandemic seems safe and feasible, with very low postoperative morbidity or mortality. To continue to offer the best care to patients who do not have COVID-19, reports on other diseases are urgently needed.

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Coronavirus disease 2019 (COVID-19) has become the largest pandemic that the world has faced in the last century.¹ After China, Europe was rapidly defined as the epicenter of the pandemic by the World Health Organization. The first epidemic outbreak in Europe was located in northern Italy, particularly in Lombardy.² During progression of the epidemic in Europe, the spread started in North America. In Canada, Quebec was considered the

epicenter of the infection. Consequently, health care systems worldwide had to adapt to this dramatic increase in COVID-19–infected patients to offer them best care. Hence, on the basis of the recommendations of scientific societies, many of elective surgical procedures were postponed. This decision was reinforced by publications from China on cancer. Indeed, reports from China

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showed an increased risk of death or intensive care unit (ICU) admission in patients with cancer.^{3,4} As a result, these precautions led to a dramatic decrease in malignancy management worldwide, including thoracic cancers.^{5,6}

However, it seems now that the world will have to address COVID-19 for an indefinite period of time, and taking care of other health disorders is still relevant. Large-scale data on cancer operations are thus more than necessary. Here, we report an international multiinstitutional cohort of patients who underwent operations for malignant thoracic diseases in 6 high-volume thoracic surgery departments that were most severely affected by COVID-19 during the study period.

Material and Methods

This study was approved by the Ethics Committee of the French Society of Thoracic and Cardiovascular Surgeons (approval number: CERC-SFCTCV-2020-07-03-14-REST).

A retrospective review of prospective databases was conducted from January 1 to April 30, 2020, from Nancy and Strasbourg (France), Freiburg (Germany), Milan and Turin (Italy), and Montreal (Canada). All of these thoracic surgery centers are located in the regions that were most severely affected by the pandemic in their respective countries. These countries officially reported their first cases of COVID-19 at the end of February, a few days apart, starting with Italy (February 21, 2020). Because patients with cancer are considered to be at higher risk in the 6 weeks after surgery, we decided to review patients starting on January 1, 2020, given that the virus likely began to spread in these regions before the first cases were declared. Nevertheless, in France, the first case of COVID-19 was retrospectively diagnosed on December 20, 2019, by polymerase chain reaction (PCR). One can thereby speculate that on January 1, 2020, the virus was already present, at least in Europe. We then divided patients into 2 groups on the basis of whether they were operated on before (group 1) or after (group 2) lockdown in each country (ie, March 9, 2020 in Italy, March 17, 2020 in France, March 22, 2020 in Quebec). In Germany, there has been no lockdown similar to that in France, Italy, and Canada. We therefore chose March 22, 2020 as the equivalent of lockdown for Germany.

After lockdown, specific measures were taken with the goal of avoiding operations on COVID-19-positive patients. In France, the day before surgery, patients were assessed by telephone for the presence or absence of symptoms related to COVID-19 or contact in the previous 14 days with individuals confirmed to have COVID-19 or to be harboring COVID-19-related symptoms. More recently, a chest computed tomographic scan without contrast enhancement was systematically performed the day before surgery to rule out a COVID-19-related infiltrate. In cases of high suspicion, patients were tested by PCR.

In Italy and Canada, health care institutions routinely performed PCR testing for COVID-19 before each hospitalization in surgical departments. In Germany, PCR

testing for COVID-19 was performed only in patients with contact or symptoms. Nevertheless, PCR-positive patients were rescheduled and retested 2 weeks later regardless of the inclusion center. Because the European Institute of Oncology in Milan was chosen to be a COVID-free area, patients with a diagnosis of COVID-19 were referred to other centers.

Since May 2020, in France, as in Italy and Canada, all patients undergoing surgery have had preoperative PCR tests. In Germany, COVID-19 PCR testing is still performed only in symptomatic patients preoperatively.

To date, all patients and family doctors have been contacted by telephone to assess the appearance of COVID-19-related symptoms or to determine PCR-confirmed COVID-19 or death.

The primary end points of our study were PCR-confirmed COVID-19 disease, rates of hospital or ICU admission (defined as severe cases), and death.

Results

Detailed characteristics of the study group are shown in [Table 1](#). In the study period, 731 patients who underwent 734 surgical procedures for pathologically proven cancer were reviewed. Upper gastrointestinal surgery for cancer was performed only at McGill University (Montreal). The majority of patients underwent surgery before lockdown ($n = 530$; 72.5%). Meanwhile wedge resections were usually performed for metastasectomy (147 of 152; 96.7%), although 5 were performed for localized non-small cell lung cancer as a result of poor pulmonary function. [Table 2](#) summarizes the case exposure of patients with COVID-19 (in hospital, in ICU, cessation of activity in the operating room) in the different hospitals in our study.

A total of 122 COVID-19 PCR tests were performed during lockdown. Most of these tests (107; 87.7%) were performed routinely before hospitalization, and 15 (12.3%) were done in symptomatic patients. Only 23 patients were screened by computed tomographic scan before hospitalization. One patient required a 15-day delay because of a positive test result before admission. No patient in the cohort underwent surgery with a positive PCR test result.

In this cohort, 9 patients had PCR-confirmed COVID-19-positive status (1.2%). Among them, 4 (0.5%) needed hospitalization for oxygen requirements. Two patients (0.3%) needed ICU and mechanical ventilatory support, and 1 patient died after 8 days in the ICU. The patient who died was 67 years old and obese (body mass index, 31.8 kg/m²), and he underwent open right lower lobectomy for adenocarcinoma (stage IA3). He became symptomatic 5 days after his discharge (influenza-like illness) and was tested for COVID-19 by PCR. After 48 hours of evolution at home, he required hospitalization and transfer to the ICU for acute respiratory distress syndrome related to COVID-19. He finally died on postoperative day 23.

The total number of deaths was 22 (3%). Every deceased patient was tested for COVID-19. Only 1 death was COVID-19 related (0.14%).

Table 1. Detailed Characteristics of the Study Group

Variable	Before Lockdown (n = 530)	After Lockdown (n = 204)	P
Center			
Nancy (n = 132)	79 (59.9)	53 (40.1)	
Strasbourg (n = 66)	46 (69.7)	20 (30.3)	
Freiburg (n = 101)	77 (76.2)	24 (23.8)	
Milan (n = 220)	162 (73.6)	58 (26.4)	
Turin (n = 89)	52 (58.4)	37 (41.6)	
Montreal (n = 126)	114 (90.5)	12 (9.5)	.001
Age, y	67 (IQR 14.8)	67 (IQR 15)	.77
Sex			
Male	297 (56)	116 (56.9)	
Female	233 (44)	88 (43.1)	.84
Body mass index, kg/m ²	25.5 (IQR 5.3)	26 (IQR 5.1)	.83
Performance status	1 (IQR 1)	1 (IQR 1)	.57
Comorbidities			
Cardiac ^a (n = 339)	237 (44.7)	102 (50)	.08
Vascular ^b (n = 195)	141 (26.6)	54 (26.4)	.67
Respiratory ^c (n = 179)	125 (23.6)	54 (26.5)	.18
Digestive ^d (n = 66)			
Neurologic ^e (n = 67)	33 (6.2)	33 (16.2)	.001
Cancer history ^f (n = 312)			
Diabetes (n = 95)	47 (8.9)	20 (9.8)	.62
Hematologic ^g (n = 21)	228 (43)	84 (41.2)	.88
Nephrologic ^h (n = 44)	74 (14)	21 (10.3)	.31
Immunosuppressive ⁱ (n = 52)	15 (2.8)	6 (2.9)	.82
	28 (5.3)	16 (7.8)	.12
	46 (8.7)	6 (2.9)	.01
Preoperative			
FEV ₁	88 (IQR 29)	90 (IQR 31.5)	.35
DLco	82 (IQR 28)	78 (IQR 24)	.34
Smoking history (n = 440)	305 (57.5)	135 (66.2)	.12
Pack-years	20 (IQR 40)	20 (IQR 40)	.8
Type of surgery			
Pneumonectomy (n = 27)	14 (2.6)	13 (6.4)	.02
Bilobectomy (n = 12)	8 (1.5)	4 (2)	.67
Lobectomy (n = 344)	245 (46.2)	99 (48.5)	.58
Segmentectomy (n = 63)	45 (8.5)	18 (8.8)	.69
Wedge resection (n = 152)	122 (23)	30 (14.7)	.01
Thymus resection (n = 27)	20 (3.8)	7 (3.4)	.91
Talc poudrage (n = 84)	63 (11.9)	21 (10.3)	.94
Chest wall resection (n = 3)	1 (0.2)	2 (1)	.21
Mediastinal tumor resection (n = 5)	5 (0.9)	0	.33
Ivor Lewis esophagectomy (n = 17)	12 (2.3)	5 (2.5)	.96
Median length of stay, d	6 (IQR 4)	5 (IQR 3)	.24
Median length of stay (without esophagectomy), d	6 (IQR 4)	5 (IQR 3)	.39
Chemotherapy			
Neoadjuvant (n = 70)	53 (10)	17 (8.3)	.47
Adjuvant (n = 176)	132 (24.9)	44 (21.6)	.64
Minimally invasive surgery	322	106	
VATS (n = 375)	285 (53.8)	90 (44.1)	.02
RATS (n = 53)	37 (7)	16 (7.8)	.69
Stage			
Tis	3 (0.6)	0 (0)	
IA1	53 (14.1)	17 (14.2)	

(Continued)

Table 1. Continued

Variable	Before Lockdown (n = 530)	After Lockdown (n = 204)	P
IA2	53 (14.1)	10 (8.3)	
IA3	29 (7.7)	3 (2.5)	
IB	47 (12.5)	22 (18.3)	
IIA	20 (5.3)	8 (6.7)	
IIB	58 (15.4)	20 (16.7)	
IIIA	54 (14.3)	11 (9.2)	
IIIB	15 (4)	11 (9.2)	
IV	46 (12.2)	18 (15)	.63
Complications (n = 216):	165 (31.1)	51 (25)	.12
Bacterial pneumonia (n = 52)	42 (7.9)	10 (4.9)	.49
PAF (n = 36)	26 (4.9)	10 (4.9)	.67
Atelectasis (n = 17)	9 (1.7)	8 (3.9)	.02
Prolonged air leak (n = 48)	39 (7.4)	9 (4.4)	.42
Anemia (n = 20)	13 (2.5)	7 (3.4)	.2
Chylothorax (n = 3)	3 (0.6)	0 (0)	.67
Follow-up time (d)	79 (IQR 59)	21.5 (IQR 26)	.001
COVID-19			
PCR confirmed (n = 9)	9 (1.7)	0	.07
Hospital admission (n = 4)	4 (0.8)	0	.58
ICU admission (n = 2)	2 (0.4)	0	>.999
Deaths (n = 1)	1 (0.2)	0	>.999
Deaths (n = 22)	17 (3.2)	5 (2.5)	.73

^aHistory of high blood pressure, atrial fibrillation, ischemic heart disease, or cardiac surgery; ^bHistory of peripheral arterial and aortic disease; ^cHistory of chronic obstructive pulmonary disease, sleep apnea, pulmonary embolism, asthma, or tuberculosis; ^dHistory of chronic liver disease, inflammatory bowel disease, or gastrointestinal surgery; ^eHistory of epilepsy; ^fHistory of any thoracic or extrathoracic malignancy; ^gHistory of leukemia, lymphoma, or chronic anemia; ^hHistory of chronic kidney failure or, more rarely, nephrectomy; ⁱHistory of any immunosuppressive treatment or immunosuppressive health disorder.

Data are presented as n (%); continuous values are presented as median (IQR). Comparisons were performed using the Mann-Whitney, Fisher nonparametric, and median tests whenever appropriate. Classification of the tumor stage was performed according to the eighth edition of the TNM classification of lung cancer (Union for International Cancer Control, 2017).

COVID-19, coronavirus disease 2019; DLCO, diffusing capacity for carbon monoxide; FEV₁, forced expiratory volume in 1 second; ICU, intensive care unit; IQR, interquartile range; PAF, postoperative atrial fibrillation; PCR, polymerase chain reaction; RATS, robotic-assisted thoracic surgery; VATS, video-assisted thoracic surgery.

The overall complication rate was 29.4% (216 cases). The most frequent complications were pneumonia (42 of 530 before lockdown and 10 of 204 after lockdown; $P = .49$), followed by prolonged air leakage (39 of 530 before lockdown and 9 of 204 after lockdown; $P = .42$) and postoperative atrial fibrillation (26 of 530 vs 10 of 204, respectively; $P = .67$). Other complications are detailed in Table 1. There was no difference in the complication rate before and after lockdown in our cohort (165 of 530 vs 51 of 204, respectively; $P = .12$). Specific mortality rates are summarized in Supplemental Table 1.

A total of 306 open operations and 428 minimally invasive surgical procedures were performed. There were statistically fewer procedures using video-assisted thoracic surgery after lockdown ($P = .02$).

The median length of stay before confinement was 6 days (interquartile range, 4.2 days) vs 5 days (interquartile range, 3.1 days) after lockdown ($P = .24$).

We compared the different precautions taken in the study hospitals. The most important precaution concerns the Milan center because it was quickly decided that the

European Institute of Oncology would not treat patients with severe forms of COVID-19 (Supplemental Table 2).

There was no difference in terms of COVID-19 results. There was also no difference in mortality between the 2 groups. Additional subgroup analyses are available in Supplemental Tables 2, 3, 4, and 5.

Comment

Our results highlight safety and feasibility of operations for malignant thoracic diseases during the COVID-19 pandemic. Indeed, mortality (3%) and morbidity (29.4%) were low, comparable to published data. More, COVID-19 infection was responsible for only 1 of the 22 deaths in the cohort (4.5%), and only 2 (0.3%) of the 731 patients needed ICU hospitalization for COVID-19 infection.

The preliminary data on Asian cohorts^{3,4} led to a dramatic decrease in scheduled surgical procedures in Europe and North America. Nearly 40% of the surgical procedures that were cancelled or postponed were operations for cancer.⁸ In the field of thoracic oncology, many recommendations have suggested delaying surgery

Table 2. Exposure of the Study Hospitals to Cases of Coronavirus Disease 2019 and the Impact on Hospital Activities

Hospital	January 2020	February 2020	March 2020	April 2020
Regional University Hospital, Nancy, France				
COVID-19 cases in hospital	-	+	+	+
COVID-19 cases in ICU	-	-	+	+
ICU converted into COVID unit	-	-	-	+
Designated COVID unit	-	-	+	+
OR converted into COVID unit	-	-	-	-
Thoracic surgeon redeployed	-	-	-	-
Stopping activity in OR	-	-	-	+ (1 wk)
European Institute of Oncology, Milan, Italy				
COVID-19 cases in hospital	-	-	+	+
COVID-19 cases in ICU	-	-	-	-
ICU converted into COVID unit	-	-	-	-
Designated COVID unit	-	-	-	-
OR converted into COVID unit	-	-	-	-
Thoracic surgeon redeployed	-	-	-	-
Stopping activity in OR	-	-	-	-
Mc Gill University, Montreal, Canada				
COVID-19 cases in hospital	-	-	+	+
COVID-19 cases in ICU	-	-	+	+
ICU converted into COVID unit	-	-	+	+
Designated COVID unit	-	-	+	+
OR converted into COVID unit	-	-	-	-
Thoracic surgeon redeployed	-	-	-	-
Stopping activity in OR	-	-	-	(+) restricted activity (emergency and oncology only)
University Hospital, Freiburg, Germany				
COVID-19 cases in hospital	-	+	+	+
COVID-19 cases in ICU	-	-	+	+
ICU converted into COVID unit	-	-	-	-
Designated COVID unit	-	-	+	+
OR converted into COVID unit	-	-	-	-
Thoracic surgeon redeployed	-	-	+	+
Stopping activity in OR	-	-	(+) restricted activity (emergency and oncology only from March 18, 2020)	(+) restricted activity (emergency and oncology only)
University of Turin, Turin, Italy				
COVID-19 cases in hospital	-	+	+	+
COVID-19 cases in ICU	-	-	+	+
ICU converted into COVID unit	-	-	+	+
Designated COVID unit	-	-	+	+
OR converted into COVID unit	-	-	+	+
Thoracic surgeon redeployed	-	-	-	-
Stopping activity in OR	-	-	-	-
Rhena Private Hospital, Strasbourg, France				
COVID-19 cases in hospital	-	+	+	+
COVID-19 cases in ICU	-	-	+	+
ICU converted into COVID unit	-	-	+	+
Designated COVID unit	-	-	+	+
OR converted into COVID unit	-	-	+	+
Thoracic surgeon redeployed	-	-	+	+
Stopping activity in OR	-	-	+ (2 wk)	+ (2 wk)

COVID, COVID-19, coronavirus disease 2019; ICU intensive care unit; OR, operating room; +, present (COVID-19 patients or special measures); -, absent.

for peripheral localized non-small cell lung cancer smaller than 2 cm (in patients with a low risk of COVID-19 contamination) or 3 to 5 cm (in patients with a high risk of COVID-19 contamination)^{5,7,8}. In the meantime, the risk of cancer growth or metastasis, even in “small tumors,” is expected, leading to lower chances of survival for patients with these potentially curable cancers. This delay in the management of localized non-small cell lung cancer, even 3 to 4 months, can transform a localized tumor of less than 1 cm (T1a) into a tumor of 3 to 4 cm (T2a), thus decreasing the probability of 5-year survival from 92% to 68%, and worsening to 53% with hilar lymph node involvement (TNM classification of lung cancer, eighth edition⁹). This concept was reinforced by a report by the COVIDSurg Collaborative.¹⁰ Indeed, the COVIDSurg Collaborative concluded that it would take approximately 45 weeks to clear the backlog of operations resulting from COVID-19 disruption, despite a 20% increase in surgical activity.¹⁰ Under these conditions, it can be estimated that the delay in treatment of these disorders will lead to more advanced disease at the time of surgery, including metastatic disease in patients who will no longer be suitable candidates for curative treatment. In support of this view, a meta-analysis focusing on delayed treatment in oncology was published in November 2020.¹¹ After inclusion of more than 1.2 million patients for different indications, a 6% to 8% increase in mortality depending on histologic type was found for a 4-week delay in surgical treatment.¹¹ Moreover, the switch from surgical treatment to systemic therapies (eg, targeted therapies or immunotherapies) as a result of postponed surgery undoubtedly has a significant medicoeconomic impact.

Our results do not support thoracic cancers and thoracic surgery as risk factors for poor outcomes in the current COVID-19 era. Indeed, the expected mortality rate related to COVID-19 in the general population, as reported by the World Health Organization, is 0.28%.¹² In our cohort, the rate of severe events was 0.3%, with a very low rate of death (0.14%). Moreover, the median age of the studied population was 67 years, and according to the World Health Organization, the overall mortality rate in this population is estimated to be 3.6% in the latest estimates. Markedly, 2 of the patients who underwent pneumonectomy (68 and 83 years old) and who were found to be COVID-19 positive had surprisingly positive courses.

Other historical epidemics and pandemics have already threatened the health care system, an example being the severe acute respiratory syndrome coronavirus outbreak that occurred between 2002 and 2004 in Hong Kong and China. It does not seem unrealistic to hypothesize that the COVID-19 pandemic will not be the last. The medical system consequently must learn from these pandemics and adapt its practices to offer care to all patients. We have highlighted here that the pursuit of treatment for thoracic cancers in highly infected regions during a pandemic period is feasible and does not lead to substantial excess mortality because only 1 of 22 deaths was COVID-19 related. Indeed, even though most ICU beds were converted into beds for COVID-19-positive patients,

we did not observe higher postoperative mortality than seen during a nonpandemic period. We did not observe an increased risk of in-hospital contamination because only 5 (0.7%) patients tested positive after their hospitalization. These findings can be partially explained by the reinforcement of the enhanced recovery after surgery¹³ program in the majority of the hospitals in our study that limited the hospital length of stay. Furthermore, because ICU beds were transformed into beds for COVID-19-positive patients, recovery rooms were transformed into a non-COVID-19 ICU zone, allowing the maintenance or transfer of sick patients in the postoperative period and limiting the risk of contamination by a COVID-19-positive patient. However, we emphasize that maintaining surgical activity during the COVID-19 pandemic depends on several factors related to hospitals, including material (mechanical ventilator), health care providers, and bed availability, as well as the intensity of the pandemic itself. Equally, the maintenance of “non-COVID-19” care channels such as endobronchial ultrasound or pulmonary function testing is a necessity to perform thoracic surgery for malignant disease.

To improve management, we compared the precautionary measures taken during the study. The most important measure was the preservation of the European Institute of Oncology in Milan. However, subgroup analysis of only 1 center compared with the others does not allow us to draw conclusions about the benefit of this precaution. Further studies will be necessary to determine the best preventive measures against COVID-19.

Our study has some limitations that must be taken in account when analyzing the results. Although the data were prospectively collected, this is a retrospective cohort study. Moreover, the heterogeneity of prevention measures taken, depending on each country, did not allow us to identify the best way to proceed. Nevertheless, it shows that different measures can be applied to provide safety to both patients and health care providers.

Conversely, our study is strengthened by its multi-institutional design, providing clinical data on a large published cohort of patients who underwent operations for malignant thoracic disease during the COVID-19 pandemic. Finally, the proportion of COVID-19 PCR tests was relatively low, and as a result we could not draw any conclusion about the consequences of COVID-19 infection on thoracic cancer surgery outcomes. Indeed, our cohort included 66 patients who did not have systematic PCR testing preoperatively during the lockdown period (only in France), so we may have underestimated the rate of COVID-19, especially asymptomatic cases. We can also point out that because of the variable incubation period of COVID-19 (between 2 and 12 days¹⁴), it does not seem reasonable to allocate a time of infection (before, during, or after hospitalization). However, the aim of this study was to evaluate the safety of maintaining surgical activity during the COVID-19 pandemic.

The maintenance of surgical activity, particularly in oncology, appears necessary in light of the excess mortality from all causes observed during the first months of 2020. Indeed, part of the excess mortality observed is

linked to the absence of or delay in the management of non-COVID-19 disorders.¹⁵ The absence of a diagnosis of myocardial infarction has been well documented,¹⁶ as has the delay in cancer diagnosis.¹⁷

In conclusion, in this large international multiinstitutional study, we have shown that maintaining surgical thoracic oncology activity in the era of COVID-19 is feasible and safe. Given that surgery is associated with the best outcomes in malignant thoracic diseases, patients with thoracic cancer patients should still be treated surgically. We emphasize that every measure should be taken to protect health care providers and to limit the risk of operating on COVID-19-positive patients. More data on other malignant disease are necessary.

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