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Safety of patients and providers in lung cancer surgery during the COVID-19 pandemic

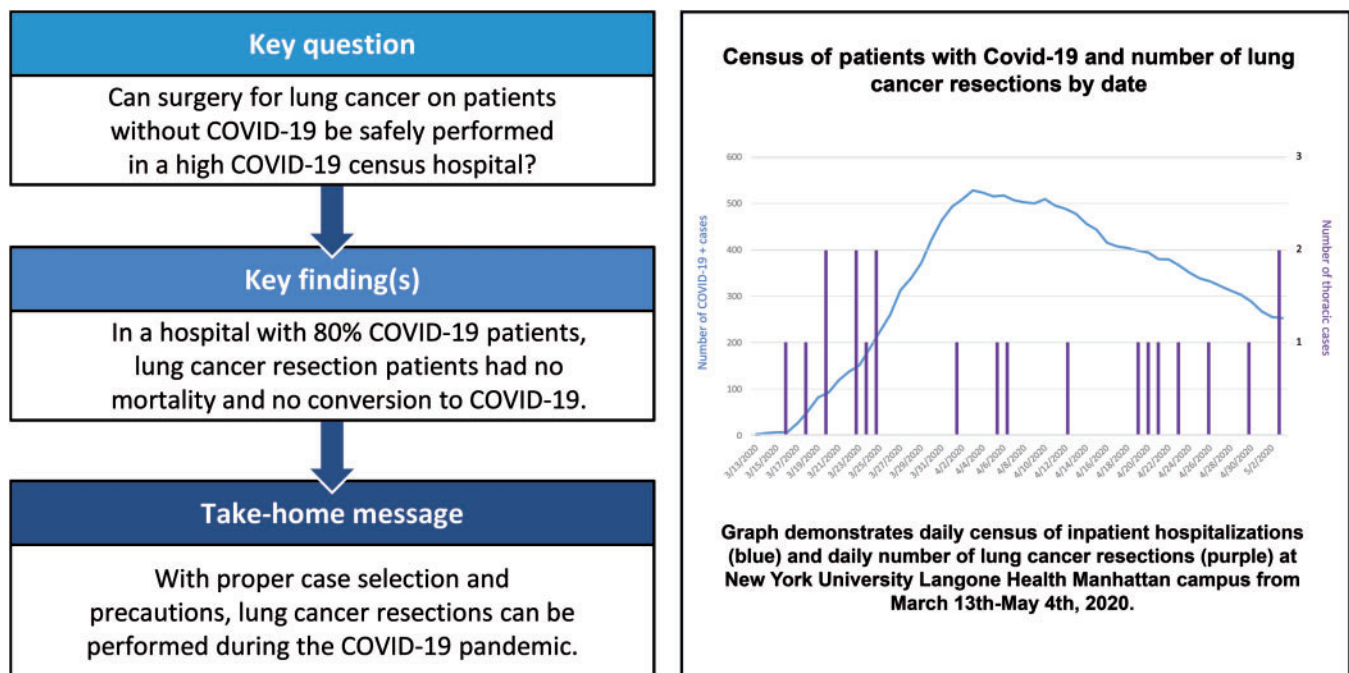
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Abstract

OBJECTIVES: The coronavirus disease 2019 (COVID-19) pandemic has resulted in patient reluctance to seek care due to fear of contracting the virus, especially in New York City which was the epicentre during the surge. The primary objectives of this study are to evaluate the safety of patients who have undergone pulmonary resection for lung cancer as well as provider safety, using COVID-19 testing, symptoms and early patient outcomes.

METHODS: Patients with confirmed or suspected pulmonary malignancy who underwent resection from 13 March to 4 May 2020 were retrospectively reviewed.

RESULTS: Between 13 March and 4 May 2020, 2087 COVID-19 patients were admitted, with a median daily census of 299, to one of our Manhattan campuses (80% of hospital capacity). During this time, 21 patients (median age 72 years) out of 45 eligible surgical candidates underwent pulmonary resection—13 lobectomies, 6 segmentectomies and 2 pneumonectomies were performed by the same providers who were caring for COVID-19 patients. None of the patients developed major complications, 5 had minor complications, and the median length of hospital stay was 2 days. No previously COVID-19-negative patient ($n = 20/21$) or healthcare provider ($n = 9$: 3 surgeons, 3 surgical assistants, 3 anaesthesiologists) developed symptoms of or tested positive for COVID-19.

CONCLUSIONS: Pulmonary resection for lung cancer is safe in selected patients, even when performed by providers who care for COVID-19 patients in a hospital with a large COVID-19 census. None of our patients or providers developed symptoms of COVID-19 and no patient experienced major morbidity or mortality.

Keywords: Coronavirus disease 2019 • Pulmonary resection • Lung cancer

ABBREVIATIONS

COVID-19	Coronavirus disease 2019
CT	Computed tomography
ICU	Intensive care unit
IQR	Interquartile range
NSCLC	Non-small-cell lung cancer
PET	Positron emission tomography
PFT	Pulmonary function test
PPE	Personal protective equipment
rtPCR	Reverse transcriptase-polymerase chain reaction
SUV _{max}	Maximum standardized uptake values
VATS	Video-assisted thoracoscopic surgical

INTRODUCTION

The global coronavirus disease 2019 (COVID-19) pandemic [1] and the resultant strain on the healthcare system have altered the current practice of medicine and how patients seek care. Delays in presentation for acute illness have been reported, with the delay due to patient concern for contracting COVID-19 or providers discouraging presenting to the hospital, resulting in preventable deaths [2]. New York was the epicentre of COVID-19 cases, accounting for one-third of the cases in the USA [3]. Due to the overwhelming surge of critically ill COVID-19 patients, governing bodies in New York City and New York State placed a moratorium on elective surgery, effective on 20 March 2020 [4] and 23 March 2020 [5], respectively. The reason for the suspension was to preserve hospital resources, such as ventilators, personal protective equipment (PPE), hospital and intensive care unit (ICU) beds and the hospital workforce. In addition, there was concern that non-COVID-19 patients admitted with other types of ailments might become infected with COVID-19.

Provision of care for cancer patients remains vital even during times of resource scarcity, such as the current pandemic. The American College of Surgeons set out guidelines to help physicians and hospitals prioritize patient selection for operative management [6]. One unique subset of cancer patients who may be at higher risk is those that require lung resection for non-small-cell lung cancer (NSCLC). The risk-benefit ratio for these patients must be carefully weighed, as contracting COVID-19 in the post-operative period confers a higher likelihood of respiratory failure or mortality [7].

The primary purpose of this study was to evaluate the safety of patients undergoing and providers involved in pulmonary resection for lung cancer during the COVID-19 crisis at New York University Langone Healthcare at the Manhattan campus. In addition, we present our decision-making process on patient selection, describe our hospital COVID-19 testing policy and perioperative care, and report our early results.

PATIENTS AND METHODS

Patient selection

This is a retrospective analysis of all patients who underwent or were considered for pulmonary resection for confirmed or suspected lung cancer at New York University Langone Health (NYULH) Manhattan campus from the time of our first admission with COVID-19, 13 March 2020 to 4 May 2020. The NYULH Institutional Review Board approved this study and the requirement for informed consent was waived (IRB #120-00744 approved 9 May 2020). Data were collected from direct chart review.

Pulmonary resection was defined as segmentectomy, lobectomy or pneumonectomy, and was performed for suspected or diagnosed NSCLC. All patients scheduled from 13 March 2020 onwards were re-evaluated by our existing multi-disciplinary thoracic oncology tumour board, in addition to a COVID-19 committee. All patients with suspicious pulmonary nodules or biopsy-proven NSCLC who presented during this time underwent a similar screening process.

Coronavirus disease 2019 review process

The multi-disciplinary thoracic oncology tumour board is held weekly. It comprised physicians from thoracic surgery, medical oncology, radiation oncology, pulmonary medicine, interventional pulmonology, radiology and pathology. The COVID-19 committee included 3 members of the tumour board (2 thoracic surgeons and a medical oncologist) who gave the final approval to all patients before undergoing surgery during the crisis.

Factors taken into consideration regarding surgical resection versus watchful waiting with serial computed tomography (CT) scans or further staging with endobronchial ultrasound lymph node biopsy included: patient/tumour factors, institutional resources and expected postoperative course. Patient and tumour factors included: tumour size, tumour appearance on CT (i.e. solid, sub-solid or ground-glass opacity), rate of growth, maximum standardized uptake values (SUV_{max}) on positron emission tomography (PET) scan, clinical-stage by CT and PET, pulmonary function test (PFT), patient comorbidities and functional status and prognosis and/or stage migration with surgical delay, all of which combined to evaluate the likelihood of tumour progression or loss of surgical candidacy versus undergoing resection sooner for each patient. High-risk features considered for resection were a solid nodule component > 2 cm, a SUV_{max} ≥ 2.5, or change in short-interval imaging due to concern for progression of disease if care was delayed. Patients with slow-growing tumours, such as carcinoid, those who refused surgery or patients with COVID-19 were deferred. Other considerations included whether a patient was enrolled in an IRB approved industry or academic-based neoadjuvant trial with strict criteria when the resection was to be performed. All patients obtained PFTs before

surgical resection. Patients who did not meet these criteria were evaluated for stereotactic body radiation therapy versus short-interval CT scan, and, if PFTs had not previously been performed, PFTs were deferred.

Institutional resources consisted of the number of hospitalized COVID-19 patients and the availability of anaesthesiologists, operating rooms, operating room staff, anaesthesia machines, number of non-COVID-19 patient beds, readiness of PPE (face shields, N-95 masks, gloves and gowns) and availability of COVID-19 tests for patients before surgery. Expected postoperative course factors considered were expected length of stay, the likelihood of postoperative respiratory failure requiring mechanical ventilation, the potential need for ICU care versus floor care and the hospital capacity at that time point.

Perioperative care

All patients underwent testing for COVID-19 within a 24-h period before undergoing surgery. COVID-19 was performed using a nasal pharyngeal swab for reverse transcriptase-polymerase chain reaction (rtPCR) assay. If the preoperative COVID-19 test was positive, the patient's operation was rescheduled 2 weeks later and retested. During the interim 2 weeks, the patients self-quarantined at home. If the retest was positive, surgery was delayed another 2 weeks. Patients underwent pulmonary resection only after obtaining a negative COVID-19 test.

Despite the negative PCR test preoperatively, all patients were treated with the same PPE precautions used for COVID-19 positive patients. PPE in the operating room consisted of a hair cover, N-95 mask, eye protection, non-sterile gown and gloves throughout the entirety of the procedure. While the operating rooms could be converted to negative pressure for any patient with COVID-19 or had unknown COVID-19 status, all patients who underwent resection were negative for COVID-19, so ventilation changes were made. However, during intubation, non-anaesthesia personnel were asked to wait outside the operating room. Once intubated, bronchoscopy was performed to position the double-lumen tube. Standard intraoperative sterile PPE was used for the operation. All operating room staff who cared for patients were COVID-19 negative by testing, with only essential staff workers present. Patients were admitted to a dedicated non-COVID-19 floor or ICU postoperatively. Standard postoperative care regarding chest tube management, pain management and discharge criteria was provided [8].

Evaluation of outcomes

The primary outcome of this study was the safety of patients and providers, defined as no development of COVID-19 symptoms, such as fever, cough, shortness of breath, chills, myalgia, diarrhoea and headaches, or change from negative to positive rtPCR test, and no major morbidity and mortality for patients. All patients were screened for COVID-19 symptoms and fevers daily throughout the hospital stay, monitored for symptoms and fevers at home, and screened again during follow-up visits. Providers were screened for COVID-19 symptoms, and all underwent rtPCR testing on a monthly basis. The follow-up time was defined as the date of surgery to the date of data collection (6 May 2020). Morbidity was evaluated based on the Clavien–Dindo classification, with minor morbidity defined as grade I–III and major morbidity defined as grade IV [9].

RESULTS

Patients evaluated for surgical resection for non-small-cell lung cancer

From 13 March 2020 to 4 May 2020, 2087 patients with a positive rtPCR test for COVID-19 were admitted to our Manhattan Tisch Hospital, with a median daily census of 299 patients (80% of hospital capacity) (Figure 1). During this period, 45 patients were evaluated for surgical resection for suspected or biopsy-proven NSCLC. After review by the multi-disciplinary thoracic oncology tumour board and the COVID-19 committee, 21 patients (47%) underwent pulmonary resection for suspected or diagnosed NSCLC and the remaining 24 (53%) patients have been deferred for surgical resection at a later date.

Pulmonary resection for suspected or biopsy-proven non-small-cell lung cancer

Characteristics. All of the 21 patients who underwent pulmonary resection for suspected or biopsy-proven NSCLC had solid or predominantly solid nodules (Table 1). Eleven patients had a $SUV_{max} \geq 2.5$, and 3 patients had a biopsy-proven adenocarcinoma. The remaining 7 patients had short-interval growth or change in the lung nodule. Two of the 21 patients underwent neoadjuvant treatment, one of whom was enrolled in a clinical trial. The median maximum tumour diameter was 1.9 cm [interquartile range (IQR) 1.5–4 cm] with a median SUV_{max} 4.6 (IQR 2–9.3).

Twenty patients (95%) were COVID-19 negative on their first test before surgery. One patient (5%) was asymptomatic but tested COVID-19 positive at the time of this scheduled surgery. This case was delayed for 2 weeks, during which time he remained asymptomatic. The patient retested negative for

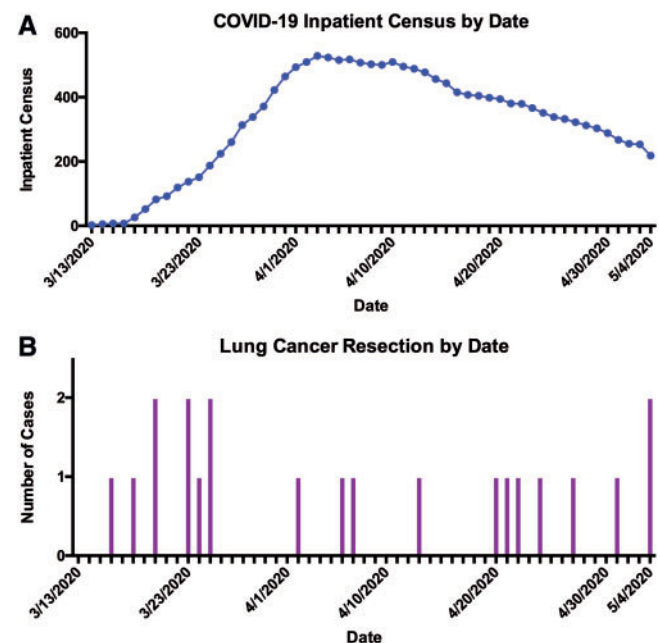


Figure 1: Daily census of patients with COVID-19 and number of lung cancer resections by date. Graph demonstrating daily census of inpatient hospitalizations (A) and daily number of lung cancer resections (B) at New York University Langone Health Manhattan campus from 13 March to 4 May 2020. COVID-19: coronavirus disease 2019.

Table 1: Characteristics of patients evaluated for pulmonary resection for suspected or biopsy-proven lung cancer

	Patients undergoing pulmonary resection (n = 21)	Patients with deferred resection (n = 24)
Gender, n (%)		
Male	7 (33)	13 (54)
Female	14 (67)	11 (46)
Age (years), median (IQR)	72 (68–78)	68 (65–75)
BMI (kg/m ²), median (IQR)	26 (23–30)	26 (24–29)
Comorbidities, n (%)		
Chronic kidney disease	1 (5)	0 (0)
Congestive heart failure	1 (5)	4 (17)
COPD	5 (24)	6 (25)
Coronary artery disease	4 (19)	6 (25)
Diabetes	2 (9.5)	9 (38)
Hypertension	14 (67)	17 (71)
Stroke	1 (5)	3 (13)
Total with any comorbidity, n (%)	15 (71)	21 (88)
Tumour maximum dimension on imaging (cm), median (IQR)	1.9 (1.5–4)	1.3 (0.9–1.7)
Tumour SUV _{max} , median (IQR)	4.6 (2–9.3)	1.9 (1.5–2.9)
Tumour characteristic, n (%)		
Solid	17 (81)	12 (50)
Part solid	4 (19)	10 (42)
Pure ground-glass opacity	0 (0)	2 (8)
Biopsy-proven malignancy including carcinoid, n (%)	7 (33)	3 (13)
Pulmonary function tests, median (IQR), % of expected		
Preoperative FEV ₁	84 (73–95)	92 (82–105.3)
Preoperative DLCO	88 (77–93)	80.5 (73.8–105.3)
Smoking history, n (%)		
Never smoker	5 (24)	8 (33)
Former smoker <10 pack-years	5 (24)	3 (12.5)
Former smoker ≥10 pack-years	11 (52)	10 (42)
Current smoker	0 (0)	3 (12.5)
Length of smoking history (pack-year), median (IQR)	30 (10–40)	30 (13–48)

BMI: body mass index; COPD: chronic obstructive pulmonary disease; DLCO: diffusing capacity of lung for carbon monoxide; FEV₁: forced expiratory volume over 1 s; IQR: interquartile range; SUV_{max}: maximum standardized uptake values.

COVID-19 and the pulmonary resection was performed. All operative procedures were performed in a minimally invasive fashion, with 17 robotic procedures (81%) and 4 video-assisted thoracoscopic surgical (VATS) procedures (19%). The choice for robotic versus VATS resection was based on surgeons' preference for routine pulmonary resections. Operative procedures consisted of 6 segmentectomies (29%), 10 lobectomies (48%), 3 completion lobectomies (14%) and 2 pneumonectomies (9%).

Evaluation of outcomes. The surgical outcomes are shown in Table 2. To date, there have been no major morbidities and mortalities (0%), with a median follow-up of 30 days (IQR 14–44). All operations were started and completed minimally invasively, with no conversions and a median blood loss of 20 ml per case. There were 5 minor complications, with 3 grade I and 2 grade III complications. No patients have developed COVID-19 symptoms. Two patients had a planned postoperative ICU admission, both of whom underwent pneumonectomy and stayed in the ICU for 2 days. No unplanned postoperative ICU admissions or ventilator requirements occurred. The median hospital stay was 2 days (IQR 1–3).

Deferred resection for suspected or biopsy-proven non-small-cell lung cancer

There were 24 patients who had their operations deferred. Their characteristics are shown in Table 1. Of the 24 patients, 6 (25%)

had pure ground-glass opacities or sub-solid nodules with a sub-centimetre solid component. Twelve patients (50%) had nodules smaller than 2 cm with no PET avidity or SUV_{max} <2.5. One patient (4%) had a 2.9-cm nodule that was biopsy-proven carcinoid. Three patients (13%) with no tissue diagnosis had a maximum tumour diameter of ≥2 cm with an elevated SUV_{max} but refused to come to the hospital for surgical resection. The remaining 2 patients (8%) tested COVID-19 positive, with 1 patient remaining symptomatic to date and the other died from COVID-19 related respiratory failure before re-scheduling surgery.

The median age was 68 years (IQR 65–75). The median maximum tumour diameter was 1.3 cm (IQR 0.8–1.7 cm) with a median SUV_{max} 1.9 (IQR 1.5–2.9). All deferred patients are either undergoing a short-interval follow-up CT scan or being re-evaluated for surgical resection. No patients have elected to receive SBRT or other local therapy. None of the 24 deferred patients were candidates for neo-adjuvant therapy or trials. Of the deferred patients who have since undergone a repeat chest CT scans or undergone resection after COVID-19 improved, there was only one patient who progressed, from clinical IIB (T3N0) to pathological IIIA (T4N0), and this delay in resection was due to patient preference. Of the remaining patients, 1 had pathological N1 disease that was not detected clinically.

Evaluation of healthcare provider safety

Three thoracic surgeons, 3 physician assistants and 3 thoracic anaesthesiologists performed all pulmonary resections for

Table 2: Characteristics and outcomes of pulmonary resections

	Patients undergoing pulmonary resection for lung cancer (n = 21)
Duration of follow-up (days), median (IQR)	30 (14–44)
Hospital length of stay (days), median (IQR)	2 (1–3)
Chest tube duration (days), median (IQR)	2 (0.8–3.3)
Patients requiring ICU, n (%)	2 (9.5)
Underwent neoadjuvant treatment, n (%)	2 (9.5)
Redo operation, n (%)	4 (19)
Type of resection, n (%)	
Segmentectomy	6 (29)
Lobectomy	13 (62)
Pneumonectomy	2 (9.5)
Estimated blood loss (ml), median (IQR)	20 (15–100)
Number of lymph nodes removed, median (IQR)	24 (19–28)
Number of lymph node stations sampled, median (IQR)	6 (5–7)
NSCLC pathological stage, ^a n (%)	
Not malignant	1 (5)
Pathology pending	3 (14)
Stage IA	9 (43)
Stage IB	1 (5)
Stage IIA	2 (9.5)
Stage IIB	1 (5)
Stage IIIA	2 (9.5)
Stage IIIB	0 (0)
Stage IIIC	0 (0)
Stage IV	2 (9.5)
Complications (Clavien–Dindo classification), n (%)	
Grade I	3 (14)
Grade II	0 (0)
Grade III	2 (9.5)
Grade IV	0 (0)
Grade V	0 (0)
Readmission rate, n (%)	0 (0)
Converted to COVID-19, n (%)	0 (0)
Developed COVID-19 symptoms, n (%)	0 (0)
Mortality, n (%)	0 (0)

^aPathological stage as defined by the 8th edition lung cancer staging [7].

COVID-19: coronavirus disease 2019; ICU: intensive care unit; IQR: inter-quartile range; NSCLC: non-small-cell lung cancer.

malignancy during this time frame. To date, none of the 9 team members have developed any symptoms, and all have tested negative by COVID-19 rtPCR testing. Providers have been rescreened every month. All other operating room personnel were present on a rotating basis, with no known conversions to COVID-19 in their routine testing. Besides, temperatures of all operating room staff were checked before entry to the operating area. Of note, 2 surgeons had daily exposure to COVID-19 positive patients by performing bronchoscopies or rounding in the ICU. Operations were performed by surgeons on non-COVID-19 patients before any procedures or before rounding on positive COVID-19 patients.

DISCUSSION

While the number of new COVID-19 cases in New York City has finally peaked, COVID-19 continues to impact healthcare provider decisions regarding the care of other non-COVID-19

patients. Since COVID-19 was declared a pandemic, our institution has seen a 37% decrease in the presentation of strokes in our emergency services. Across the USA, high volume cardiac catheterization centres had noted a 38% decrease in ST-elevation myocardial infarction activations, likely secondary to patients avoiding medical care due to concerns of COVID-19 transmission [10]. In addition to patient concern, physicians are also worried about the safety of their patients contracting COVID-19 in the hospital, as well as their personal risk of exposure at work. Given the apprehension of patient exposure to COVID-19, data examining the safety of performing pulmonary resections are necessary to assess the risk for patients.

Little data are reported on the safety of performing surgery amidst the COVID-19 pandemic. Data from Iran on 4 patients with non-thoracic surgery who contracted COVID-19 in the perioperative period resulted in a high fatality rate of 75% [11]. Cai *et al.* [7] demonstrated that 7 patients tested positive for COVID-19 after lung resection, with a 43% mortality rate, while Li *et al.* [12] had 25 patients with COVID-19 after thoracic surgery with a 20% mortality rate. Only one published report from an institution in Italy evaluated the safety of surgery during COVID-19, performing 71 lung resections with no reported COVID-19 postoperative conversion [13], however, no details regarding any other outcomes, any selection criteria, hospital census or overall policy was elucidated.

Our findings show the feasibility and safety of performing surgical resection for lung cancer at a hospital with a high census of COVID-19 patients (80% capacity) that is located in the epicentre of the crisis. Twenty-one patients with biopsy-proven non-carcinoid NSCLC or high suspicion for lung cancer underwent resection, compared to 89 pulmonary resections performed in the same period in 2019. Patients had no major postoperative complications or mortality, and no patient or provider contracted COVID-19. All procedures were performed using a minimally invasive approach with a short median hospital stay.

Factors that may have led to our results included our existing culture of safety, availability of PPE at all times, COVID-19 testing for all providers, daily temperature and symptom checks on all operating room staff to supplement the PCR testing, provision of N-95 masks to all personnel, limiting staff members in the operating room during intubation, using minimally invasive techniques, and postoperative management in dedicated 'non-COVID-19' areas. For patient and provider safety, it was important that we had the capacity to swab every surgical candidate for rtPCR testing the day before or the morning of the scheduled operation and tested all hospital employees in various phases. This ability to test was imperative to optimize patient outcomes by operating when they are COVID-19 negative, as well as to decrease hospital workers' exposure to COVID-19. We prioritized resections to patients with higher risk features (solid nodule component > 2 cm, an SUV_{max} ≥ 2.5 or change on short-interval imaging) associated with a greater rate of malignancy and disease progression [14, 15]. The only exceptions for deferred cases were biopsy-proven carcinoid, which is slow-growing cancer with a low likelihood of metastasis [16], those that refused surgical resection, and the 2 patients that tested positive for COVID-19. The remainder of the patients elected to be followed up with short-interval CT scans and planned surgical resection in the near future, as opposed to treatment with SBRT.

This study is significant as it had the largest reported number of patients undergoing pulmonary resection for lung cancer in the USA at a hospital with a high COVID-19 census. Providers cared for both COVID-19 patients and COVID-19-negative cancer patients. The results are encouraging since no patient

converted to COVID-19 or suffered a major complication, with zero mortality. These data are promising on a wider scale for other surgical procedures during this pandemic, as we demonstrated feasibility and safety in cancer patients undergoing lung resections. This group represents a high-risk patient population who are immunocompromised and underwent high-risk surgery. This study is limited by a selected group of patients who underwent surgery. While many groups have developed a scoring system [17], our institution used tumour board and a COVID-19 committee to evaluate all lung cancer patients for surgical resection, which is a subjective selection process. Additionally, only a small number of patients underwent resection with outcomes limited to early follow-up. However, this does not diminish from our primary early outcomes. As the COVID-19 pandemic continues to spread and concerns of a second surge loom, we must establish a safe strategy for lung cancer surgery that protects both patients and healthcare providers.

Conflict of interest: none declared.

Author contributions

Stephanie H. Chang: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Writing—original draft; Writing—review & editing. **Michael Zervos:** Conceptualization; Data curation; Methodology; Writing—review & editing. **Amie Kent:** Conceptualization; Formal analysis; Investigation; Methodology; Writing—original draft; Writing—review & editing. **Abraham Chachoua:** Conceptualization; Methodology; Writing—review & editing. **Costas Bizakis:** Conceptualization; Data curation; Methodology; Writing—review & editing. **Harvey Pass:** Conceptualization; Data curation; Methodology; Writing—review & editing. **Robert J. Cerfolio:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing—original draft; Writing—review & editing.

Reviewer information

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