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Safety of lung cancer surgery during COVID-19 in a pandemic epicenter

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ABSTRACT

Background: The influence of SARS-CoV-2 on surgery for non–small cell lung cancer needs to be understood to inform clinical decision making during and after the COVID-19 pandemic.

Objective: This study reports on the 90-day rate of infection as well as the morbidity and mortality of lung surgery for cancer in a tertiary care hospital located in a pandemic epicenter.

Methods: We conducted a retrospective review of a prospective database to identify consecutive patients who underwent lung cancer resection before (January 1, 2020–March 10, 2020, group 1; 57 patients) and during the COVID-19 pandemic (March 11, 2020–June 10, 2020, group 2; 41 patients). The primary end point was the occurrence of SARS-CoV-2 infection during the first 90-days after surgery. The secondary outcome measure was 90-day perioperative morbidity and mortality.

Results: Patient characteristics were not significantly different between the groups. Ninety-day COVID-19 infection rates was 7.3% (3 out of 41) for patients undergoing an operation during the pandemic and 3.5% (2 out of 57) in patients operated on immediately before the pandemic. All patients tested positive 10 to 62 days after the index surgical procedure following hospital discharge. Four COVID-19–positive patients were symptomatic and 4 out of 5 patients required hospitalization, were men, previous or current smokers with hyperlipidemia, and underwent a sublobar resection. Univariate analysis did not identify any differences in postoperative complications before or during the COVID-19 pandemic. Ninety-day mortality was 5% (2 out of 41) for lung cancer surgery performed during the pandemic, with all deaths occurring due to COVID-19, compared with 0% (0 out of 57) mortality in patients who underwent an operation before the pandemic.

Conclusions: During the COVID-19 pandemic, COVID-19 infections occurred in 7.3% of patients who underwent surgery for non–small cell lung cancer. In this series all infections occurred after hospital discharge. Our results suggest that COVID-19 infections occurring within 90 days of surgery portend a 40% mortality, warranting close postoperative surveillance. (J Thorac Cardiovasc Surg 2022;164:378-85)

During December of 2019, an outbreak of COVID-19 caused by SARS-CoV-2 started in Wuhan, China.1 On March 11, 2020, the World Health Organization officially declared COVID-19 a worldwide pandemic. In the United States, New York State emerged as the epicenter of the COVID-19 pandemic with the first confirmed diagnosis

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See Commentaries pages 386 and 387.

CENTRAL MESSAGE

Postoperative COVID-19 infection portends a higher mortality following lung resection. However, lung resection during the COVID-19 pandemic can be done safely with minimal risk of transmission.

PERSPECTIVE

Few studies evaluate lung cancer surgery during the COVID-19 pandemic. We compared short-term outcomes following lung resection during and before the pandemic. There was no difference in morbidity and the COVID-19 infection rate was low. All infections occurred after discharge with a 40% mortality rate. Postoperative COVID-19 precautions and surveillance are critical after lung resection.
on March 1, 2020. On March 7, 2020, a state of emergency was declared by the governor of New York after 89 new cases were reported. To date, New York City has accounted for more than 900,000 COVID-19 cases. During the first wave of the pandemic, the city represented more than 25% of COVID-19 cases in the United States. Due to the overwhelming surge of critically ill COVID-19 patients, governing bodies in New York State placed a moratorium on elective surgery to preserve hospital resources, such as ventilators, personal protective equipment, 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. ICUs filled to capacity and operating rooms were converted into critical care areas to accommodate the rapidly increasing COVID-19 patient population, one-third of whom required mechanical ventilation.

The American College of Surgeons set out guidelines to help physicians and hospitals prioritize patient selection for operative management. Retrospective series have demonstrated operative mortality rates as high as 20% to 50% in patients undergoing elective surgery during the pandemic. One unique subset of cancer patients who may be at higher risk is composed of those who require lung resection for non–small cell lung cancer (NSCLC). The risk to benefit ratio for these patients must be carefully weighed because contracting COVID-19 during the postoperative period confers a high likelihood of respiratory failure or death. There is little information on the perioperative outcomes of surgical resection for lung cancer during the COVID-19 pandemic. The objective of this study is to report the incidence and outcome of COVID-19 after surgical resection of lung cancer in New York City during the COVID-19 pandemic.

METHODS
We conducted a retrospective review of a prospectively assembled thoracic surgery database to identify patients undergoing surgical resection for lung cancer clinically staged as stage I to IIIA, with or without preoperative induction therapy, between January 1, 2020, and June 10, 2020. June 10, 2020, was chosen because it was the end of the first wave in New York (Figure 1). Patients were categorized into 2 groups, prepandemic and pandemic, to compare the surgical outcomes while significant reallocation of resources took place. Group 1 was defined as the patients undergoing an operation between January 1, 2020, and the day immediately before the start of the pandemic as defined by the World Health Organization to be March 11, 2020. Group 2 was defined as the pandemic period starting on March 11, 2020, through June 10, 2020, when COVID-19 cases in New York City had substantially decreased (Figure 1). Patients in group 2 were selected for surgical resection after review by an institutional review board charged with review and approval of all surgical procedures to facilitate appropriate allocation of resources. This study was approved by the Weill Cornell Medicine Institutional Review Board (protocol No. 20-08022559) and was deemed exempt from informed consent.

We identified 98 patients who met our inclusion criteria. The hospital records were reviewed for demographic and clinical characteristics, including age, sex, clinical stage, and use of neoadjuvant therapy. Performance status of all patients was graded according to Eastern Cooperative Oncology Group guidelines, and comorbidities were graded using the Charlson Comorbidity Index (CCI). Records were also reviewed for perioperative and relevant pathology data, including surgical approach, extent of resection, pathologic stage, and completeness of resection (ie, R status). As per our practice, appropriate margins were obtained and systematic sampling was defined in accordance with National Comprehensive Cancer Network guidelines as removal or sampling of at least 3 N2 stations. Adverse events were defined according to National Cancer Institute Common Terminology Criteria for Adverse Events during the first 90 days after surgery.

COVID-19 Testing
Due to limitations of testing capabilities before April 1, 2020, testing for SARS-CoV-2 was restricted to patients with symptoms suggestive of COVID-19. As of April 1, 2020, testing logistics were adequate and were required as part of preadmission testing on all subsequent patients regardless of symptom profile. Surgery was delayed for any patient testing positive during preadmission testing. Any patient testing positive during admission was immediately transferred to a COVID-19 ICU within the hospital.

Perioperative Care
Thoracic surgery patients were relocated into a newly created space that had previously functioned as a postanesthesia care unit and was designated a COVID–19-negative area. This 18-bed unit consisting of 16 open beds and 2 negative pressure rooms was selected due to proximity to operating suites and accessibility. The unit accepted patients with non–COVID–19-related medical or surgical critical illnesses. Following surgery, all patients recovered in the newly formed COVID–19-negative ICU space. Given limited availability of resources early during the pandemic, repeat testing was only performed for any patient who developed symptoms of fever, chest pain, increasing oxygen requirement, or high clinical suspicion for COVID–19. Patients remained in the COVID–19–negative unit until the time of discharge with efforts made to discharge patients home rather than other medical facilities in an effort to limit potential exposure at alternative facilities.

Follow-up
After hospital discharge, patients were evaluated at 2-week intervals for the first 3 months, then every month. In lieu of office-based follow-up appointments, virtual patient visits were conducted with in-office visits limited to patients requiring physical presence such as wound issues or other complaints unable to be satisfactorily evaluated remotely. COVID–19-specific symptom evaluations (eg, fever and hypoxia) were conducted on every patient postoperatively. Postdischarge COVID–19 testing was performed in any patient with respiratory symptoms and possible COVID–19 exposure. Other studies, such as computed tomography scanning, were done only if clinically indicated. All data were collected, entered into a prospective database, and updated at regular intervals until the patient’s final follow-up or death.

End Points
The primary end point was the incidence of polymerase chain reaction–proven postoperative COVID–19 during the first 90 days after surgery. Secondary end points included the incidence of postoperative adverse events or deaths during the first 90 days after surgery (ie, 90-day mortality).

Abbreviations and Acronyms

| Abbreviation | Definition |
|--------------|------------|
| CCI          | Charlson Comorbidity Index |
| ICU          | intensive care unit |
| NSCLC        | non–small cell lung cancer |
Statistical Analysis

Descriptive statistics (including frequency, percent, median, and interquartile range) are presented for basic demographic, clinical, and pathologic characteristics. Variables of interest were examined by the \( \chi^2 \) test or Fisher exact test for categorical variables and Mann-Whitney \( U \) test for continuous variables. All analyses were performed in IBM SPSS statistics version 27 (IBM-SPSS Inc).

RESULTS

Clinicopathologic Characteristics

There were 57 patients in group 1 and 41 patients in group 2. Demographic and clinical variables, including preoperative comorbidities are shown in Table 1. The majority was white, aged 70 years (range, 44-88 years), and women with early-stage adenocarcinoma. There were no major differences in comorbidities between group 1 and group 2 except for a higher incidence of hypertension in group 2 (\( P = .008 \)). There was no difference between the 2 groups in clinical stage distribution, utilization of neoadjuvant therapy, or final pathologic stage distribution. Resection was accomplished with minimally invasive approaches (robotic or video-assisted thoracoscopic surgery) in 95% of patients in both groups (Table 2). Lobar resections were performed in 62% of patients and an R0 resection was accomplished in all but 1 patient, occurring in group 1. There was no difference in major complications between the 2 groups (Table 3). Three of the 4 reoperations were due to bleeding, with 1 patient requiring reoperation for postoperative air leak. Overall readmission rates were not statistically different between groups (\( P = .541 \)) (Table 2). There were no in-hospital deaths in either group. Average length of stay was 4 days (range, 2-22 days).

Postoperative Complications and Incidence of COVID-19 Infection

The 90-day COVID-19 infection rate for all patients was 5.1%. Postoperative 90-day COVID-19 infection rates between the prepandemic and pandemic groups were not

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FIGURE 1. The number of COVID-19 cases in New York City between January and June 2020, capturing the peak number of cases in the epicenter. Time frames for prepandemic and pandemic study groups are displayed. Patients who were infected with COVID-19 postoperatively are represented by pins (filled circles) indicating the date of surgery. Corresponding colored arrowheads depict the date each patient tested positive for COVID-19 during the postoperative period with positive test date ranging from 10 to 62 days postoperatively. COVID-19, Coronavirus Disease 2019; SARS-CoV-2, severe acute respiratory syndrome–related coronavirus-2.
statistically different, but more than doubled for patients operated on during the pandemic (group 1, 3.5% [2 out of 57]; group 2, 7.3% [3 out of 41]; P = .398) (Table 2). Four COVID-19–positive patients were symptomatic and 1 was identified through routine exposure testing. No patient had known intrahospital exposure or developed symptoms during the index surgical hospitalization so were not tested before discharge. Subsequently all patients who tested positive did so after discharge from the index surgery. Four out of 5 patients infected with COVID-19 postoperatively required hospitalization. Two of the COVID-19–positive patients died. Univariate analysis did not identify any differences in postoperative complications or factors predictive of COVID-19 infection (Table 3). Four out of 5 patients who tested positive for COVID-19 following lung resection were men, previous or current smokers with hyperlipidemia, and underwent a sublobar resection. All were older than age 65 years with the average age being 72 years (range, 66-76 years) (Table 4). CCI was calculated for patients who tested positive for COVID-19 following lung resection and was not predictive of mortality. Three patients had a CCI of 5, 1 had CCI of 6, and 1 had CCI of 10. The patients who died of COVID-19 had CCI of 5 and 10. No patient who later developed COVID-19 displayed respiratory symptoms or fever requiring testing during the index hospitalization (Table 4). Two patients that tested positive for SARS-CoV-2 died within 30 days of surgery, 3 out of 5 patients who tested positive after 30 days fully recovered at last follow-up and did not require long-term treatment for COVID-19 infection.
DISCUSSION

There is a paucity of studies investigating the perioperative outcomes after resection for lung cancer during the COVID-19 pandemic. Retrospective studies reported COVID-19 infection mortality rates in patients with lung cancer upward of 50% even without resection. Additiona-ly, this vulnerable group is at risk of SARS-CoV-2 exposure in hospital and might be particularly susceptible to subsequent pulmonary complications, due to the proinflam-matory cytokine and immunosuppressive responses to surgery and mechanical ventilation. With this in mind, few if any studies have evaluated the incidence of SARS-CoV-2 infections and 90-day outcomes in patients who underwent lung resection for cancer in the United States. In this study, we report on the frequency of postoperative COVID-19 infection and mortality associated with infection in patients undergoing lung resection during the first wave of the pandemic, as well as postoperative morbidity. A brief overview of this study was presented at the 2021 American Association for Thoracic Surgery meeting and is available in Video 1. As a comparator control group, we selected patients who had surgery for lung cancer immediately before the pandemic assuming that they would have similar demographic and preoperative comorbidities to those undergoing operation during the pandemic lockdown. During the lockdown period, like most institutions we experienced a significant decrease in surgical volume in part due to patient-related factors like decreased screening but also due to departmental case selection criteria that placed precedence on resecting nonground glass lesions. Both factors contributed to the observed decrease in surgical volume in addition to the systemic limitations placed on surgical case volume.

Despite the fact that the COVID-19 community infection estimates in New York City were above 20%, our postoperative infection rate was slightly more than 5%. These results are likely the result of strict perioperative cohorting of all postoperative patients in a COVID-19–free unit staffed by nurses and physicians who did not rotate through units caring for COVID-19–positive patients. Most prior studies reported infection rates within 30 days after surgery. In France, Leclère and colleagues performed a retrospective analysis of 115 patients to study the rate of COVID-19 infection following surgery for NSCLC resection during the first 30 days. They reported a 30-day COVID-19 infection rate of 5% and a small, but significant increase in hospital readmissions and no increase in 30-day mortality among COVID-19–positive patients. These good results are comparable to those reported in the current report. Notably, the community infection rate in Paris was significantly lower than in New York City (4%-9% vs 20%, respectively) and importantly, in this report, postdischarge COVID-19 infection was not systematically evaluated beyond 30 days. Chang and colleagues published a retrospective review of 21 patients who underwent resection for confirmed or suspected pulmonary malignancy during a similar time period in New York City. In their study, patients were screened for COVID-19 preoperatively. There was no postoperative COVID-19 infections within a median follow-up of 30 days. These impressive results are in line with our own low 30-day infection rate, and underscore the importance of preoperative testing.

| Complication          | Preop (n = 57) | Pandemic (n = 41) | P value |
|-----------------------|---------------|------------------|---------|
| Reoperation           | 1 (2)         | 3 (7)            | .170    |
| Air leak              | 4 (7)         | 2 (5)            | .663    |
| Pneumothorax          | 7 (12)        | 2 (5)            | .211    |
| Chyle leak            | 1 (2)         | 0 (0)            | .394    |
| Pleural effusion      | 2 (3)         | 4 (10)           | .203    |
| Pulmonary embolism    | 1 (2)         | 0 (0)            | .394    |
| New-onset arrhythmia  | 4 (7)         | 3 (7)            | .955    |
| Acute kidney injury   | 4 (7)         | 1 (2)            | .310    |
| Deep wound infection  | 0 (0)         | 1 (2)            | .236    |
| Respiratory failure   | 1 (2)         | 0 (0)            | .394    |
| Ileus                 | 1 (2)         | 1 (2)            | .813    |

Values are presented as n (%).

| Patient ID | Age (y) | Sex | Preoperative screening | CCI | Surgery | Cell type | Stage | LOS | POD detected | Outcome      |
|------------|---------|-----|------------------------|-----|---------|-----------|-------|-----|---------------|--------------|
| 1          | 66      | Male| No                     | 6   | Sublobar resection | Adenocarcinoma | IIB   | 3   | 62            | Recovered    |
| 2          | 72      | Male| No                     | 5   | Lobectomy        | Adenocarcinoma | IB    | 7   | 32            | Recovered    |
| 3          | 70      | Male| No                     | 5   | Sublobar resection | Adenocarcinoma | IA    | 2   | 13            | Died POD24   |
| 4          | 76      | Male| No                     | 10  | Sublobar resection | Adenocarcinoma | IA    | 3   | 10            | Died POD53   |
| 5          | 75      | Female| Yes                  | 5   | Sublobar resection | Adenocarcinoma | IA    | 4   | 18            | Recovered    |
Our data also suggest that the risk of postoperative COVID-19–related deaths may be higher within 30 days. The overall postoperative COVID-19 mortality in our series was 40% (2 out of 5) similar to that reported by Cai and colleagues. In the study conducted in Wuhan, postoperative COVID-19 infection was associated with mortality of 42.8%. Both patients who died tested positive within 30 days postoperatively, which suggests that the postoperative period may be a critical time of exposure that likely requires routine COVID-19 testing. This high mortality underscores the importance of continued efforts to identify risk factors associated with morbidity and mortality of COVID-19 to risk-stratify surgical patients preoperatively. It is possible that patients with lung cancer in general are at risk for COVID-19 infection regardless of surgery. A study from Spain by Rogado and colleagues demonstrated that COVID-19 mortality was greater for patients with lung cancer (9 out of 17 [52.3%]) than patients who were admitted for COVID-19 without lung cancer (192 out of 1878 [10%]; P < .0001). A New York study identified 69 consecutive outpatients with lung cancer who were diagnosed with COVID-19, of those 42 patients (62%) required hospitalization and 16 patients died. Therefore, the mortality seen in our cohort may have occurred independent of surgical resection. This is an important point given that a delay in resection is independently associated with increased rates of upstaging and decreased median survival for patients with clinical stage I NSCLC.

Recently, an international consortium of thoracic surgeons published guidelines for the safe resumption of surgery during the COVID-19 pandemic. The authors recommended continuation of elective surgical procedures whenever possible based on institutional triggers for scaling volume up or down depending on COVID-19 admission status, triaging of cases as driven by a multidisciplinary team, preoperative screening of all patients for infection with SARS-CoV-2 and the utilization of virtual care for postdischarge follow-up. Additionally, the Society of Thoracic Surgeons COVID-19 Task Force recently released a guidance statement for increasing the delivery of surgery. The authors advocate for continuing to address urgent and emergency surgeries with a graded increase in elective case volume. Furthermore, the task force recommends routine testing via nasopharyngeal swab, and delaying of any confirmed or suspected COVID-19–positive case by at least 2 weeks when feasible. Other collaborative statements and our own institutional data have echoed these recommendations. In addition, more than 95% of our resections were performed minimally invasively. The resulting short hospital stay and minimal complications may have made an influence on our 0 hospital-acquired infections and should be noted when choosing the appropriate patients. Guidelines for surgery during possible future waves of COVID-19 variants in vaccinated patients are undetermined. Although our sample size is low, our results highlighting an increased mortality rate with infection justifies that all patients should be tested before operation regardless of vaccination status and that precaution of community spread postoperatively will still be critical for safe surgery. Additionally, postsurgical patients regardless of vaccination status should maintain strict adherence to mask wearing and social distancing given the risks associated with exposure during this period in such a high-risk patient population. We hope that our experience may lend confidence to the idea that lung cancer surgery can be safely and effectively performed using adequate planning and adherence to protocols with specific focus on postoperative surveillance.

Limitations of this study include the small sample size and insufficient means of preoperative testing during the early phases of the pandemic and absence of systematic screening of asymptomatic patients postoperatively. Our results may have not been possible without the extensive hospital resources dedicated to continuation of elective surgery during the lockdown period. Similar results may not be achievable in institutions with more limited resources.

Webcast
You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/21%20AM/AM21_TH07/AM21_TH07_2%20-%20Dr%20Villena%20and%20Discuss%20-%20V2.mp4.
Conflict of Interest Statement
Dr Altorki has ownership interest in Angiocire Biosoence and Viewpoint Medical and conducts supported research for AstraZeneca and Roche/Genentech. Dr Port has ownership interest in Angiocire Biosoence, TMRW, and Viewpoint Medical. Dr Stiles receives consulting fees/honoraria from AstraZeneca, BMS, Pfizer, Genentech, Ribon Therapeutics, Gala Therapeutics, Flame Biosciences, and Lung Cancer Research Foundation. All other authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: lung cancer, coronavirus, COVID, thoracic surgery, resection

Discussion
Presenter: Dr Jonathan Villena-Vargas

Dr Michael Zervos (New York, NY). Hello, my name is Mike Zervos and I’m a thoracic surgeon. I work out of NYU Langone in midtown Manhattan. I have the distinct pleasure of knowing Jonathan and working closely with him. Our institutions are just a few blocks away. Jonathan’s a little further uptown, but we were both placed in an unusual circumstance during the whole pandemic, and we as institutions and surgeons needed to figure out how we were going to actually take care of some of our non–COVID-19 patients, and more specifically our lung cancer patients. Jonathan, great job on that presentation. I think it was a really good job and thank you for that contribution. As an institution, we actually looked at our own data during that time, so we had similar outcomes and similar conclusions. I have a couple questions for Jonathan.

First, do you think your surgical approach had something to do with the fact that you were able to streamline these patients and get them through the hospitalization without infection?

Dr Jonathan Villena-Vargas (New York, NY). Thank you, Dr Zervos. I absolutely think that doing the surgery minimally invasively and getting these patients out with a minimum operative stay of 3 to 4 days was a big factor in being able to do this safely. The patients did not have to linger around, and we had one of the cleanest and general intensive care unit where patients from cardiac and thoracic would be and where the only patients that went in there were COVID-19 negative, and the only providers were providers that didn’t deal with COVID-19. Therefore, having a patient come in and out in 3 to 4 days and not lolling around but going home and being protected absolutely had an impact.

Dr Zervos. I think that these are all very important points. And honestly, there are a lot of precautions that we needed to take. I think it’s especially risky to perform
thoracic surgery and it’s even riskier to have to do it during a pandemic. A lot of the things that were very important were doing the polymerase chain reaction testing the day of the surgery, or even the day before. We had actually instituted a committee that would approve the surgeries during that time, which I thought was very helpful.

And then we made sure that our staff were all properly protected with the personal protective equipment that they needed, limited the traffic in and out of the rooms, and did a very similar thing where we maintained a COVID-19 safe zone through the hospital, so we were able to do a fair amount of this surgery and get them through. I think doing these surgeries minimally invasively, whether you’re doing them thoracoscopically or robotically doesn’t really matter as long as you’re doing it in a way that can get the patients through easily. The bottom line is—and I want to conclude with this statement—none of the patients actually acquired COVID-19 in the hospital while they got their surgery. This is a community acquired, infectious disease and these patients all got COVID-19 after they left the hospital.

We didn’t have any of those patients, but regardless the bottom line is that there is absolutely no reason for people to defer their care. I know people were not getting their cardiac catheterization procedures, they were not getting their colonoscopies, they were not getting their mammograms and screenings done because everyone was scared. And these data, your data and ours, prove that it’s actually safe to do that. I think that’s the bottom line and our conclusion is that it is important not to delay your care and that if you do need care, that it is safe to happen during this time.

Dr Villena-Vargas. Completely agree. Thank you, Dr Zervos.