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Clinical features and prognosis of patients with COVID-19 after lung surgery: A retrospective clinical study

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Abstract

Aim: To evaluate whether the history of lung surgery in patients was associated with poor prognosis of coronavirus disease 2019 (COVID-19).

Methods: Clinical data of patients with COVID-19 in a single-center were retrospectively analyzed. Patients with and without lung surgery were matched in 1:4 ratio to compare the differences in clinical characteristics, laboratory results, computed tomography findings, treatment regimens, and prognosis between them.

Results: Four patients had a history of lung surgery. The time from surgery to COVID-19 onset ranged from 3 to 10 days, with a median of 6.75 days. The mortality rate in the surgical group was higher than that in the nonsurgical group (25.0% vs. 6.3%).

Conclusion: Patients contracting COVID-19 after lung surgery presented a higher death rate; hence, it is necessary to omit lung surgery in patients with active COVID-19 infection.

KEYWORDS
coronavirus disease 2019, immunosuppression, lung cancer, lung function, lung surgery

1 | INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) declared the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) outbreak as a pandemic.[1] Patients infected with SARS-CoV-2 may develop coronavirus disease 2019 (COVID-19), and about 15.9-29% of them develop acute respiratory distress syndrome (ARDS) in a short period of time characterized by respiratory distress, hypoxemia, shock, or other organ failure, and even respiratory failure.[2–4] After lung surgery, patients inevitably suffer from lung function loss that cannot be restored to normal levels for a long time.[5–7] Commonly, most patients undergo lung surgery for lung cancer. Cancer patients are susceptible to SARS-CoV-2 and have worse prognosis than the general population.[8] The clinical features and prognosis of COVID-19 in this particular population have been mentioned only in a few articles.[9–11] We summarized the clinical features and prognosis of patients with COVID-19 after lung surgery at a single center.

2 | METHODS

A retrospective analysis was performed in the isolation critical care wards at Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Wuhan, China, from January 28, 2020 to March 25, 2020. Management of these patients was conducted by physicians from the National Medical Rescue Team of China. This study enrolled 257 patients with COVID-19. The diagnosis of COVID-19 was confirmed by reverse transcription polymerase chain reaction or serological tests. Patients who needed dialysis for renal failure, took immunosuppressive drugs after kidney transplantation, had malignant tumors other than lung cancer, had other diseases that could affect the prognosis and outcome, as well as those with incomplete clinical information were excluded. Among the included patients, four patients had undergone lung surgery within two weeks. According to sex, age, and complications, such as hypertension, diabetes, and coronary heart disease, 16 patients were included in the analysis by 1:4 case-control

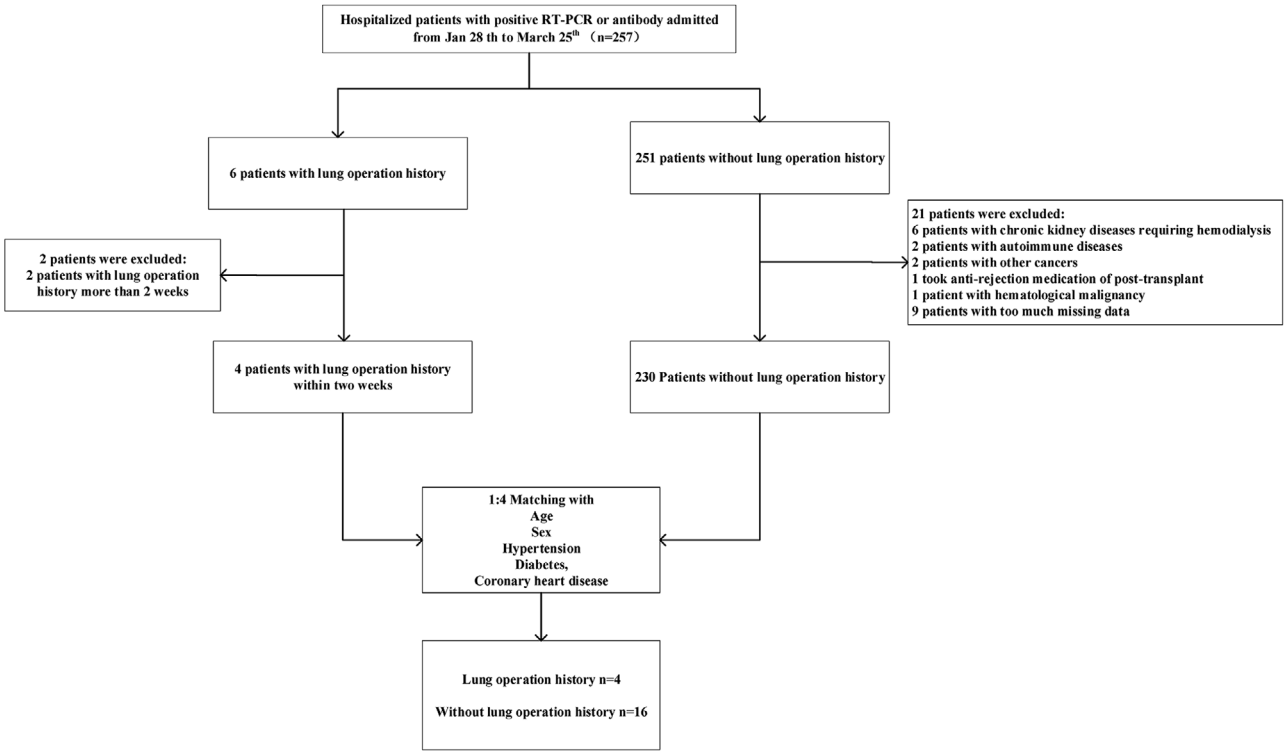

FIGURE 1 Research flow chart

matching in nonsurgical groups. The research flow chart is shown in Figure 1.

Descriptive data were expressed as mean (standard deviation) or median (interquartile range) of the continuous variables and number (%) for the categorical variables. We used the two-sample *t*-test or the Mann-Whitney *U* test to assess the differences between the two groups depending on the parametric or nonparametric data of the continuous variables, and the Fisher's exact test for the taxonomic variables. A *P*-value < .05 was considered statistically significant. The statistical analysis was performed using software Prism 7 (GraphPad Software, La Jolla, CA) or SPSS (Statistical Package for the Social Sciences) version 25.0 software (SPSS Inc). This study was approved by the Ethics Committee of Peking University Third Hospital (irb00006761-m2020060).

3 | RESULTS

The mean age of the four patients with a history of pulmonary surgery was 58.50 ± 2.38 years, and the male to female ratio was 1:1. Lobectomy was performed in three patients, and wedge resection and segmentectomy in one patient; all patients received thoracoscopic surgery. Three patients were diagnosed with non-small cell lung cancer, one with sclerosing pulmonary cell tumor. None of the patients received radiotherapy or chemotherapy after surgery. All patients presented fever, and all patients had body temperature > 38°C. The onset time of COVID-19 was from 3 to 10 days after surgery, with a median time of 6.75 days. Other symptoms were accompanied with fever, including nonproductive cough (two), rigors (one), chest distress (one), chest pain (one), productive cough (one), myalgia (one), and diarrhea (one). One patient died and three recovered and discharged from the hospital. The basic information and clinical characteristics of the four patients are shown in Table 1.

The chest computer tomography (CT) manifestations of the four patients are shown in Figure 2, all patients showed ground-glass opacity or patchy shadowing and the infection was predominant in the lobe contralateral to the side of surgery in three patients. The symptoms gradually improved and patchy shadow has been absorbed in three patients. In patient 4, lung effusions aggravated as disease deteriorated; despite receiving mechanical ventilation, the patients eventually died from respiratory failure on the 42th postoperative day.

The comparison of demographic information between the two groups is shown in Table 2. Incidence of hypertension in the surgical and nonsurgical groups (1 of 4 [25.0%] vs 5 of 16 [31.3%]; $P = 1.0$) showed no statistical difference, and the participants of neither group had diabetes, coronary heart disease, or cerebrovascular disease. The mortality rate of the surgical group (1/4, 25.0%) was higher than that of the nonsurgical group (1/16, 6.3%).

We compared the laboratory indexes of the two groups (Figure 3). Due to the limitation of sample size, we did not conduct statistical analysis. However, we still find that albumin, hemoglobin, lymphocytes, IL-6, and ferritin were lower in the surgery group.

TABLE 1 Clinical characteristics, treatment, and outcomes of patients with lung surgery

	Patient 1	Patient 2	Patient 3	Patient 4
Gender	Male	Female	Male	Female
Age	61	60	57	56
Operation	LUL lobectomy	LUL wedge resection +LLL segmentectomy	RUL lobectomy	RUL lobectomy
Histological type	SCC	Ade + Ade	Ade	PSP
Pathological stage	pT2N2M0, IIIA	pT1bN0M0, IA	pT1bN0M0, IA	NA
Radiotherapy	No	No	No	NA
Chemotherapy	No	No	No	NA
Surgery to onset of symptoms	3 days	7 days	7 days	10 days
Highest temperatures, ℃	38.2	38.3	38.5	38.4
Headache	No	No	No	No
Chills	No	No	No	No
Rigors	No	Yes	No	No
Cough	Yes	No	No	Yes
Productive cough	Yes	No	No	No
Sore throat	No	No	No	No
Chest distress	Yes	No	Yes	No
Chest pain	No	No	Yes	No
Dyspnea	No	No	Yes	No
Fatigue	No	No	No	No
Myalgia	Yes	No	No	No
Diarrhea	No	No	No	Yes
Antiviral therapy	Yes	Yes	Yes	Yes
Antibiotics	Yes	Yes	Yes	Yes
TCM	Yes	Yes	Yes	Yes
Immunoglobulin	Yes	No	Yes	Yes
Systemic corticosteroids	Yes	No	Yes	Yes
Oxygen therapy				
High-flow oxygen	No	No	No	Yes
NMV	No	No	No	Yes
IMV	No	No	No	Yes
Outcome	Discharge	Discharge	Discharge	Death

Abbreviations: Ade, adenocarcinoma; LLL, left lower lobe; LUL, left upper lobe; NA, not applicable; PSP, pulmonary sclerosing pneumocytoma; RLL, right lower lobe; RUL, right upper lobe; SCC, squamous cell carcinoma; TCM, traditional Chinese medicine.

TABLE 2 Demographic of the two groups

Variables	Lung surgery group (n = 4)	Nonsurgery group (n = 16)	*P*
Number of patients, n (%)	4 (20)	16 (80)	
Gender (male/female)	2/2	8/8	1.0
Age, mean (SD), years	58.50 (2.38)	58.56 (3.20)	.97
Pre-existing comorbidities			
Hypertension, n (%)	1 (33.3)	5 (29.2)	1.0
Diabetes mellitus, n (%)	0	0	
Coronary artery disease, n (%)	0	0	
Cerebrovascular disease, n (%)	0	0	

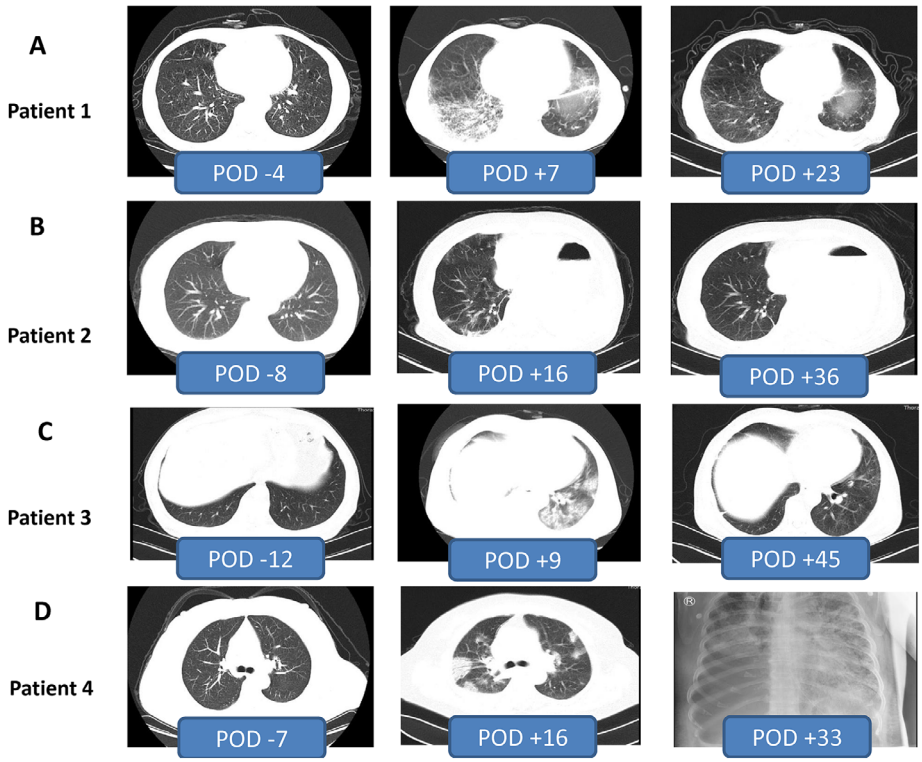

FIGURE 2 CT manifestations in four Patients with COVID-19 after lung surgery. (A) A 61-year-old male underwent VATS left upper lobectomy and lymphadenectomy. CT images on day 10 postoperation show patchy shadow in the right lung. CT images on day 23 postoperation show the shadows have been absorbed. (B) A 60-year-old female underwent VATS wedge resection of left upper lobe with basal segmentectomy and lymphadenectomy. CT images on day 16 postoperation show patchy shadow in right lower lobe. CT images on day 36 postoperation show the patchy shadow has been absorbed.(C) A 57-year-old male underwent VATS right upper lobe lobectomy and lymphadenectomy. CT images on day 9 postoperation show patchy shadow in left lower lobe. CT images on day 45 postoperation show the patchy shadow has been absorbed.(D) A 56-year-old female underwent VATS right lower lobe lobectomy. CT images on day 16 postoperation show bilateral multifocal ground-glass opacities, and x-ray on day 33 postoperation show aggravated exudation of the left lung and right pneumothorax [Colour figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

Peng et al[10] found that the death rate of 11 patients with COVID-19 after chest surgery was 27.3%; Cai et al[11] reported a mortality rate of 28.6% in seven patients undergoing lung surgery. In our study, the mortality rate was 25.0% in the surgical group, which was much higher than the 6.3% in the nonsurgical group. These results may be associated with the loss of lung function and decreased immune function following lung surgery.

SARS-CoV-2 uses angiotensin-converting enzyme II (ACE-2) as a cell entry receptor.[12] ACE-2 is expressed in a variety of different tissues, including upper and lower respiratory tract, myocardium, and gastrointestinal mucosa.[13] Because of the high expression of ACE-2 in the lung tissue, the lungs are mainly affected in COVID-19. The pathological findings of patients with COVID-19 showed a decrease in lung cells and the formation of a clear membrane, suggesting ARDS.[14,15] Since adult lung stroma is not renewable, lung function will inevitably be lost after lung surgery. Gu et al[5] found that forced expiratory volume in 1 second decreased by 13.58% (±9.98) 3 months after lobectomy, and by 8.49% (±10.36) 1 year after lobectomy. The carbon monoxide diffusing capacity decreased by 14.56% (±13.35) 3 months after lobectomy, and by 8.86% (±14.03) 1 year after lobectomy. Kim et al[6] and Nomori et al[7] reported similar results. The loss of lung function theoretically depends on the amount of lung tissue removed during surgery.[16] Peng et al[10] reported that the number of pulmonary segmentations greater than or equal to five was found to be associated with death by COVID-19. In this study, all patients had more than three lung segments removed, and developed COVID-19 symptoms within 10 days after surgery. Although we did not confirm the lung function level of the patients by pulmonary function examination, it was predicted that the lung function level of the surgical group was lower than that of the normal population, which could affect the prognosis.

The decrease in immune function after surgery can be evaluated by the decrease in lymphocytes and increase in inflammatory factors. Lymphocytosis often occurs immediately after lung surgery and is associated with postoperative pneumonia.[17] Ogawa et al. found that it takes 2 weeks for peripheral blood lymphocyte function to recover after surgery.[18] In this study, all patients developed COVID-19 within 2 weeks after surgery. Although the absolute value of lymphocytes of the surgical group was lower than the nonsurgical group, lymphocytopenia is a characteristic of SARS-CoV-2 infection and indicates the severity

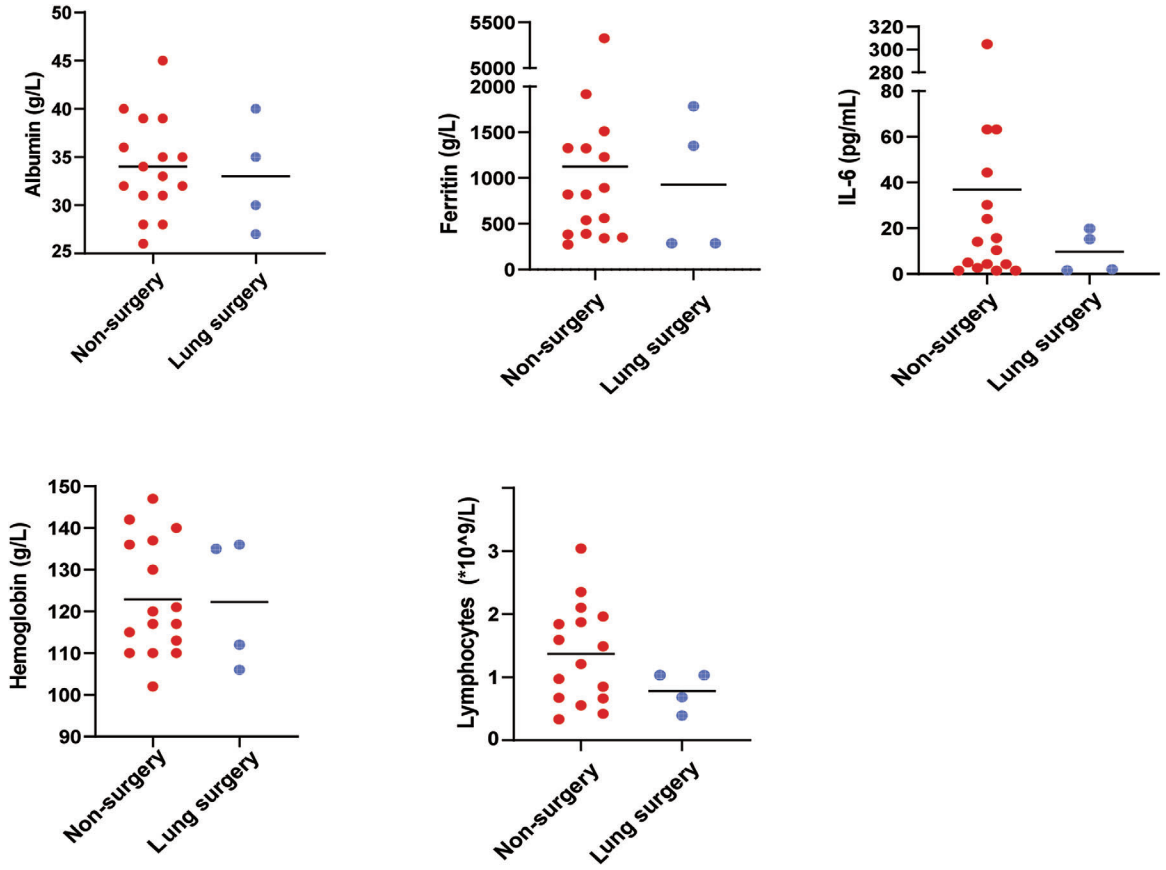

FIGURE 3 The laboratory indexes of patients with COVID-19 in nonsurgery group and lung surgery group. The values of albumin, ferritin, IL-6, hemoglobin, lymphocytes of patients with COVID-19 in nonsurgery group (red), and lung surgery group (blue) on admission are presented [Colour figure can be viewed at wileyonlinelibrary.com]

of the disease.[3,19] Moreover, postoperative lymphocytic decline could complicate the conditions.

Cytokine storms may be the pathogenesis of COVID-19, and the elevation of IL-6 indicates the level of inflammatory response.[20] Whitson et al[21] found that the level of IL-6 significantly increased after thoracotomy and reached a peak on the first day after surgery, but did not increase significantly in the thoracoscopic surgery group. Wolf et al[22] found similar results. In this study, there was not a higher IL-6 levels in the surgical groups. Similarly, other indicators reflecting the severity of COVID-19, such as ferritin,[23] also did not get a higher level.

Majority of patients had undergone lung surgery for lung cancer. In our study, three (75%) patients had lung cancer. Zhang et al[24] showed that 35.7% of 28 cancer patients with COVID-19 developed severe life-threatening complications, and 28.6% died. The authors suggest that immunosuppression in tumor patients is associated with a poorer prognosis. Mehta et al[25] also reported similar results.

5 | CONCLUSION

Patients contracting COVID-19 after lung surgery presented a higher death rate; hence, it is necessary to omit lung surgery in patients with active COVID-19 infection.

6 | LIMITATIONS

This was a single-center retrospective study with a small sample size, and the results need to be verified by a large sample size study. Heterogeneity existed in four patients undergoing lung surgery, not all of which were tumor patients. Most of the patients were hospitalized after a considerably long duration, and most had taken antiviral and antibacterial drugs outside the hospital, which might have influenced the signs and test results. The proportion of critically ill patients in our wards was high, which might have influenced the results of the analysis.

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AUTHOR CONTRIBUTIONS

Qinggang Ge and Shaohua Ma participated in the design of the study. Jie Bai contributed to the collection, analysis, and interpretation of data. Hongling Chu performed the statistical analysis.

DATA AVAILABILITY STATEMENT

After publication, we can provide the data to others with the permission of the corresponding author. A proposal with detailed description of study objectives and statistical analysis plan will be needed for evaluation of the reasonability of requests. The corresponding authors have the right to decide whether to share the data or not based on the research objectives and plan provided.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

ETHICAL STATEMENT

This study was approved by the ethics committee of Peking University Third Hospital (IRB00006761-M2020060).

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