Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Pulmonary Parenchymal Changes in COVID-19 Survivors

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ABSTRACT

BACKGROUND As the COVID-19 pandemic moves into the survivorship phase, questions regarding long-term lung damage remain unanswered. Previous histopathologic studies are limited to autopsy reports. We studied lung specimens from COVID-19 survivors who underwent elective lung resections to determine whether postacute histopathologic changes are present.

METHODS This multicenter observational study included 11 adult COVID-19 survivors who had recovered but subsequently underwent unrelated elective lung resection for indeterminate lung nodules or lung cancer. We compared these against an age- and procedure-matched control group who never contracted COVID-19 (n = 5) and an end-stage COVID-19 group (n = 3). A blinded pulmonary pathologist examined the lung parenchyma focusing on 4 compartments: airways, alveoli, interstitium, and vasculature.

RESULTS Elective lung resection was performed in 11 COVID-19 survivors with asymptomatic (n = 4), moderate (n = 4), and severe (n = 3) COVID-19 infections at a median 68.5 days (range 24-142 days) after the COVID-19 diagnosis. The most common operation was lobectomy (75%). Histopathologic examination identified no differences between the lung parenchyma of COVID-19 survivors and controls across all compartments examined. Conversely, patients in the end-stage COVID-19 group showed fibrotic diffuse alveolar damage with intra-alveolar macrophages, organizing pneumonia, and focal interstitial emphysema.

CONCLUSIONS In this study to examine the lung parenchyma of COVID-19 survivors, we did not find distinct postacute histopathologic changes to suggest permanent pulmonary damage. These results are reassuring for COVID-19 survivors who recover and become asymptomatic.

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One year into the COVID-19 pandemic, more than 116 million people worldwide have been infected with SARS-CoV-2 and more than 2.5 million lives have been lost.[1] Postmortem autopsies or pathologic studies from patients with end-stage lung disease from COVID-19 report severe fibrosis, diffuse alveolar damage (DAD), perivascular T-cell infiltration, severe endothelial injury, intracellular viral particles, and cell membrane disruption in lung tissue.[2-4] Whether there are long-lasting histopathologic changes in the lung parenchyma of COVID-19 survivors is unknown.[5,6]

A growing number of people have survived COVID-19, but some have experienced a prolonged and strenuous recovery. In population-based studies, an estimated 35% of survivors had not returned to their usual state of health 14 to 21 days postinfection, and some patients remained symptomatic several months after infection,[7-10] even showing persistent radiographic findings such as

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TABLE 1 Summary of Demographic Data, Clinical Characteristics, COVID-19 Course, and Operative Details of 14 Patients

Characteristics	COVID-19 survivors (n = 11)	COVID-19 end-stage lung disease (n = 3	Negative control patients (n = 5)
Age, y	65 (36-78)	56 (53-77)	72 (62-78)
Female sex	7 (64)	1 (33)	3 (60)
Race/ethnic group			
White	7 (64)	2 (67)	3 (60)
African American	2 (18)	NA	2 (40)
Hispanic/Latino	2 (18)	1 (33)	NA
Body mass index, kg/m^2	27.9 (23.8-34.7)	21.9 (21.3-24)	28.7 (24.6-34.7)
Smoking			
None	2 (18)	2 (67)	NA
Current	NA	NA	NA
Former	9 (82)	1 (33)	5 (100)
Pack-years	25.5 (6-52.5)	29.5	50 (18-67.5)
Comorbidities			
Chronic obstructive pulmonary disease	2 (18)	NA	NA
Chronic kidney disease	1 (9)	1 (33)	NA
Heart disease	2 (18)	NA	NA
Hypertension	4 (36)	1 (33)	2 (40)
Obesity	3 (27)	NA	NA
Type 2 diabetes	1 (9)	1 (33)	NA
Other[a]	4 (36)	3 (100)	4 (80)
COVID-19 symptoms			
Anosmia	1 (9)	NA	NA
Chills	2 (18)	NA	NA
Congestion	4 (36)	NA	NA
Cough	6 (55)	2 (67)	NA
Fatigue	3 (27)	NA	NA
Fever	4 (36)	2 (67)	NA
Headache	2 (18)	NA	NA
Muscle/body aches	2 (18)	NA	NA
Nausea	1 (9)	NA	NA
Pneumonia	2 (18)	3 (100)	NA
Shortness of breath	1 (9)	2 (67)	NA
Sore throat	3 (27)	NA	NA
Classification of COVID-19 course			
Asymptomatic	4 (36)	NA	NA
Moderate	4 (36)	NA	NA
Severe	3 (27)	3 (100)	NA
Days from infection to thoracic procedure or death[b]	68.5 (24-125), n = 12	87 (87-142)	NA

[a]Other comorbidities included obstructive sleep apnea, Crohn disease, hyperthyroidism, hyperlipidemia, and hepatitis C; [b]One patient underwent 2 elective thoracic surgeries, and those 2 specimens (n = 12 total specimens) were included. Continuous data are presented as median (range) and categorical data as n (%). NA, not applicable.

ground-glass opacities.[5] Although a lung biopsy is unlikely to be performed on an otherwise healthy survivor, there is a unique opportunity to examine the lung parenchyma of COVID-19 survivors who subsequently underwent elective thoracic operation or lung resection for different indications such as solitary lung nodules or lung cancer. Examining the lung parenchyma of this patient population can provide important insights into this disease and its long-term pulmonary impact.

In this context, we studied the histopathologic changes in a unique subset of patients who recovered from COVID-19, became asymptomatic, and underwent lung resection for other unrelated indications. We sought to identify the spectrum of disease in COVID-19 survivors, which would help inform expectations in a growing surviving population currently exceeding millions.

PATIENTS AND METHODS

STUDY DESIGN AND PARTICIPANTS. This multicenter, observational, retrospective, cohort study was

conducted at Loyola University Medical Center and the University of Chicago Medicine. The study was approved by the Loyola University Chicago and the University of Chicago Institutional Review Boards (LU214441 and IRB210055).

We included 11 adult patients (>18 years) who had previously contracted COVID-19 confirmed by a positive reverse-transcription polymerase chain reaction and were asymptomatic at the time of their subsequent elective lung resections between July 2020 and February 2021 (COVID-19 survivors). For comparison, we also included 3 patients who had prolonged symptoms and did not fully recover from COVID-19 (COVID-19 end-stage lung disease). The negative control group included 5 patients matched for age and elective thoracic procedure who underwent lung resection between 2019 and 2020 and did not have a history of COVID-19. Patient clinical, histologic, and radiologic data were collected from electronic medical records.

COVID-19 DISEASE. Details of the COVID-19 course, including date of positive reverse-transcription polymerase chain reaction test result, symptoms, and hospital and intensive care unit (ICU) admissions, were included. COVID-19 survivors were classified by their symptoms during infection into 3 groups: asymptomatic, moderate, or severe based on prior literature.[11-15] Asymptomatic patients did not experience symptoms of COVID-19.[11,12] Moderate COVID-19 cases were defined by symptoms such as fever, chills, aches, cough, headache, nausea, sore throat, fatigue, and congestion not requiring ICU admission.[12-15] Severe disease was determined by admission to the ICU.[15]

PATHOLOGIC REVIEW. All specimens were handled according to routine institutional histopathology processing protocols. Sections of uninvolved lung parenchyma distant from the main tumor were taken at the time of grossing for each of the cancer resection specimens. For the explanted lung specimen, representative sections were taken from the peripheral, central, and hilar regions of each lobe. In brief, 5-μm, formalin-fixed paraffin-embedded sections were stained with hematoxylin and eosin. Trichrome stains were also performed on representative sections of the explanted lung. Stained sections were reviewed by board-certified pathologists (V.A. and P.M.) experienced in thoracic pathology. Representative photos were taken at ×2.5, ×10, and ×20 magnifications.

Randomized and deidentified slides were provided to a blinded, experienced thoracic pathologist (A.N.H.) to assess whether any specific pathologic changes could be seen in the COVID-19 survivors compared with the negative controls. Representative slides from the patients with COVID-19 end-stage lung disease were used as comparators to demonstrate to the blinded pathologist both acute and chronic changes directly attributable to COVID-19. Histologic features were assessed in a standardized fashion across 4 histologic compartments: airways, alveoli, interstitium, and vasculature.

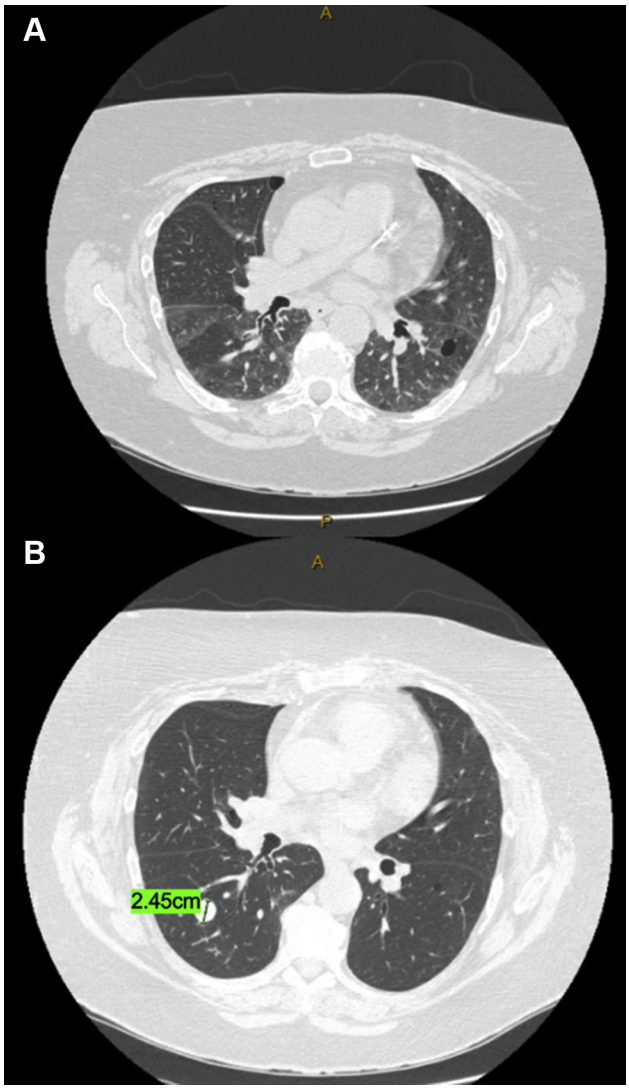

FIGURE 1 Representative computed tomographic (CT) images from a patient who recovered from severe COVID-19 infection and then subsequently underwent a right lower lobectomy. (A) Axial CT images 3 weeks after the COVID-19 diagnosis show bilateral patchy ground-glass opacities. (B) Axial CT from positron emission tomography/CT images 6 weeks later show resolution of the bilateral ground-glass opacities and the 2.45-cm lung nodule prompting the right lower lobectomy.

STATISTICAL ANALYSIS. Results are descriptively reported with percentages or medians with ranges as appropriate.

RESULTS

PATIENT CHARACTERISTICS. COVID-19 survivors. Among COVID-19 survivors, median age was 65 years

(range, 36-72 years), median body mass index was 27.9 kg/m^2 (range, 23.8-34.7 kg/m^2), and 7 (64%) were women. COVID 19 was moderate in 4 survivors (36%), 3 (27%) had a severe course requiring ICU admission, and the remainder (36%) were asymptomatic. Common preexisting conditions included hypertension (36%), obesity (27%), and heart disease (18%) (Table 1). Although no COVID-19 survivors were current smokers, 82% were former smokers. At time of operation, all patients had resolution of COVID-19 radiographic sequelae (Figure 1) and all were asymptomatic from a COVID-19 perspective.

COVID-19 end-stage lung disease patients. Included were 3 patients with COVID-19 end-stage lung disease: a 56-year-old previously healthy man (patient 17), a 53-year-old man (patient 18) with type 2 diabetes, hyperlipidemia, and hypertension, and a 77-year-old woman (patient 19) with chronic kidney disease and chronic lymphocytic leukemia (Table 2).

Negative control patients. Specimens from 5 patients matched by age and procedure without a prior COVID-19 diagnosis served as control tissues and were obtained from lung cancer resection specimens in a similar fashion to the COVID-19 survivors. The controls all had a history of smoking.

No patient received any COVID-19 vaccine at the time of this study.

OPERATIVE DETAILS AND INDICATIONS. COVID-19 survivors. A total of 12 operations were performed in 11 COVID-19 survivors, resulting in 12 specimens available for analysis. The median time from infection to elective thoracic operation was 68.5 days (range, 24-125 days) (Figure 2). The most common procedure was lobectomy (75%), followed by wedge resection (25%) (Table 2). The indications for surgical procedure included management of indeterminate pulmonary nodules (58%), resection of biopsy-proven lung cancer (33%), and spontaneous pneumothorax (8%). There were no postoperative complications in the COVID-19 survivors.

COVID-19 end-stage lung disease patients. Patient 17 underwent a thoracotomy, decortication, and bullectomy for empyema and persistent air leak 87 days after infection and remained ventilator dependent. Patient 18 underwent a bilateral lung transplant 142 days after infection. There were no postoperative complications. Patient 19 died of acute COVID-19 without undergoing thoracic operation.

Negative control patients. All 5 control patients underwent elective thoracic operations for lung cancer, with

TABLE 2 Detailed Demographics of All 19 Patients

Patients	Age, y	Sex	Characterization of COVID-19 Course	Type of Thoracic Procedure	Reason for Procedure
Negative control patients					
1	78	Female	NA	Wedge resection	Indeterminate nodule
2	62	Female	NA	Right lower lobectomy	Malignant neoplasm
3	78	Male	NA	Wedge resection	Indeterminate nodule
4	72	Female	NA	Left upper lobectomy	Malignant neoplasm
5	68	Male	NA	Right middle lobectomy	Adenocarcinoma
COVID-19 survivors					
6	67	Male	Asymptomatic	Right middle lobectomy	Malignant neoplasm
7[a]	51	Female	Asymptomatic	Left upper lobectomy; right upper lobectomy	Indeterminate nodule; indeterminate nodule
8	36	Male	Asymptomatic	Wedge resection and pleurodesis	Spontaneous pneumothorax
9	68	Male	Asymptomatic	Right upper lobectomy	Indeterminate nodule
10	53	Female	Moderate	Right upper lobectomy	Adenocarcinoma
11	72	Female	Moderate	Right upper lobectomy	Adenocarcinoma
12	65	Female	Moderate	Right lower lobectomy	Indeterminate nodule
13	50	Male	Moderate	Wedge resection	Indeterminate nodule
14	65	Female	Severe	Right upper lobectomy	
15	72	Female	Severe	Wedge resection	Indeterminant nodule
16	69	Female	Severe	Right lower lobectomy	Indeterminant nodule
COVID-19 end-stage lung disease					
17	56	Male	Severe	Thoracotomy, decortication, bullectomy	Empyema and persistent air leak
18	53	Male	Severe	Lung transplant	ARDS and pulmonary fibrosis
19	77	Female	Severe	NA	NA

[a]Patient 7 underwent 2 different elective thoracic operation at different times and therefore added 2 histologic specimens to the totals of COVID-19 survivors (n = 11 patients, n = 12 specimens). NA, not applicable.

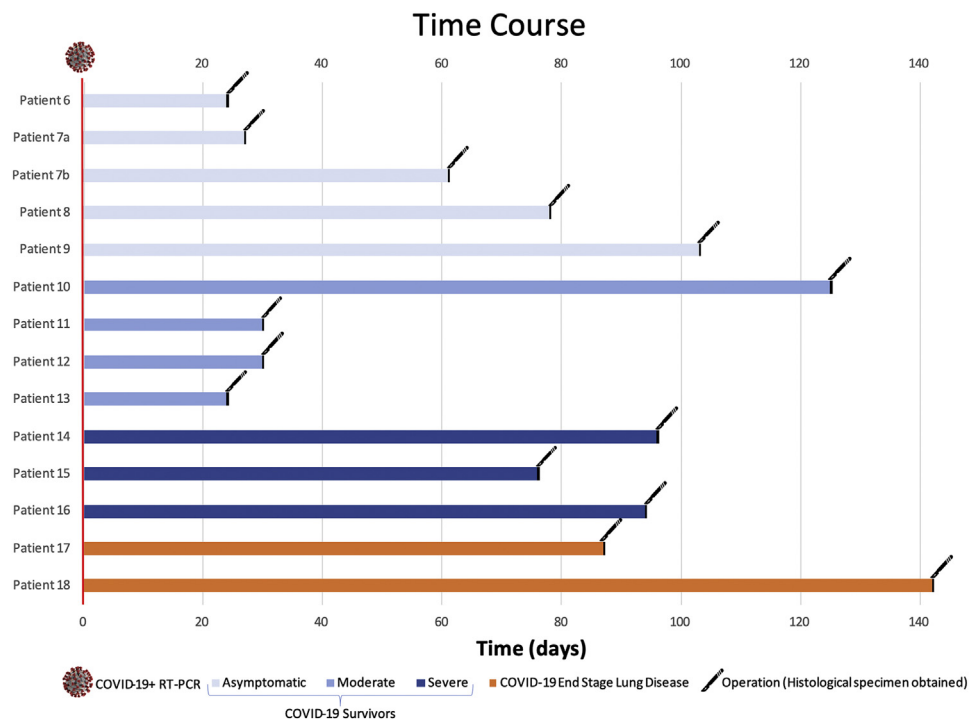

FIGURE 2 Amount of time from COVID-19 infection to operation. Time from positive COVID-19 reverse-transcription polymerase chain reaction (RT-PCR) test to elective thoracic operation date for COVID-19 survivors and patients with COVID-19 end-stage lung disease, with the exception of patient 19 who did not undergo an operation.

the most common procedures being lobectomy (60%) and wedge resection (40%).

HISTOLOGY. Airways. In COVID-19 survivors and controls, there was evidence of small-airway disease, including basement membrane fibrosis, which was present in 67% of COVID-19 survivors and in 60% of control patients (Table 3; Figures 3A, 3B). Airway inflammation was minimal in COVID-19 survivors and controls (Figures 3A, 3B). Examination of the airways in the patient who died of acute COVID-19 was somewhat limited by postmortem changes, but overall, there was scant-to-mild lymphocytic inflammation and minimal changes to the basement membrane or smooth muscle (Figure 3C). In patient 17, there was evidence of basement membrane fibrosis and moderate mixed inflammation in the submucosa, with intraepithelial extension suggestive of potential superimposed infectious processes (Figure 3D).

Alveoli. There were high rates of emphysema in COVID-19 survivors (92%) and controls (100%) (Figures 4A, 4B). Smoker's macrophages, metaplastic changes, and occasional poorly formed granulomas were seen in the alveolar spaces in a subset of both groups as well (Table 3). In patient 19, alveolar COVID-19 disease was characterized by findings of DAD (Figure 4C). In patient 18, scattered intra-alveolar macrophages and rare foci of organizing pneumonia were seen within the alveoli (Table 3).

Interstitium. Areas of mild fibrosis were seen in COVID-19 survivors and controls, with 50% of COVID-19 survivors having focal fibrosis and 60% of control patients having some areas of fibrosis (Figures 4A, 4B). The pattern of fibrosis seen in COVID-19 survivors and control patients was largely attributable to smoking-related changes. The interstitium of patient 19 was inflamed with predominantly lymphocytic inflammation and edema (Figure 4C). This was in contrast to patient 17, in whom the interstitium was diffusely fibrotic (Figure 4D) with a brisk inflammatory infiltrate composed primarily of lymphocytes and was not the same pattern of fibrosis seen in COVID-19 survivors and controls.

Vasculature. Histologic evidence of mild pulmonary hypertension was present in 42% of COVID-19 survivors and in 60% of controls, but the vasculature was otherwise unremarkable (Figures 5A, 5B). There was no significant vasculitis in any of the assessed COVID-19 survivors or the end-stage patients. While scattered microthrombi and gross pulmonary emboli have been reported in the acute COVID-19 setting,[16] the vessels in

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TABLE 3 Summary of Histologic Findings

Patients	Airway	Alveoli	Interstitium	Vessel
Negative control patients				
1	Unremarkable	Emphysema, pigmented macrophages, focal organizing pneumonia	Mild interstitial fibrosis, carcinoid (micro)tumorlet	PH
2	Basement membrane fibrosis/ small airway disease	Mild emphysema, bronchiolar metaplasia	Anthracosis, focal lymphoid aggregates, focal mild fibrosis	Unremarkable
3	Goblet cell hyperplasia	Emphysema, rare giant cells	Anthracosis	PH
4	Basement membrane fibrosis	Mild emphysema, edema, rare poorly formed granulomas with giant cells	Variably fibrotic with some severely fibrotic areas, foci of interstitial lymphoid infiltrate, anthracosis	PH, granuloma in vessel wall
5	Unremarkable	Mild emphysema	Anthracosis	Unremarkable
COVID-19 survivors				
6	Unremarkable	Emphysema, atypical adenomatous hyperplasia, rare pigmented macrophages	Anthracosis	Unremarkable
7a	Respiratory bronchiolitis	Emphysema, pigmented macrophages, Langerhans cell histiocytosis	Smoking-related interstitial fibrosis, scattered lymphoid aggregates	Unremarkable
7b	Respiratory bronchiolitis, peribronchiolar fibrosis	Emphysema, pigmented macrophages, focal edema	Smoking-related interstitial fibrosis	Unremarkable
8	Mild peribronchiolar inflammation	Emphysema, focal poorly formed granulomas	Mild interstitial thickening, perivascular lymphoid aggregates	Unremarkable
9	Peribronchiolar fibrosis	Emphysema, with patchy chronic inflammation, focal edema	Patchy widened, smoking-related interstitial fibrosis	PH
10	Unremarkable	Mild emphysema	Mild interstitial fibrosis, anthracosis	PH
11	Basement membrane fibrosis	Emphysema, rare foamy macrophages	Rare foci of fibrosis, anthracosis	PH
12	Basement membrane fibrosis/ small airway disease	Scattered poorly-formed granulomas and mild patchy inflammation	Poorly formed granulomas, anthracosis	PH
13	Mild small airway disease	Emphysema, scattered foamy macrophages	Unremarkable	PH
14	Unremarkable	Emphysema	Congestion, focal lymphoid infiltrate	Unremarkable
15	Peribronchial inflammation and fibrosis	Emphysema, rare organizing pneumonia	Mild interstitial inflammation, patchy fibrosis	Unremarkable
16	Unremarkable	Mild emphysema, edema, focal fibrin	Unremarkable	Unremarkable
COVID-19 end-stage lung disease				
17	Submucosal lymphohistiocytic infiltrate	Intra-alveolar macrophages, collapse	Diffuse fibrosis (fibrotic DAD), focal changes suggestive of interstitial emphysema, patchy chronic inflammation, calcifications	Recanalized thrombi
18	Basement membrane fibrosis, submucosal lymphohistiocytic and eosinophilic inflammation, intraepithelial neutrophils suggestive of superimposed infection	Organizing pneumonia, collapse, abundant hemosiderin-laden macrophages, microcystic change with bronchiolar squamous metaplasia	Diffuse fibrosis (fibrotic DAD), moderate lymphocytic/ mononuclear inflammation, pulmonary interstitial emphysema	Large recanalized thrombus
19	Postmortem sloughing of epithelium, submucosal edema, mild lymphocytic inflammation	Diffuse alveolar damage, mild hemorrhage, reactive pneumocytes	Mild but diffuse interstitial lymphocytic inflammation, edema	Focal perivascular edema

DAD, diffuse alveolar damage; PH, pulmonary hypertension.

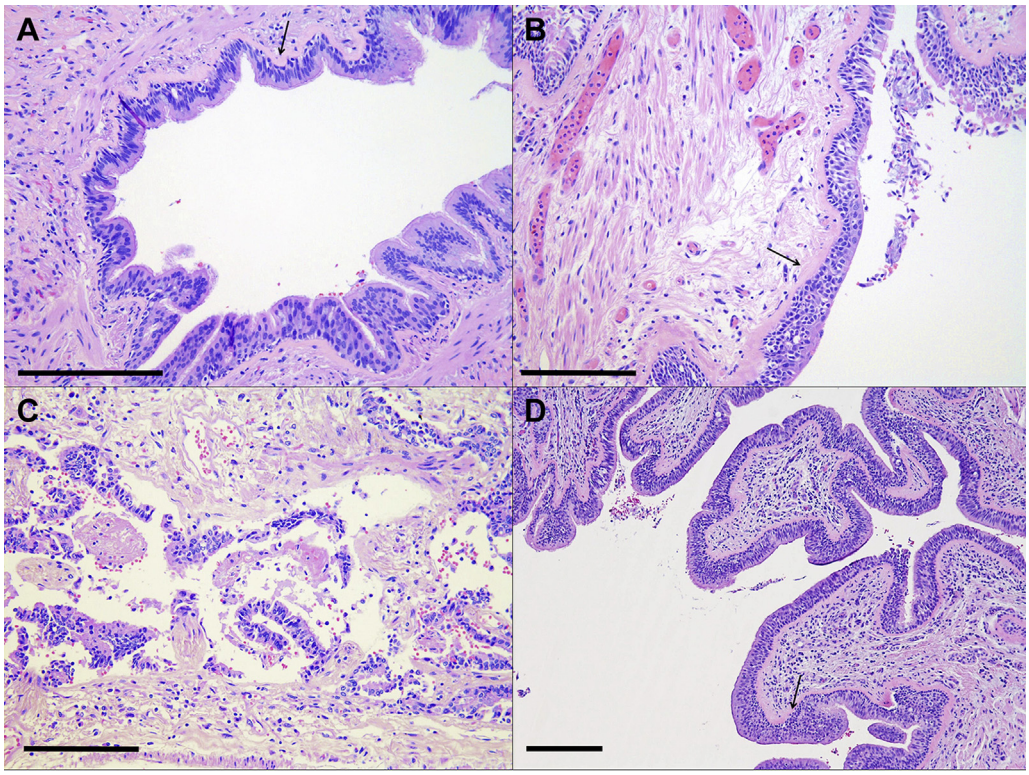

FIGURE 3 Representative histologic images (hematoxylin and eosin stain; original magnification ×20) of the airways. (A) COVID-19 survivor (patient 11) with basement membrane fibrosis (arrow) and scant submucosal inflammation. (B) Negative control (patient 5) shows similar basement membrane fibrosis (arrow). (C) COVID-19 end-stage lung disease (patient 19) exhibits postmortem sloughing and scant lymphocytic inflammation in the submucosa. (D) COVID-19 end-stage lung disease (patient 17) with basement membrane fibrosis (arrow) and moderate submucosal and intraepithelial inflammation. Scale bars (bottom left corner): ~250 μm.

patient 19 were patent, with no significant inflammation or occlusive thrombi (Figure 5C). Areas of recanalized thrombi were, however, rarely seen in patient 17 (Figure 5D).

Blinded pathologist review. An experienced pulmonary pathologist blinded to the clinical histories for each patient was unable to distinguish between COVID-19 survivors and controls in any of the assessed compartments. In addition, no significant differences were appreciated between the COVID-19 survivors who had an asymptomatic, moderate, or severe disease course in any of the assessed compartments.

COMMENT

In this observational study of patients who survived COVID-19, recovered, and became asymptomatic and then underwent an elective lung resection for other indications, we examined the potential for any postacute histopathologic lung changes in COVID-19 survivors. We found no discernible histopathologic changes suggesting permanent parenchymal damage in recovered COVID-19 survivors.

It is reassuring that none of the COVID-19 survivors included in this study had any lasting damage that was directly attributable to COVID-19. These findings fill an important gap in our understanding of the COVID-19 pandemic,[17] especially as we move into its survivorship phase. Clinicians and patients alike now have observational evidence that once patients recover from their disease, they are unlikely to have permanent lung parenchymal sequelae at least up to 4 months from the infection, which was the maximal duration of this study.

A strength of this study is the rigorous use of a blinded pathology methodology in analyzing the difference between COVID-19 survivors' lung tissue and non-COVID-19 infected controls, while also providing a COVID-19 end-stage lung disease comparison group. With this approach, we were able to obtain unbiased, dependable results that showed no discernible differences between the lungs of patients with COVID-19 and

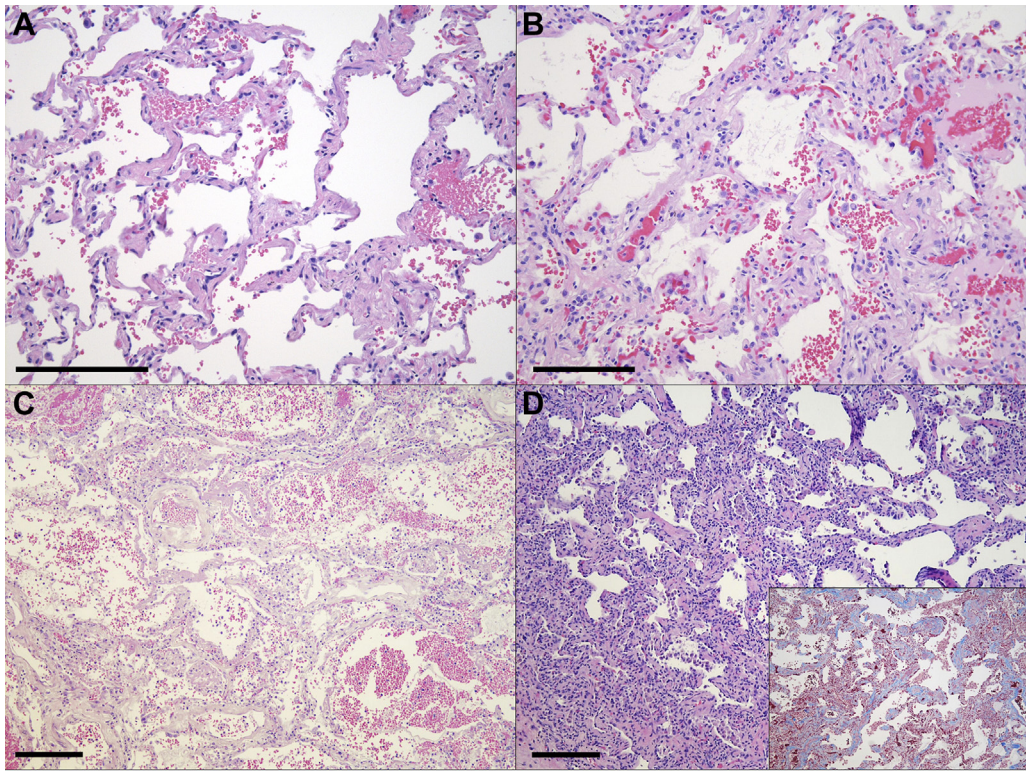

FIGURE 4 Representative histologic images (hematoxylin and eosin stain) of the alveoli and interstitial regions. (A) COVID-19 survivor (patient 10) with mild, variable interstitial thickening (original magnification ×20). (B) Negative control (patient 5) shows similar interstitial thickening (original magnification ×20). (C) COVID-19 end-stage lung disease (patient 19) exhibits diffuse alveolar damage (original magnification ×10). (D) COVID-19 end-stage lung disease (patient 17) with scattered intra-alveolar macrophages and fibrotic diffuse alveolar damage (original magnification ×10), with interstitial fibrosis supported by positive trichrome staining in the interstitium (inset original magnification ×10). Scale bars (bottom left corner): ~250 μm.

controls. In addition, the systematic examination across the 4 histologic compartments provided a complete picture of the airways, alveoli, interstitium, and vasculature, all of which can be affected as shown in the comparison group with COVID-19 end-stage lung disease.

On the other hand, the patients with COVID-19 end-stage lung disease likely represent those who have progressed to fibrosis as a result of organization of the original acute lung injury, a phenomenon that has been reported both before the COVID-19 pandemic[18,19] and in severe cases of acute COVID-19.[20] The reasons some patients progress to COVID-19 end-stage lung disease while others recover with pathology undiscernible from controls is unclear. We included in the present study the spectrum of COVID-19 disease courses from asymptomatic to severe disease requiring ICU admission. It is noteworthy that even in those with severe disease, their recovery was complete without notable lasting parenchymal damage.

COVID-19 can severely injure vascular endothelium and can progress to acute respiratory distress syndrome and viral pneumonia regardless of age or preexisting conditions.[21] This was the case for the end-stage patients included in this study. The changes in these patients were consistent with fibrotic DAD[22-25] as well as diffuse lymphocytic inflammation, pulmonary interstitial emphysema, and recanalized thrombi. The cumulative changes in these 3 patients were entirely attributable to the subsequent organization of diffuse acute lung injury (ie, DAD and organizing pneumonia) and need for prolonged mechanical ventilation.

This investigation further reveals important information regarding the safety of lung resection in COVID-19 survivors. No postoperative complications occurred in the patients in this series. We found that the lung parenchyma did not exhibit clinically relevant changes that would hamper or prolong postoperative recovery after lung resection. This is valuable information to surgeons and patients when discussing potential

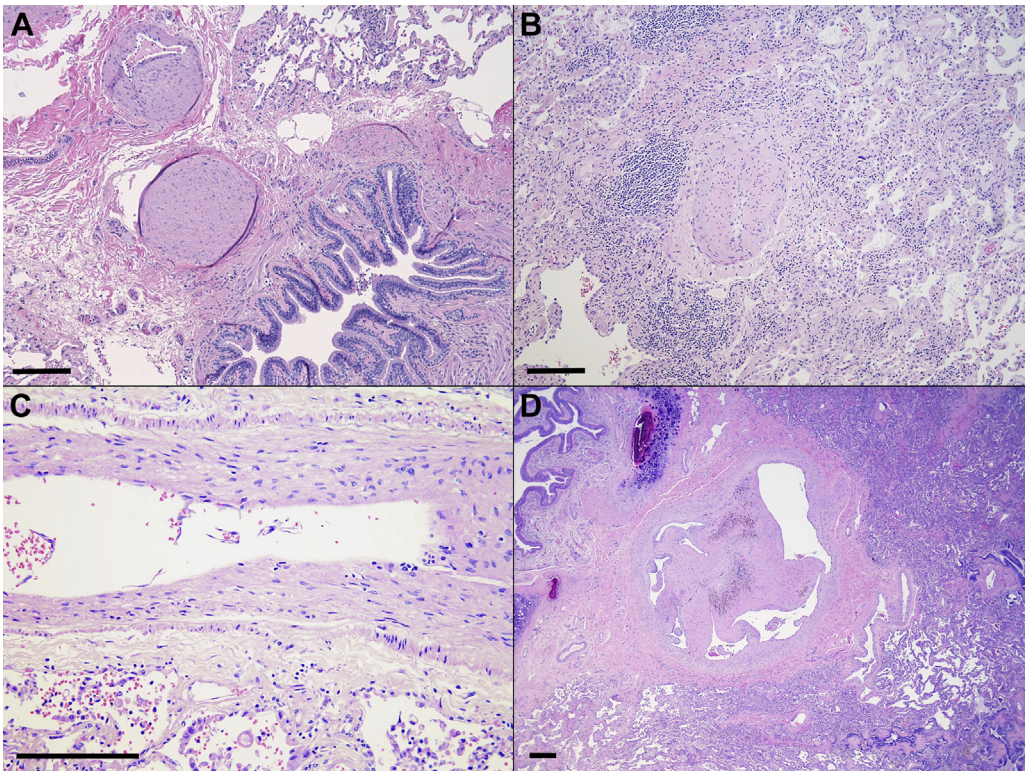

FIGURE 5 Representative histologic images (hematoxylin and eosin stain) of pulmonary vasculature. (A) COVID-19 survivor (patient 10) with pulmonary hypertension (original magnification ×10). (B) Negative control (patient 4) with similar pulmonary hypertension as well as mild interstitial inflammation (original magnification ×10). (C) COVID-19 end-stage lung disease (patient 19) with minimal vascular changes (original magnification ×20). (D) COVID-19 end-stage lung disease (patient 17) shows a recanalized thrombus (original magnification ×20 magnification). Scale bars (bottom left corner): ~250 μm.

surgical risks in this growing subset of patients. In addition, previous studies have suggested that elective operations be postponed by 6 weeks to maximize safety.[26]

This study has several limitations. This is an observational study subject to inherent confounding and selection bias. It is possible that the surgeons selected patients to undergo lung resection who would have a low probability of long-standing parenchymal changes. Second, most of the patients had smoking-related parenchymal changes that may obscure any possible COVID-19-related changes. However, the absence of any discernible differences and the inability of a blinded pathologist to differentiate between COVID-19 survivors and controls makes subtle changes less likely.[4,27]

In addition, we did not have data on pulmonary function tests before and after COVID-19 infection, which can meaningfully add to the overall functional assessment of these patients beyond the histopathologic assessment.

Finally, the study is limited by its sample size, although we included patients along the spectrum of COVID-19 disease course.

Notwithstanding these limitations, these results report the histopathology of COVID-19 survivors' lungs and expand the literature surrounding the survivorship of COVID-19.

In conclusion, we did not find any distinct postacute histopathologic changes among COVID-19 survivors, who have recovered and became asymptomatic, to suggest permanent pulmonary damage. COVID-19 survivors, who are asymptomatic at time of surgical evaluation, can undergo lung resection safely without added risk, and their histopathologic findings in the otherwise benign lung parenchyma are indistinguishable from controls. This suggests that patients who have asymptomatic, moderate, or severe acute COVID-19 courses can have a full recovery. Future studies examining why some patients achieve full recovery while others go on to develop end-stage lung disease are warranted.

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