Successful Lung Transplantation for Severe Post COVID-19 Pulmonary Fibrosis

David J. Hall, MD, Jefree J. Schulte, MD, Erik E. Lewis, MD, Swaroop R. Bommareddi, MD, Charles T. Rohrer, MD, Samir Sultan, DO, James D. Maloney, MD, Malcolm M. DeCamp, MD, Daniel P. McCarthy, MD, MBA, MEM

PII: S0003-4975(21)01841-5
DOI: https://doi.org/10.1016/j.athoracsur.2021.10.004
Reference: ATS 35719


Received Date: 21 September 2021
Accepted Date: 17 October 2021


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Running Head: Lung Transplant for Covid-19 Fibrosis

David J Hall, MD1; Jefree J Schulte, MD2; Erik E Lewis, MD1; Swaroop R Bommareddi, MD1; Charles T Rohrer, MD2; Samir Sultan, DO3; James D Maloney, MD1; Malcolm M DeCamp, MD1; Daniel P McCarthy, MD, MBA, MEM1*

Division of Cardiothoracic Surgery, Department of Surgery1;
Department of Pathology and Laboratory Medicine2;
Division of Allergy, Pulmonary, and Critical Care Medicine, Department of Medicine3;
University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

Word Count: 1500 words

Address correspondence to:
Daniel P McCarthy, MD, MBA, MEM
Division of Thoracic and Cardiovascular Surgery
Clinical Sciences Center
600 Highland Ave, H4/318
Madison, WI 53792
Email: mccarthyd@surgery.wisc.edu
ABSTRACT

Lung transplantation has been well described for COVID-19 patients in the acute setting, but less so for the resulting pulmonary sequelae. We share one of the first cases of lung transplantation for post COVID-19 pulmonary fibrosis. A 52-year-old female developed COVID-19 in July 2020 and mounted a partial recovery, but went on to have declining function over the ensuing three months and developed fibrocystic lung changes. She underwent bilateral lung transplantation and recovered rapidly, was discharged home POD 14, and has done well in follow-up. We demonstrate that lung transplantation is an acceptable therapy to treat post COVID-19 pulmonary fibrosis.

Abstract Word Count: 100 words
Over the past year, the lung failure and transplantation community has met unprecedented challenges in the care of patients affected by COVID-19. The pandemic has not only led to an increase in patients with acute lung injury, but also a population of survivors who develop the long-term sequelae of COVID-19. Many of the early lung transplants for COVID-19 were performed for patients with acute lung failure on extracorporeal membrane oxygenation (ECMO) support rather than for long-term effects of the disease.\textsuperscript{1-6} Herein we report one of the first cases of lung transplantation for post COVID-19 pulmonary fibrosis.

An otherwise healthy 52-year-old female developed COVID-19 pneumonia in July 2020. At baseline she was worked full-time and jogged several miles per day. Following infection, she progressed to severe acute respiratory distress syndrome and was treated with remdesivir, tocilizumab, and corticosteroids. She spent seven days on BIPAP with a fraction of inspired oxygen (FiO\textsubscript{2}) of 100\% at rest followed by an additional five weeks on CPAP alternating with humidified high flow nasal cannula (HFNC). After six weeks, she was discharged to a long-term assisted care facility where she wore HFNC with an FiO\textsubscript{2} of 70\% at rest and BIPAP with an FiO\textsubscript{2} of 50\% during short walks and time on a recumbent bicycle. Follow up COVID-19 PCR testing was negative in August 2020 and she additionally became COVID IgG Ab positive. Unfortunately, she developed progressive pulmonary fibrosis prompting referral for consideration of advanced lung failure therapies.

She was transferred to our institution in October 2020 for transplant evaluation. Imaging (\textbf{Figure 1}) demonstrated fibrotic changes predominantly in the bilateral upper lobes with some apical cystic change and traction bronchiectasis with mild bilateral hilar mediastinal
lymphadenopathy. Her exertional hypoxia progressed to the point of precluding safe ambulation despite HFNC at 100% FiO$_2$ and 55LPM. In an effort to maintain transplant candidacy and avoid severe deconditioning, venovenous ECMO was initiated with a right internal jugular 28Fr dual-lumen cannula.

Following less than 24h of ECMO, she underwent bilateral sequential lung transplantation on central venoarterial ECMO via bilateral thoracosternotomy. Intraoperatively, there were no significant pleural adhesions, but robust mediastinal and hilar lymphadenopathy with stigmata of acute inflammation was identified. The procedure was uncomplicated and ischemic times were 268 min for the left lung and 391 min for the right lung. Post-operatively, she did not require vasopressor support. Bronchoscopy on POD1 demonstrated intact anastomoses, and her P/F ratio was >400. She was extubated early on POD2 and the remainder of her stay was unremarkable, with quick progression and discharge to home on POD14. She is now over ten months status post lung transplantation and has done well with no evidence of rejection and stable pulmonary function tests – most recent FEV$_1$ 1.81L (86% predicted) and FVC 2.26L (89% predicted).

**Gross Pathologic and Histologic Findings**

The right native lung weighed 492g and the left weighed 377g. The bilateral lung surfaces were intact with smooth, glistening pleura. The pleura demonstrated innumerable sub-centimeter nodules, or cobblestoning, bilaterally. Scattered emphysematous blebs were also present. The cut surfaces of the bilateral lungs showed diffuse consolidation involving all lung lobes. There were focal hemorrhagic changes and focal peripheral bronchiectasis without bronchopneumonia.
The histologic sections were notable for diffuse fibrosing interstitial pneumonia (Figure 2A-D). The sub-pleural compartment showed more dense fibrosis and microscopic honeycomb change. Also in the peripheral lung, there were dilated cystic spaces with giant cell reaction, consistent with reaction to interstitial air. In the central portion of the lungs, the fibrosis diffusely widened the existing alveolar spaces in a nonspecific interstitial pneumonia (NSIP)-like pattern of fibrosis. In other areas, the fibrosis showed a sieve-like pattern with alveoli arranged in parallel slits. Overall, the pattern of fibrosis was inconsistent with a named interstitial lung disease.

COMMENT

At the time of this patient’s operation, fewer than twenty lung transplants had been performed worldwide for COVID-19.1-6 While the natural history of COVID-19 and pulmonary remodeling following infection are poorly understood, severe pulmonary fibrosis itself is a widely-accepted indication for lung transplantation. As the pandemic continues into its second year and beyond, the lung failure and transplant community will shift to treating survivors with long-term effects. Herein we share one of the first lung transplants performed for pulmonary fibrosis following COVID-19 pneumonia, who had a successful and rapid post-operative recovery.

Initial reports of explanted lungs detailed the pathologic changes that developed in patients after the initial onset of symptoms of COVID-19.1,2,5,6 Some describe generic interstitial fibrosis, while others mention that hyaline membranes were present, raising the possibility of organizing diffuse alveolar damage instead of a true interstitial fibrosis.2,5 Bharat and colleagues reported cystic space formation was common and that some of the cystic spaces demonstrated “complete fibrosis”.1 Similar to these previous reports, our patient showed cystic space formation with giant
cells, but uniquely, we also identified true microscopic honeycomb change in the absence of hyaline membrane formation.

In contrast to previously published reports of lung transplants for severe COVID ARDS, our patient wasn’t transplanted for ARDS but instead for irreversible post-COVID fibrosis. She met listing criteria established for interstitial lung disease and was over three months into her disease course, having become seronegative for COVID-19 and antibody positive, and with no evidence of acute superimposed disease process on her final native lung pathology. Post-COVID pulmonary fibrosis has been well-characterized in recent literature based on clinical, radiologic, and pathologic information to describe the non-idiopathic pulmonary fibrosis associated with COVID infection. Our experience is one of the first in what may become a large series of patients transplanted for fibrosis as a long-term effect of COVID-19, and we urge the transplant community as a whole to explore how to best care for this important population.
REFERENCES


FIGURE LEGENDS

Figure 1: Pre-transplant representative chest imaging demonstrating fibrotic changes in the bilateral upper lobes greater than lower lobes with some apical cystic change and traction bronchiectasis with mild bilateral hilar mediastinal lymphadenopathy.

Figure 2 A-D: Representative photomicrographs from pathologic examination of the explanted lungs. A) Peripheral section of the lung showing the subpleural area with dense fibrosis and microscopic honeycombing (H&E, 20X). B) Peripheral cystic spaces with giant cell reaction (H&E, 100X) C) Lung parenchyma showing a NSIP-like pattern of fibrosis (H&E, 40X). D) Sieve-like pattern of fibrosis in the central lung (H&E 40X).