

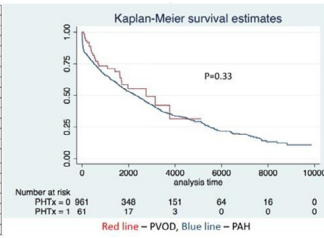


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disease severity of PVOD is higher than PAH. Despite that more PVOD patients required ECMO support post-operative, patient survival and other long-term outcomes such as lung function or rejection were not different between from PAH patients.

	(PAH)(970)	(PVOD)(51)	p-value
Recipient age (year)	39.84(15.27)	39.87(21.55)	0.99
Gender (f)	656(67.82%)	35(68.63%)	0.13
BMI	24.04(5.06)	24.35(5.1)	0.64
Post Lta PAF (mmHg)	88.63(22.79)	71.54(22.38)	<0.01
Post Lta PAP (mmHg)	49.01(13.7)	38.76(13.49)	<0.01
Post Lta mPAP (mmHg)	57.5(16.36)	47.38(16.65)	<0.01
Post Lta PCWP (mmHg)	12.89(7.6)	11.39(7.67)	0.24
Post Lta Cardiac output	4.3(1.54)	4.79(2.09)	0.03
Previous cigarette smoking	186(18.11%)	29(57.54%)	0.16
LAS at matching	45.82(14.28)	47.09(14.79)	0.53
Time on wait list (days)	337.56(511.14)	153.7(208.34)	<0.01
Ischemic time (hours)	5.18(1.81)	5.69(1.91)	0.02
On ECMO after lung transplant	418(2.86)	81(1.57)	<0.01
Acute rejection	623(28(11.24%))	107(81(1.99%))	0.29
Post Lta HD	141(89(15.24%))	7(8(11.48%))	0.37
reintubated	160(15(10.87%))	20(12(2.79%))	0.75
PCO2	109(7.05(3.76%))	67(6(7.7%))	0.06
Length of stay	35.71(41.35)	33.38(31.40)	0.67
FEV1 post Lta (Predicted)	68.49(12.78)	70.91(17.31)	0.39
FVC post Lta (Predicted)	79.3(12.84)	79.11(18)	0.19
PCO2 post Lta (Predicted)	35.79(3.77)	36.94(4.14)	0.86



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Esophageal Disorders in Lung Transplant Recipients: Association with Chronic Lung Allograft Dysfunction and Survival

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Purpose: Chronic lung allograft dysfunction (CLAD) is a major cause of morbidity and mortality in lung transplant recipients and is often triggered by aspiration events, potentiated by esophageal and gastric disorders. The two major classes of esophageal disorders include: 1) disorders of peristalsis and 2) esophagogastric junction outflow obstruction (EGJOO). Previous small studies have shown conflicting relationships between esophageal function and the development of CLAD. Herein, we sought to investigate the relationship between esophageal disorders and long-term outcomes in a large retrospective cohort of lung transplant recipients.

Methods: All lung transplant recipients from 2000-2018 with available esophageal manometry testing within first 7 months post-transplant were included in this study. Subjects were categorized into three groups: 1) no esophageal disorders, 2) disorder of peristalsis, and 3) EGJOO (defined by the 2007 Chicago Classification System). Disorders of peristalsis were further divided into major disorder (absent contractions) and minor disorder (irregular contractions). Univariable Cox proportional hazards models were used to determine the relationship between esophageal disorders and the development of CLAD and allograft failure (death/retransplant).

Results: Of 487 subjects, 47 (10%) had a disorder of peristalsis (8 major, 39 minor) and 57 (12%) had EGJOO. Older subjects were more likely to have an esophageal disorder (p=0.001). A major disorder of peristalsis was associated with an increased risk of CLAD [HR 2.78 (95% CI 1.23-6.28); p=0.01] and allograft failure [HR 3.17 (95% CI 1.49-6.77); p=0.003]. A minor disorder of peristalsis was not significantly associated with CLAD or allograft failure. EGJOO was associated with an increased risk of CLAD [HR 1.63 (95% CI 1.11-2.40); p=0.01] and allograft failure [HR 1.73 (1.18-2.54); p=0.005].

Conclusion: In a large retrospective cohort we observed that lung transplant recipients with major disorders of peristalsis and EGJOO were at an increased risk of CLAD and death/retransplant. In contrast, people with minor disorders of peristalsis were not at an increased risk of these outcomes. These findings will help with risk-stratification of lung transplant recipients and personalization of treatment for aspiration prevention.

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Case Report of Donor Transmitted SARS-CoV-2 Infection During Lung Transplantation

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Introduction: Avoiding SARS-CoV-2 infection in the peri-operative period is a challenge for lung transplantation during the COVID19

pandemic. Testing donor lung BAL samples for SARS-CoV-2 as part of pre-transplant workup may avoid donor-derived infections.

Case Report: A 36-year-old woman with interstitial lung disease secondary to desquamated interstitial pneumonia during infancy underwent bilateral lung transplant. She was highly allosensitized (cPRA >89%, ccPRA 97%) prompting intra-operative plasmapheresis (PLEX) and rabbit thymoglobulin induction immunosuppression. Post-operatively, her immunosuppression consisted of institution-standard tacrolimus, mycophenolate, and methylprednisolone. For HLA desensitization belatacept, rituximab, intravenous immunoglobulin (IVIG), and carfilzomib regimens were added. She was extubated post-op day 2. Her course was complicated by worsening hypercarbia, hypoxia and respiratory secretions. Post-op day 11, she was reintubated with tracheostomy placement. Chest imaging showed bilateral heterogeneous pulmonary opacities. BAL sampling was positive for SARS-CoV-2 with concern for donor transmission given adherent hospital precautions. Pre-transplant donor and recipient nasopharyngeal (NP) SARS-CoV-2 screenings were negative. Donor transmission was confirmed by positive PCR testing of banked pre-operative donor lung BAL samples. Dexamethasone and remdesivir were started. Tacrolimus and mycophenolate were continued for immunosuppression. She developed acute antibody-mediated rejection (AMR) with new donor specific antigens (DSA) likely related to her SARS-CoV-2 infection. Her AMR was managed with IVIG and PLEX x 10 with PLEX followed by SARS-CoV-2 convalescent plasma. Her DSA's resolved and ventilatory support was weaned. She was discharged home post-op day 56 and was doing well on room air 6 months out.

Summary: This case emphasizes a potential to miss donor SARS-CoV-2 infection in standard pre-operative evaluation. Despite absence from the NP mucosa viable SARS-CoV-2 virions may be present in donor lung tissue, increasing risk of infection to recipients. Peri-transplant SARS-CoV-2 infection carries a high risk of morbidity. Of note, our case occurred prior to the UNOS mandate for donor lung SARS-CoV-2 screening by lower respiratory sampling. This mandate will decrease risk for similar cases in the future.

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Use of High Dose Corticosteroids Reversed COVID-19 Associated ARDS in a Patient Listed for Lung Transplantation

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Introduction: In acute respiratory distress syndrome (ARDS) patients with irreversible lung damage, lung transplantation from a ventilator and/or extracorporeal membrane oxygenation support (ECMO) is feasible. Recently, selection criteria for lung transplant candidates with a COVID-19 associated ARDS have been published. Here, we report the efficacy of high dose corticosteroids as ultimate salvage therapy, despite Meduri scheme attempts, in a patient listed for transplantation.

Case Report: A 50-year-old female with a medical history of Multiple Sclerosis (relapsing-remitting type under treatment with anti-alpha4-integrin therapy), was tested positive for COVID-19. She deteriorated and was admitted to the hospital. High flow oxygen and dexamethasone (six milligram daily), were started but unfortunately, she developed a severe ARDS with need for mechanical ventilation and ECMO support. Corticosteroids according to the Meduri scheme and ciprofloxacin were started. Weaning trials were initiated but failed and CT-thorax showed consolidation and presumed fibrosis. After 37 days on ECMO, she was evaluated and listed for bilateral lung transplantation. A corticosteroid pulse therapy of 1000 mg of methylprednisolone IV for three days during antibiotic coverage with piperacillin/tazobactam was started and within three days the clinical condition of the patient improved and she could be weaned from ECMO (51 days of ECMO) and delisted from the lung transplantation

waiting list. Nowadays, patient does not require oxygen, is at home and revalidating.

Summary: Here, we report the efficacy of a regimen with high dose corticosteroids as ultimate salvage therapy, despite Meduri scheme attempts, in a patient listed for transplantation. Corticosteroids are beneficial for immunomodulation and may reduce hyperinflammation. Our trial with administration of high dose corticosteroids pulse therapy in COVID-19 ARDS patients refractory to corticosteroids according to “classical schemes” has been successful and is informative. Further studies, will hopefully further elucidate responders and non-responders to high dose corticosteroid pulse therapy and preferably answer the question if prophylactic use of antibiotics and antifungals (in view of possible complications such as pulmonary aspergillosis and mucormycosis) is prudent in this vulnerable group.

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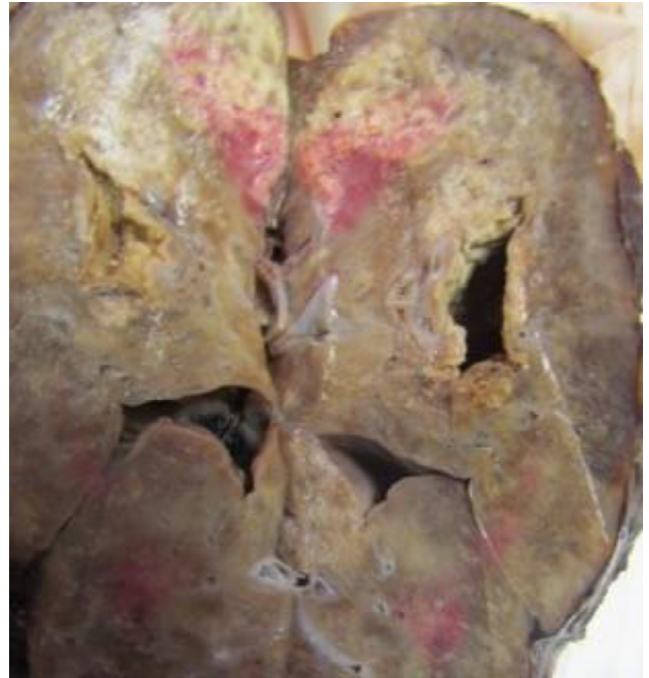
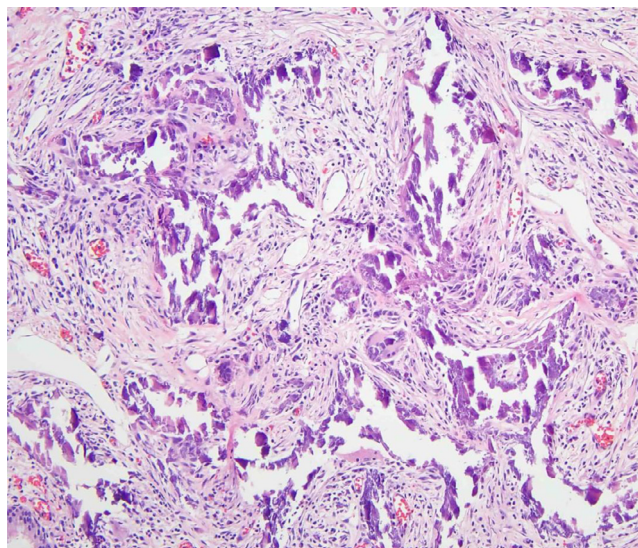
Chronic COVID 19 Related Disease Requiring Lung Transplantation with Calcified Cavitory Lesions in Explanted Lungs

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Introduction: Bilateral cavitory lung lesions with calcification in a patient with chronic COVID requiring transplantation are described.

Case Report: 46-year-old woman presented for lung transplant with respiratory failure due to COVID-19 pneumonia following remdesivir, dexamethasone, tocilizumab and baricitinib therapy. Cavitory upper lobe lung lesions were noted on imaging with negative cultures. She was started on VV ECMO as a bridge to bilateral lung transplant. Explanted lungs were consolidated and fibrotic with bilateral upper lobe calcification surrounding cavitory lesions. Varied microscopic pathology included NSIP pattern of inflammation, and foci of airway centered inflammation with giant cells suggesting chronic hypersensitivity reaction. The calcification was reminiscent of dendriform/metastatic calcification, and involved areas of necrotic/mummified parenchyma.

Summary: Cavitation as a late stage complication of COVID19 has been described in rare cases and is considered atypical. The constellation of findings in our case, including cavitory lesions with associated dendriform like calcifications are unique and maybe attributable to COVID19 itself +/- exacerbation of underlying chronic lung disease +/- intercurrent infection, or COVID19 related cavitation with superimposed secondary changes due to ECMO treatment. Bilateral lung transplantation has a reasonable short-term prognosis for patients with end stage respiratory failure secondary to COVID19; examination of these native lungs may expand our concept of COVID19 related chronic lung injury patterns.



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Peri-Operative Desensitization for Highly Sensitized Lung Transplant Recipients Following COVID-19 Acute Respiratory Distress Syndrome (ARDS) - Report of Two Cases

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Introduction: Sensitized lung transplant (LTx) candidates have longer waiting times, decreased likelihood of transplant, and increased risk of death while on the waitlist. Patients with SARS-Cov-2 ARDS on ECMO support due to end-stage lung disease have a short window of opportunity for LTx. We report two cases in which the Toronto LTx peri-operative strategy was performed with good outcomes in highly sensitized Covid-19 patients.

Case Report: **Case 1:** 31-yo female patient with Covid-19 ARDS, transferred for LTx evaluation after 46 days on VV-ECMO. She was pregnant when she presented with Covid -19 acute respiratory failure, and underwent an urgent C-section due to fetal distress. She required blood transfusions during ICU stay. At LTx assessment: PRA class I: 95%; class II: 0%. A decision to proceed with LTx with perioperative desensitization was made considering the low probability of finding a suitable donor. After seven days on the waiting list, she underwent bilateral LTx. Virtual cross-match (XM) positive (B35); CDC-XM negative. Desensitization protocol was performed with perioperative plasma exchange (PLEX) without basiliximab induction, followed by five sessions of PLEX and intravenous immunoglobulin 1 mg/kg. Due to postoperative acute cholecystitis with positive cultures after biliary drainage, anti thymocyte globulin (ATG) infusion (3 mg/kg) was held, and infusion postponed until four weeks post LTx. Tacrolimus, mycophenolate, and prednisone were used as maintenance immunosuppression. The patient was discharged home on PO day 53 with excellent graft function. **Case 2:** 35-yo female patient with Covid-19 ARDS, transferred for LTx after 69 days on VV-ECMO. History of 3 previous pregnancies and multiple blood transfusions due to transitory coagulopathy during her ICU stay. PRA class I: 83%; class II: 94%. VCM positive (B7, Cw7, DRB1*11:01, DR52, DQA1*05/DQB1*03). Desensitization protocol was performed, but ATG infusion was held due to *C. albicans* bloodstream infection and colonization with pan-resistant *K. pneumoniae*. DSAs at six weeks were negative. She remains hospitalized for mechanical ventilation withdrawal and inpatient rehabilitation.