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Results: A total of 931 recipients were included in this study, 868 (93.2%) and 63 (6.8%) were IPF and CVF, respectively. IPF recipients were on average older (65 vs. 56 years, $p < 0.001$), white race (83% vs. 51%, $p < 0.001$), and less likely to be male (73% vs. 86%, $p = 0.04$). BMI was similar between the IPF and CVF, 27.6 and 27.2 kg/m², as was the mean PAP 24 and 21 mmHg. The CVF cohort had lower predicted FVC (32% vs. 47%, $p = 0.01$), and had less tobacco use (36% vs 61%, $p < 0.001$). Mean creatinine level was clinically similar, though statistically higher in the IPF cohort, (0.83 vs 0.64, $p < 0.001$). CVF recipients were on the waitlist for a shorter median duration (10 vs 32 days, $p < 0.001$) with a higher LAS (85 vs 41, $p < 0.001$). Notably, more CVF recipient were be on ECMO at time of listing (29% vs 2%, $p < 0.001$) and require ventilatory support (27% vs. 2%, $p < 0.001$). CVF recipients were more likely to receive a double lung transplantation compared to IPF (83% vs 64%, $p = 0.002$), with similar ischemia times, 5.5 vs 5.1 hrs ($p = 0.17$). Mortality at 30 days was comparable between CVF and IPF (7.0% vs. 2.3%, $p = 0.09$), though 20 patients in the CVF cohort had missing data.

Conclusion: Patients with end-stage lung disease secondary to CVF are higher acuity, and more likely to require ECMO and ventilatory support as a bridge to lung transplantation. Early mortality, while comparable to non-COVID related fibrotic lung disease, remains almost 3 times higher with CVF. In the era of publicly reported survival outcomes, the transplant community may need to reconsider how we approach this new and devastating diagnosis of CVF.

(235)

Radiographic and Histopathologic Lessons from COVID-19 Explants

L. Benninger,¹ P. Johns,² S. Chandrashekar,³ and S. Nandavaram.⁴ ¹Cleveland Clinic, Cleveland, OH; ²University of Florida, Gainesville, FL; ³Emory Health Care, Atlanta, GA; and the ⁴University Of Kentucky, Lexington, KY.

Purpose: COVID-19 acute respiratory distress syndrome (ARDS) can result in irreversible lung damage. Lung transplant is a viable option for such select patients. Our aim is to describe the radiologic features prior to lung transplant and post transplant explant pathology, in such patients.

Methods: A single center retrospective chart review was performed of adults who underwent lung transplant for COVID-19 ARDS from 7/1/2020 until 7/31/2021. Demographic data, imaging reports at the time of listing and explant pathology were collected.

Results: 25 patients were included and none of them had pre-existing lung disease. Chest CT reports obtained at the time of transplant listing and post transplant lung explant reports were reviewed. Most common radiographic and explant features were traction bronchiectasis and NSIP pattern interstitial fibrosis, respectively.

Conclusion: To our knowledge, this is the largest descriptive report on COVID 19 explants. Though NSIP pattern is the most common finding on explants, only 48% of patients had fibrosis on CT scan prior to listing. Hence, other findings reflective of end stage lung disease such as traction bronchiectasis, GGO's should be considered along with respiratory mechanics while assessing the need for lung transplant for COVID-19 ARDS.

Demographic Variables

| | |
|--|-----------------|
| Age (years) | 51 [IQR(44-54)] |
| Male | 80% (n=20) |
| Female | 20% (n=5) |
| Extracorporeal Life Support Bridge to Transplant | 92% (n=23) |
| Mechanical Ventilation bridge to transplant | 96% (n=24) |
| Nasal Cannula Oxygen Supplementation | 4% (n=1) |
| Alive at the time of this study | 100% (n=25) |

| CT Chest Radiographic Features at the time of transplant listing | |
|--|------------|
| Traction Bronchiectasis | 84% (n=21) |
| Consolidations | 80% (n=20) |
| Pneumothorax | 72% (n=18) |
| Fibrosis | 48% (n=12) |
| Ground Glass Opacities (GGO's) | 40% (n=10) |
| Pleural Effusions | 40% (n=10) |
| Cystic Changes | 28% (n=7) |
| Pneumomediastinum | 16% (n=4) |

| Lung Explant Pathology | |
|--|------------|
| NSIP (non specific interstitial pattern) interstitial fibrosis | 76% (n=19) |
| UIP (usual interstitial pattern) interstitial fibrosis | 4% (n=1) |
| Pulmonary Vascular Injury | 72% (n=18) |
| Alveolar Hemorrhage | 56% (n=14) |
| Organizing Pneumonia | 44% (n=11) |
| Pleuritis | 40% (n=10) |
| Cystic Cavitary Changes | 32% (n=8) |
| Bronchopneumonia | 32% (n=8) |
| Pulmonary Embolism | 16% (n=4) |
| Abscess | 4% (n=1) |

(236)

The Effect of COVID-19 Infection on Transplant Function and Development of CLAD in Lung Transplant Patients: A Multicenter Experience

E. Roosma,¹ J.P. Van Gemert,² A.E. De Zwart,² C.C. Van Leer-Buter,³ M. E. Hellemons,⁴ E. Berg,⁵ B. Luijk,⁵ O.W. Akkerman,² E.A. Verschuuren,² and C.T. Gan.² ¹Department of Respiratory Diseases, Martini Ziekenhuis, Groningen, Netherlands; ²Department of Respiratory Diseases, Tuberculosis and Lung Transplantation, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands; ³Department of Virology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands; ⁴Department of Respiratory Diseases, Erasmus Transplant Institute Rotterdam, University Medical Center Rotterdam, Netherlands; and the ⁵Department of Respiratory Diseases, University Medical Centre Utrecht, Utrecht, Netherlands.

Purpose: Concerns have been raised on the impact of the coronavirus disease (COVID-19) on lung transplant (LTx) patients. The aim of this study was to evaluate the effect on the clinical course and transplant function pre- and post-COVID-19 infection in LTx patients.

Methods: Data were retrospectively collected from adult LTx patients with a proven COVID-19 infection from three Dutch transplant centres, between February 2020 and September 2021. Spirometry results were collected pre-COVID-19 infection and within 3 and 6 months post-COVID-19 infection.

Results: A total of 59 LTx patients had been tested positive for COVID-19. The median age was 58 years (IQR 49-66), 64% was male and median time since transplantation was 5 years (IQR 2-11). Thirty-three patients (56%) were hospitalized, 30 (51%) were in need for supplemental oxygen therapy, 17 (29%) were admitted to the intensive care unit (ICU) and 13 (22%) required invasive mechanical ventilation. Thirteen patients died (22%), 10 in ICU (77%), 3 (23%) on general wards. Post-COVID-19 spirometry results were available in 45 (76%) patients within three months post-infection and in 34 (58%) 6 months post-infection. Spirometry results and the prevalence of chronic lung allograft dysfunction (CLAD) are shown in Table 1. CLAD pre-COVID-19 was not associated with higher mortality (12% vs 10%, $p = 0.162$).

Conclusion: In LTx patients COVID-19 infection results in high hospitalization and mortality rate. FVC and FEV1 was declined three months after infection and gradually improved at 6 months post-COVID-19 infection. However, FVC remained significantly lower after 6 months, demonstrating

a more restrictive pattern. The prevalence of CLAD did not change after COVID-19 infection. Further follow-up is required to obtain more detailed information about CLAD.

Table 1 Transplant function pre- and post-COVID-19 infection

| | Pre-COVID-19 | 3 months post-COVID-19 | p-value | 6 months post-COVID-19 | p-value |
|--------------------|--------------|------------------------|---------|------------------------|---------|
| Number of patients | 59 | 45 | | 34 | |
| FEV1, L | 2.62 ± 0.80 | 2.49 ± 0.86 | 0.005 | 2.51 ± 0.75 | 0.077 |
| FVC, L | 3.68 ± 1.06 | 3.44 ± 1.17 | 0.002 | 3.52 ± 1.00 | 0.033 |
| FEV1/FVC ratio | 72 ± 13 | 73 ± 15 | 0.084 | 72 ± 13 | 0.876 |
| CLAD, n (%) | 22 (37) | | | 13 (38) | |

Continuous variables are expressed as mean and standard deviation. CLAD = chronic lung allograft dysfunction.

(237)

SARS-CoV-2 Vaccine Response in Lung Transplant Recipients: A French Multicenter Study

G. Dauriat,¹ L. Beaumont,² B. Renaud-Picard,³ M. Salpin,⁴ B. Coiffard,⁵ I. Danner-Boucher,⁶ A. Leborgne,⁷ S. Feuillet,¹ M. Penhouet,⁶ M. Reynaud-Gaubert,⁵ F. Gallais,⁸ J. Messika,⁴ A. Roux,² and J. Le Pavec.⁹ ¹Department of Pneumology and Lung Transplantation, Marie Lannelongue Hospital, Le Plessis Robinson, France; ²Pneumology, Adult Cystic Fibrosis Center and Lung Transplantation Department, Foch Hospital, Suresnes, France; ³Pneumology Unit and Strasbourg Lung Transplant Program, University Hospital of Strasbourg, Strasbourg, France; ⁴Department of Respiratory Medicine and Lung Transplantation, APHP-Bichat Hospital, Paris, France; ⁵Department of Respiratory Medicine and Lung Transplantation, APHM, Hôpital Nord, Marseille, France; ⁶Department of Pulmonology, Cystic Fibrosis Reference Centre, University Hospital, Nantes, Nantes, France; ⁷Department of Pulmonology, University Hospital, Toulouse, Toulouse, France; ⁸Laboratory of Virology, University Hospital of Strasbourg, Strasbourg, France; and the ⁹Dept of Pulmonology and Lung Transplantation, Marie Lannelongue Hospital, Le Plessis Robinson, France.

Purpose: Many scientific societies recommend SARS-CoV-2 vaccination for solid-organ transplant recipients. The immunogenicity of two or three vaccine doses in lung transplant (LTx) recipients is unclear. The aim of this study was to evaluate the humoral response to the vaccine in LTx and heart-lung transplant (HLTx) recipients.

Methods: We conducted a prospective study of LTx and HLTx recipients at seven centers in France. Anti-spike-protein antibody titers after two or three SARS-CoV-2 vaccine injections were measured.

Results: We studied 2186 patients (1091 [51%] males) with a median age of 49 [45-55] years. Double LTx was performed in 1792 (82%) patients. The main reasons for LTx were chronic obstructive pulmonary disease (n=656, 30%), fibrosis (n=459, 21%), and cystic fibrosis (n=350, 16 %). Median time from LTx to vaccination was 59 [29-108] months and mean time from the last vaccine dose to serological testing was 3 months [1.5-3.8]. We used WHO definitions to classify antibody titers as negative (< 30 BAU/mL), suboptimal (30-260 BAU/mL), or protective (> 260 BAU/mL). Of the first 1081 patients, 270 (25%) were partially vaccinated and 649 (60%) fully vaccinated (three doses or history of COVID-19 then two doses); Among these patients, 133 (12%) were infected by covid. Of the 649 fully vaccinated patients, 461 (71%), 84 (13%), and 97 (15%) had negative, suboptimal, and protective antibody titers, respectively. The proportion of patients with protective titers was 8% vs. 18% in patients vaccinated within 5 years vs. 5 or more years after LTx, respectively. Among covid-infected patients, 48% developed a protective rate, whether fully or partially vaccinated.

Conclusion: LTx recipients usually fail to develop protective antibody titers in response to SARS-CoV-2 vaccination. Once further data are collected, we will seek to identify risk factors for a poor antibody response.

(238)

TTV Load is Associated with SARS-CoV-2 Vaccination Response in Lung Transplant Recipients

E.A. Verschuuren,¹ R. Hoek,² R.D. de Vries,³ D. van Baarle,⁴ M. van der Heiden,⁴ J. van Gemert,⁵ E. Gore,⁶ H.G. Niesters,⁶ M.E. Erasmus,⁷ M.E. Hellemons,² S. Scherbeijn,⁸ C.H. Geurts van Kessel,⁹ and C. van Leer Buter.¹⁰ ¹UMC Groningen Transplant Centre, University of Groningen, Groningen, Netherlands; ²dept. of Pulmonary Medicine, Erasmus Medical Center, Rotterdam, Netherlands; ³dept. of Viroscience, Erasmus Medical Center, Rotterdam, Netherlands; ⁴dept. of Medical Microbiology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands; ⁵dept. of Pulmonary Diseases, University Medical Center Groningen, University of Groningen, Groningen, Netherlands; ⁶dept. of Medical Microbiology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands; ⁷Department of Cardiothoracic Surgery, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands; ⁸dept of Viroscience, Erasmus Medical Center, Rotterdam, Netherlands; ⁹dept. of Viroscience, Erasmus Medical Center, Rotterdam, Netherlands; and the ¹⁰dept. of Medical Microbiology, University Medical Center Groningen, University of Groningen, Groningen, Netherlands.

Purpose: Although the currently approved COVID-19 vaccines are highly effective, SARS-CoV-2-specific immune responses are diminished in lung transplant recipients (LTR), probably due to immunosuppression (IS). There is currently no marker of IS that can be used to predict vaccination responses. Here, we study if torque tenovirus (TTV) can be used as a predictive marker.

Methods: The humoral response to the mRNA-1273 vaccine was assessed in 103 LTR, who were vaccinated 4 to 237 months after Lung transplantation. Spike (S)-specific IgG levels were measured at baseline, 28 days after first, and 28 days after the second vaccination. TTV loads were determined by RT-PCR and Pearson's correlation coefficient was calculated to correlate serological responses to TTV load.

Results: Humoral responses to the vaccine COVID-19 vaccination were found in 41/103 (40%) LTR at 28 days after the second vaccination. 62 /103 (60%) had no detectable antibodies. TTV loads at baseline correlated with S-specific antibodies and the percentage of responders (= < 0.001) (Fig 1). TTV loads also strongly correlated with the time since transplantation, indicating that participants with lower TTV loads were longer after transplantation.

Conclusion: This study shows an association between baseline TTV load and mRNA-1273-induced S-specific antibodies. If the TTV load is indeed a predictor of vaccination responses, this can be used in the future as a potential guidance for optimizing vaccination regimens. Therefore, we recommend that TTV load measurements are included in further vaccination efficacy studies in immunocompromised cohorts.

Table 1

| | TTV ≥ 6.5 log copies/ml (n=26) | TTV 5.13 -6.5 log copies/ml (n=25) | TTV 3.78-5.13 log copies/ml (n=26) | TTV < 3.78 log copies/ml (n=26) | P value |
|------------------------------------|--------------------------------|------------------------------------|------------------------------------|---------------------------------|----------|
| % (low) responders | 7.6 % (n=26) | 40% (n=10) | 53.8% (n=14) | 57.7% (n=15) | P=0.0007 |
| Age (median IQR) | 61.5 (51-65) | 59 (38.5-63.5) | 61 (39.5-66.3) | 61 (50.5-67.5) | P=0.70 |
| Time from transplant (median, IQR) | 17.5 (11-57.5) | 41 (22.8-71) | 81 (50.3-170.8) | 97 (57-159) | P=0.0001 |
| MMF-free treatment (n=13) | 11.5% (n=3) | 16% (n=4) | 7.7% (n=2) | 15.4% (n=4) | NS |