COVID-19 Lung Transplant Registry

Version 1.2 (22 April 2021)

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Participating Sites:
To be determined

Background:
COVID-19, which is caused by SARS-CoV-2, is a respiratory illness that causes a range of illness from asymptomatic infection to severe multi-organ failure and death. Hospitalization and death is highest in older patients and those with underlying medical conditions. A subset of patients with severe COVID-19 develop a robust severe systemic inflammatory response which can result in ARDS and lung injury. While many patients will recover, a small subset will progress to more severe disease. Among these patients with permanent damage to the lung, rendering them ventilator- or ECMO-dependent. Lung transplantation has been the sole option for such patients with end-stage lung disease. With the advent of the first lung transplant for patients with non-resolving COVID-19-associated respiratory failure, there has been global interest in performing lung transplant for this unique population of COVID-19 patients. While the numbers of cases of lung transplant for COVID-19-associated respiratory failure have increased significantly, there is a paucity of data on these patients. As such, we propose the development of a registry of patients who have undergone lung transplant for COVID-19-associated respiratory failure. This registry will capture information on pre-transplant status, surgical requirements and post-transplant outcomes. The registry will be open to any site anywhere in the world that wants to submit data and will be collected in an such a way to limit collection of protected health information to facilitate

easy of participation. The registry will be housed at Northwestern University Feinberg School of Medicine, will have IRB approval by the NU IRB. Regular summary data from the database will be shared will all groups who participate in the study. Data will be presented at national and international meetings as well as a published manuscript with summary information. Sites will have to register with the NU team to get access to REDCap.

Study Population:
Inclusion: Individuals of any age who undergo single or bilateral lung transplant for COVID-19-associated respiratory failure will be included in the study. Listing for transplant has to occur after diagnosis of COVID-19 and complications of COVID-19 have to be the primary reason for transplant.

Exclusion: This study will not include individuals who were considered for transplant and subsequently became infected with COVID-19. Patients who were listed for or were being evaluated for lung transplant before COVID-19 diagnosis will not be included.

We expect to collect data on less than 500 subjects.

Data Collection:
Data to be collected is outlined in Appendix A. Data will be collected by study teams and entered into the NU REDCap database. This is a password-controlled database that allows members of the NU study team to see only data. Sites will identify the data and enter their patients data on a public REDCap form. They will include their name and email address to allow the NU team to send a link to the form to the individual to return later and complete missing data. Submitters will not have access to their data. The Registry Coordination Team will have access to the primary database as will statisticians (Lihui Zhao) who will help with the data analysis. While the majority of data will be collected retrospectively, patients may be followed prospectively to assess 1, 3, 6 and 12 month outcomes. Data collection will begin as soon as IRB approved and will continue indefinitely. Interval assessments will be made at least once per year and when fewer than 5 new patients are added in the prior year, data will stop being collected.

No patient identifiers will be collected in the REDCap database on individual patients and only summary data will be presented publicly.

For patient level data for NU, we will develop and EDW report with relevant material for our patients that have received a lung transplant for COVID-19. Manual chart review will be required for some specific data (i.e. onset of symptoms, complications). A coded identifier list that includes patient name, date of birth and study number will be collected separate from the REDCap database and will be stored in a password-protected file on NU server.

Access to date will be through the REDCap website and only individuals from Northwestern will be able to view or export data for data analysis. Data will be retained for 10 years after publication of the final manuscript and then be destroyed. Access to the database will be maintained by the NU team and access can be removed if individuals as needed.

Potential Risk:
The potential risk would be loss of confidentiality. This risk is minimized since there are no linkers to individual patients maintained in the REDCap database and no patient identifiers will be collected in the REDCap database. For NU subjects, a separate coded identifier list will be maintained separately from the REDCap database as detailed about; this will minimize the risk of loss of confidentiality.

Potential Benefit:
The data will be a potential benefit to society and future patients to inform subsets of patients who may benefit from transplant.

Informed Consent:
We will request a waiver of informed for consent as it is essential that complete data is collected and subjects are globally distributed which makes access to them challenging. Further, the research meets the following criteria for allowing waiver of consent:

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the individuals whose data you are analyzing;
- The research could not practicably be carried out without a waiver of consent;
- We will not collect identifiable private information

HIPPA Authorization:
We will seek a waiver of HIPPA authorization as we will not collected protected health information. Further, the research meets the following criteria for allowing a waiver of authorization:

- The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
  (1) an adequate plan to protect the identifiers from improper use and disclosure;
  (2) an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
  (3) adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the

use or disclosure of protected health information would be permitted by the HIPAA Privacy Rule;
- The research could not practicably be conducted without the waiver or alteration; **and**
- The research could not practicably be conducted without access to and use of the protected health information. For non-NU subjects, no PHI be collected as part of the REDCap database captured by NU and we will have no access to any PHI. For NU subjects, the team will maintain the PHI, in the form of a coded identifier list, separate from the REDCap database.

No mental health data will be collected as part of this study.

Publication Policy:
All publications will be approved by the Registry Coordinating Team (RCT). Requests to access subsets of data by contributing investigators must be made in writing to the RCT which will review and approve of the concept. Data and analysis will have to be done by the NU team with results shared with the requestor.

All abstracts and publications will list only members of the RCT and others that have contributed to data collection or analysis of the available data. In general, Saima Aslam and Max Weder will be co-primary authors and Michael Ison will be listed as the senior author. One member of the teams contributing data from the top 10 sites may be invited to be co-authors and sites with more than 10 patients contributed by have 2 authors.

Appendix A. Data to Be Collected via REDCap

Submitter Details

1. Transplant Institution
2. Initials of person completing questionnaire
3. Email of person completing questionnaire

Pre-Transplant Module

4. Patient gender at birth
    a. Male
    b. Female
5. Patient age at time of listing
6. Patient race
    a. White, Caucasian
    b. African American
    c. Asian
    d. Native Indian
    e. Other _____
    f. Not listed
7. Ethnicity
    a. Hispanic
    b. Non-Hispanic
8. Country Patient is from: US, Other: provide
9. For US patients: Does patient live in the same state as the transplant center? YES/No
10. Did the patient have co-morbidities prior to contracting COVID?
    a. Yes
    b. No
11. If answered yes, check all that applies (conditional on above):
    a. Essential hypertension
    b. Diabetes
    c. Obesity, BMI>30-35
    d. Obesity, BMI >35
    e. Hyperlipidemia
    f. Coronary artery disease
    g. Peripheral vascular disease
    h. Depression or anxiety
    i. Chronic kidney disease
    j. Immunosuppressed state
    k. History of smoking
    l. Blood disorders (sickle cell disease, thalassemia)
    m. Other pertinent diagnoses _____

12. Did the patient have any history of lung disease prior to contracting COVID
    a. Yes
    b. No
13. If answered yes to question #8, what was the lung diagnosis (conditional on above)?
    a. Asthma
    b. COPD/ emphysema
    c. Sarcoidosis
    d. ILD: IPF
    e. ILD: non-IPF
    f. Cystic fibrosis
    g. Pulmonary arterial hypertension
    h. Other: _____
14. Was the patient oxygen dependent prior to contracting COVID?
    a. Yes
    b. No
15. If answered yes to question 16, enter oxygen flow rate prior to contracting COVID (conditional on above)
    a. ____ LPM
16. Was the patient listed for lung transplant prior to contracting COVID
    a. Yes
    b. No
17. If patient was listed for lung transplant prior to contracting COVID, what was the leading indication for listing (conditional on above)?
    a. COPD/ emphysematous lung disease
    b. Interstitial lung disease, IPF
    c. Interstitial lung disease, non-IPF
    d. Cystic fibrosis
    e. Pulmonary arterial hypertension
    f. Other _____
18. If patient was listed for lung transplant prior to contracting COVID, what was the most recent lung allocation score prior to the COVID diagnosis?

19. Estimated time interval between initial COVID diagnosis and time of listing (days)
20. Time interval from first positive PCR to first negative PCR (days)PCR Testing Information
    a. Site of First Positive Result: Upper (Nasal, Oral)/Lower Track
21. First Negative Upper (Nasal, oral) Result: Days since initial result
22. First Negative Deep Result: Days since initial result
23. How many negative tests were required to clear for transplant: None, one, two, three or more
24. Was the COVID PCR positive at the time of listing?
    a. Yes
    b. No

   c. Site: Upper/Deep (conditional on above)
   d. Enter cycle threshold value, if known
25. Was the COVID PCR positive at the time of transplant?
   a. Yes
   b. No
   c. Unknown
   d. Site: Upper/Lower (conditional on above)
   e. Enter the cycle threshold value, if known
26. Antibody testing prior to transplant: Yes/No
   a. Spike, Nucleocapsid, Other (List target)
   b. Detectable antibodies: Yes/No
   c. Days from first positive PCR test to antibody test (conditional on above)
27. Enter time on mechanical ventilation up to date of transplant (days)
28. Was the patient ventilator dependent at the time of transplant? Yes/No
   a. Enter FiO2 in the ventilator at time of transplant (conditional on above)
   b. Enter static lung compliance at the time of transplant (ml/cmH2O)
29. Enter days on ECMO up to date of transplant:
30. Was the patient ECMO dependent at the time of transplant? Yes/No
   a. FiO2 on ECMO circuit at the time of transplant, if known (conditional on above)
31. Patient mobility at the time of transplant
   a. Patient fully ambulatory
   b. Patient ambulatory with assistance
   c. Patient not ambulatory, but able to participate in physical therapy
   d. Patient not ambulatory and not able to participate in physical therapy
32. Did the patient require paralytics within 7 days of transplant
   a. Yes
   b. No
33. How was transplant consent obtained
   a. Patient
   b. Next of Kin

34. What medical therapy was provided to treat COVID in your patient (check all that applies)
   a. Remdesivir
   b. Dexamethasone
   c. Convalescent plasma
   d. Monoclonal antibody treatment
   e. IL-6 Therapy (Tocilizumab, Sarilumab)
   f. Other: Describe

35. Infection in the last 2 weeks prior to transplant:
   a. Bacterial: List pathogen

b. Fungal: List pathogen
c. Viral: List pathogen
d. Other: List

36. Lung allocation score at the time of transplant (if available)

Transplant Event Module

1. Days from First Positive PCR test and day of Transplant: (Days)
2. Intraoperative ECMO Use: Yes/No
    a. VA or VV (conditional on above)
    b. ECMO duration (minutes) until transfer to PACU
    c. ECMO in use post-Op: Yes/No
3. Cardiopulmonary Bypass Used: Yes/No
    a. Duration of Cardiopulmonary Bypass (Minutes):
4. Ischemic Time (hours)
5. Intra-operative transfusions:
    a. Cell Saver Used: Yes/No
    b. pRBC: Number of Units
    c. FFP: Number of Units
    d. Platelets: Number of Units

Post-Transplant Course Module

Induction immunosuppression	Yes/ no
What agent was used for induction immunosuppression?	1, Basiliximab | 2, Alemtuzemab | 3, Thymoglobulin | 4, Daclizumab | 5, Methylprednisolone | 6, Other
Current maintenance immunosuppression consists of following: (multiple choices)	1, Tacrolimus | 2, Mycophenolate mofetil | 3, Prednisone | 4, Sirolimus | 5, Cyclosporine | 6, everolimus | 7, belatacept
Any Additional Therapies Utilized between Transplant and initial discharge (multiple choice)	1 Eculizumab, 2 Rituxumab, 3 Plasma Pharesis, 4 IVIG
Were COVID-19 specific therapeutics used post-transplant?	Yes/ no
What COVID-10 specific therapeutics were used post-transplant? (multiple choices)	1, remdesivir | 2, monoclonal antibody | 3,convalescent plasma | 4, IL-6 inhibitor 5, JAK inhibitor 6, other
What other COVID-19 specific therapeutic was used post-	

transplant?	
Was post-transplant surveillance for SARS-CoV-2 done via PCR	Yes/ no
If Yes	Were any positive – day post-transplant, site

Post-transplant length of stay in the ICU (days)	
Post-transplant total length of stay (days)	
Number of post-transplant days on mechanical ventilation	
Post-transplant days of ECMO	
Was patient discharged to home or a rehabilitative facility?	1, Home, 2, Rehabilitative facility
Duration of Inpatient Rehab (Days)	
Post-transplant complications within 30 days of transplant (multiple choices)	1, Airway dehiscence | 2, Airway ischemia/necrosis | 3, Bronchial stricture/stenosis requiring intervention | 4, recurrent COVID-19| 5, post-transplant pneumonia | 6, bacteremia | 7, septic shock | 8, Grade 3 PGD within 72 hours of transplant | 9, Pulmonary Embolism | 10, other
Details of "other" complications within 30 days of transplant	
Post-transplant complications 31-90 days post transplant	1, Airway dehiscence | 2, Airway ischemia/necrosis | 3, Bronchial stricture/stenosis requiring intervention | 4, recurrent COVID-19| 5, post-transplant pneumonia | 6, bacteremia | 7, septic shock | 8, Grade 3 PGD within 72 hours of transplant | 9, Pulmonary Embolism | 10, other
Patient alive at 6-months post-transplant?	1, Yes | 2, No | 3, Pending 6-month follow-up
Cause of death within 6 months of transplant	
Post-transplant complications months 3-6 post-transplant	1, Airway dehiscence | 2, Airway ischemia/necrosis | 3, Bronchial stricture/stenosis requiring intervention | 4, recurrent COVID-19| 5, post-transplant pneumonia | 6, bacteremia | 7, septic

	shock | 8, Grade 3 PGD within 72 hours of transplant | 9, Pulmonary Embolism | 10, other
Free text re: complications months 3-6 post-transplant	
Post-transplant rejection months 1-6 post-transplant?	Yes/No
Type of rejection?	1, ACR | 2, AMR
Grade of rejection (if more than one, please select most severe)	List ISHLT criteria
Number of rejection episodes	
Patient alive at 12-months post-transplant?	1, Yes | 2, No | 3, Pending 12-month follow-up
Cause of death within 12 months of transplant	
Post-transplant complications month 6-12 post-transplant	1, Airway dehiscence | 2, Airway ischemia/necrosis | 3, Bronchial stricture/stenosis requiring intervention | 4, recurrent COVID-19| 5, post-transplant pneumonia | 6, bacteremia | 7, septic shock | 8, Grade 3 PGD within 72 hours of transplant | 9, Pulmonary Embolism | 10, other
Free text re: complications month 6-12 post-transplant	
Post-transplant rejection month 6-12 post-transplant?	Yes/No
Type of rejection?	1, ACR | 2, AMR
Grade of rejection (if more than one, please select most severe)	List ISHLT criteria
Number of rejection episodes	