VANDERBILT School of Medicine

VANDERBILT UNIVERSITY MEDICAL CENTER

# Considerations for Transplantation of Patients with COVID-19

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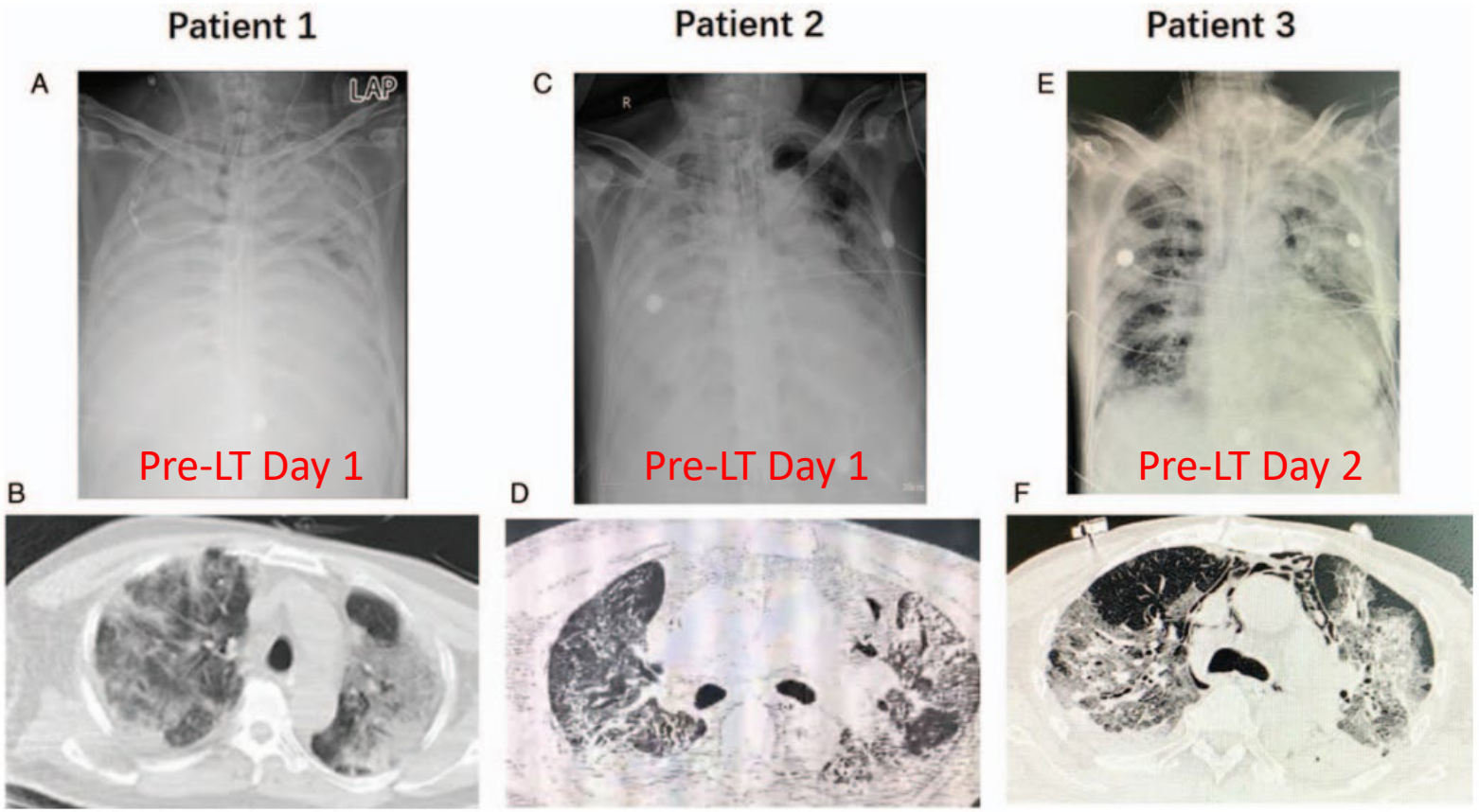
# Lung transplantation as therapeutic option in acute respiratory distress syndrome for coronavirus disease 2019-related pulmonary fibrosis




Chen J, et al. Chinese Medical Journal 2020;133(12)

# Lung Transplantation for COVID-19: Patient Characteristics

| Characteristics | Patient 1 | Patient 2 | Patient 3 |
|---|---|---|---|
| Sex | Male | Male | Male |
| Age (years) | 66 | 58 | 73 |
| BMI (kg/m$^2$) | 27 | 24 | 21 |
| Location | Shenzhen | Wuxi | Wuxi |
| Date of illness | January 3, 2020 | January 23, 2020 | January 26, 2020 |
| Date of confirmation of COVID-19 | January 11, 2020 | January 27, 2020 | February 2, 2020 |
| Comorbidities | Hypertension | HBV infection | DM, CKD, CHD, AF, and COPD |
| Date of MV (days pre-LT) | January 19, 2020 (27) | February 7, 2020 (22) | February 20, 2020 (20) |
| Date of ECMO (days pre-LT) | February 1, 2020 (15) | February 22, 2020 (7) | February 21, 2020 (19) |
| Convalescent plasma | Yes | Yes | Yes |
| Steroids (mg/d) | MP 80 | MP 60 | MP 40 |
| Oxygen index pre-LT (mmHg) | 60 | 104 | 114 |
| Mean PAP (mmHg) | 52 | 48 | 40 |
| ECMO mode pre-LT | VAV (5)+ | VV (3.5)+ | VV (4)+ |
| (flow rate, L/min) | Intra-operative VA (4) | Intra-operative VA (3) | Intra-operative VA (4) |
| Virus-negative samples | NP, BALF, and sputum | NP, BALF, sputum, and serum | NP, BALF, sputum, and serum |
| Lymphocytes pre-LT ($\times 10^9$/L) | 0.41 | 0.70 | 0.58 |
| D-dimer (μg/mL) | 12.75 | >20 | 13.34 |
| SOFA score pre-LT | 16 | 14 | 18 |
| Date of LT (days of illness onset) | February 15, 2020 (42) | February 29, 2020 (37) | March 10, 2020 (44) |
| Graft location (km) | Guangzhou City (128) | Kaifeng City (790) | Guangzhou City (1470) |
| Incision and LT type | Clamshell, RSLT + HT | Clamshell, Bilateral LT | Clamshell, Bilateral LT |
| Intra-operative cardiac event | VF | No | AF |
| Cold ischemic time (right lung/left lung, min) | 360/550 | 480/575 | 400/480 |
| Total surgery duration (min) | 450* | 300 | 295 |
| Post-LT survival | Death on POD 1 | Survival | Survival |
| $PaO_2/FiO_2$ (mmHg), POD 1 | – | 350 | 420 |
| ECMO weaning (post-LT, h) | – | 37 | 40 |
| Explanted lung virology | Mildly positive | Mildly positive | – |
| Follow-up reach to POD | – | POD 22 | POD 12 |

# Meet the Two COVID-19 Patients Who Received Double-Lung Transplants at Northwestern Medicine

NORTHWESTERN MEMORIAL HOSPITAL

JULY 30, 2020

# Florida patient is third-ever coronavirus survivor to undergo double-lung transplant

After contracting the coronavirus, a man's lungs were decimated. He could not survive without a lung transplant.

# Vandy performs first heart-lung transplant on COVID patient

Oct 13, 2020

UTHealth | The University of Texas Health Science Center at Houston

# Double-lung transplant for COVID-19 patient performed by team of UTHealth physicians

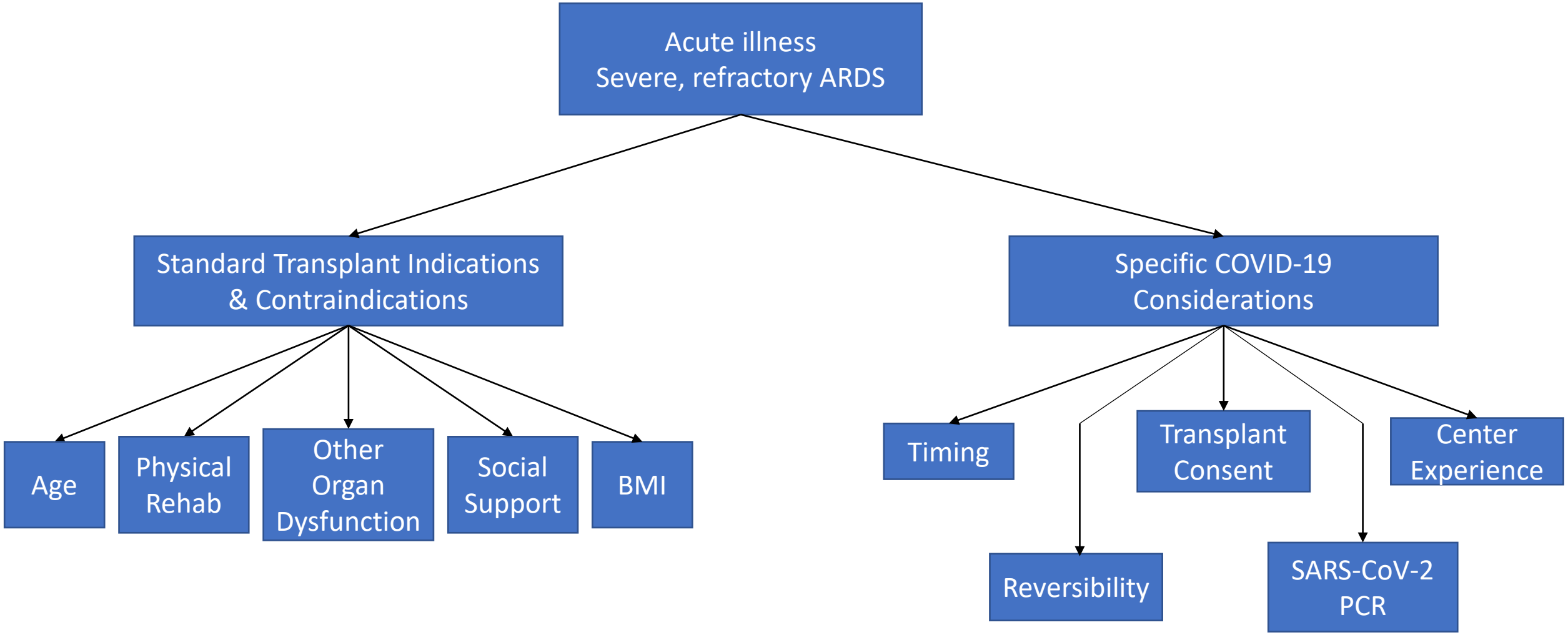
24-Sep-2020 11:10 AM EDT, by University of Texas Health Science Center at Houston

https://www.nm.org/about-us/northwestern-medicine-newsroom/press-releases/2020/meet-the-two-covid19-double-lung-transplant-patients

https://www.tampabay.com/news/health/2020/08/07/florida-patient-is-third-ever-coronavirus-survivor-to-undergo-double-long-transplant/

https://www.newswise.com/coronavirus/double-lung-transplant-for-covid-19-patient-performed-by-team-of-uthealth-physicians

https://www.tullahomanews.com/news/coronavirus_news/vandy-performs-first-heart-lung-transplant-on-covid-patient/article_ecd8def4-0d7b-11eb-976e-479b8e7f61ec.html


Acute illness
Severe, refractory ARDS
Standard Transplant Indications & Contraindications
Specific COVID-19 Considerations
Age
Physical Rehab
Other Organ Dysfunction
Social Support
BMI
Timing
Transplant Consent
Center Experience
Reversibility
SARS-CoV-2 PCR

# ECMO for COVID-19 Infection: Patient Characteristics

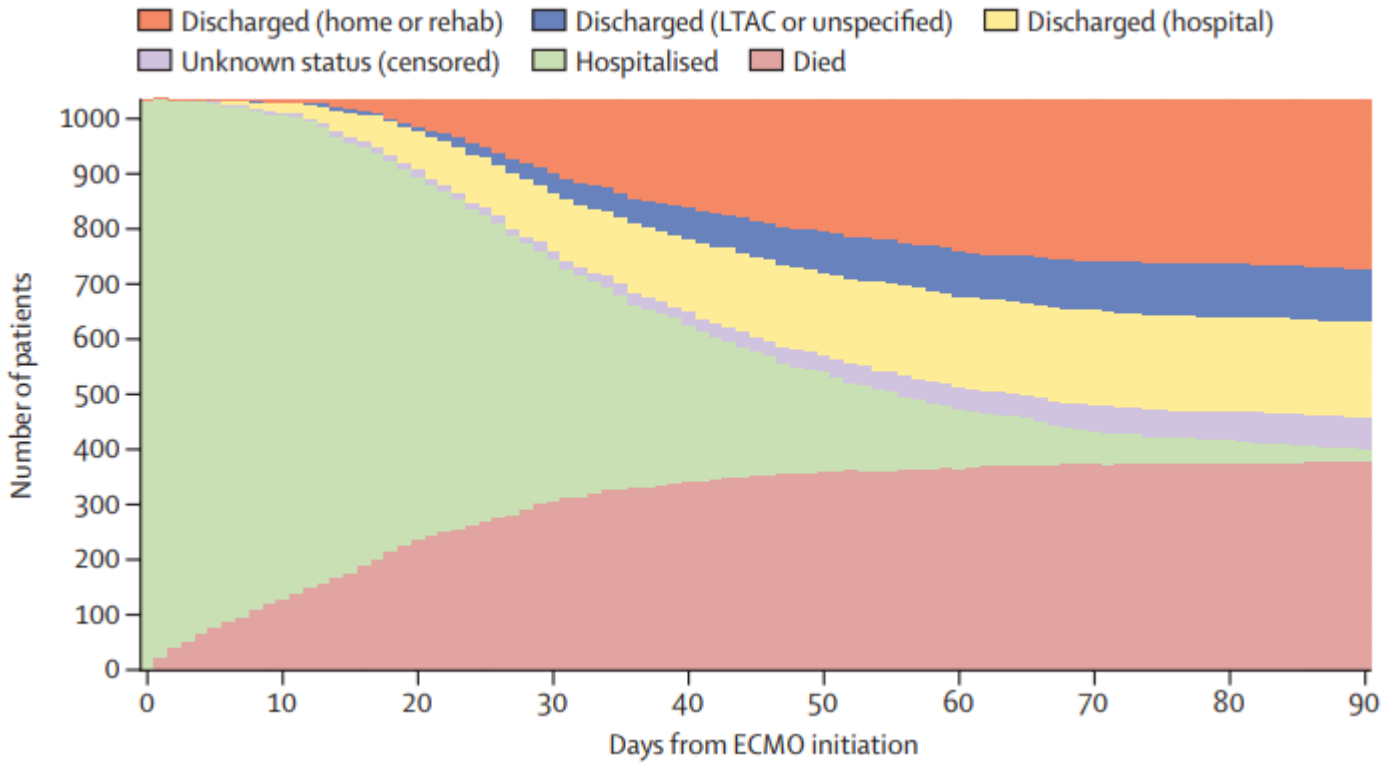
| | Full cohort (n=1035) | ARDS cohort* (n=779) |
|---|---|---|
| Age (years) | 49 (41–57) | 50 (42–57) |
| BMI (kg/m²)† | 31 (27–37) | 32 (28–37) |
| Sex‡ | | |
| Male | 764 (74%) | 572 (74%) |
| Female | 269 (26%) | 206 (26%) |
| Pre-ECMO comorbidities | | |
| No comorbidity | 311 (30%) | 243 (31%) |
| Cancer | 11 (1%) | 10 (1%) |
| Immunocompromised | 24 (2%) | 21 (3%) |
| Diabetes | 245 (24%) | 187 (24%) |
| Pre-existing cardiac disease | 24 (2%) | 13 (2%) |
| Pre-existing respiratory disease | 29 (3%) | 21 (3%) |
| Pre-existing renal insufficiency | 21 (2%) | 14 (2%) |
| Asthma | 110 (11%) | 91 (12%) |
| Pregnancy | 22 (2%) | 13 (2%) |
| Obesity (BMI >30 kg/m²) | 487 (47%) | 362 (47%) |
| Acute illness | | |
| ARDS | 819 (79%) | 775 (100%) |
| Acute heart failure | 50 (5%) | 25 (3%) |
| Myocarditis | 22 (2%) | 7 (1%) |
| Acute kidney injury | 301 (29%) | 247 (32%) |

| | Full cohort (n=1035) | | ARDS cohort* (n=779) | |
|---|---|---|---|---|
| | N | Median (IQR) or n (%) | N | Median (IQR) or n (%) |
| Non-invasive ventilation | | | | |
| Non-invasive ventilation before intubation | 1032 | 606 (59%) | 776 | 434 (56%) |
| BiPAP | 1032 | 185 (18%) | 776 | 119 (15%) |
| CPAP | 1032 | 140 (14%) | 776 | 80 (10%) |
| HFNC | 1032 | 357 (35%) | 776 | 285 (37%) |
| Pre-ECMO intubation (days) | 914 | 4·0 (1·8–6·4) | 688 | 4·3 (2·0–6·5) |
| Conventional ventilation† | 951 | 942 (99%) | 729 | 721 (99%) |
| PEEP (cm $H_2O$) | 868 | 14 (12–16) | 661 | 15 (12–18) |
| PIP (cm $H_2O$) | 699 | 33 (30–38) | 532 | 34 (30–38) |
| $FiO_2$ | 888 | 1·0 (0·90–1·0) | 672 | 1·0 (0·90–1·0) |
| $PaO_2$:$FiO_2$ (mm Hg) | 868 | 72 (59–94) | 657 | 72 (60–93) |
| $PaCO_2$ (mm Hg) | 896 | 60 (50–74) | 678 | 60 (50–74) |
| Pre-ECMO support | | | | |
| Prone positioning | 1019 | 612 (60%) | 766 | 464 (61%) |
| Neuromuscular blockade | 1015 | 729 (72%) | 762 | 567 (74%) |
| Inhaled pulmonary vasodilators | 1019 | 293 (29%) | 766 | 242 (32%) |
| Any vasoactive support | 1015 | 606 (60%) | 758 | 447 (59%) |
| Norepinephrine | 1015 | 561 (55%) | 762 | 416 (55%) |

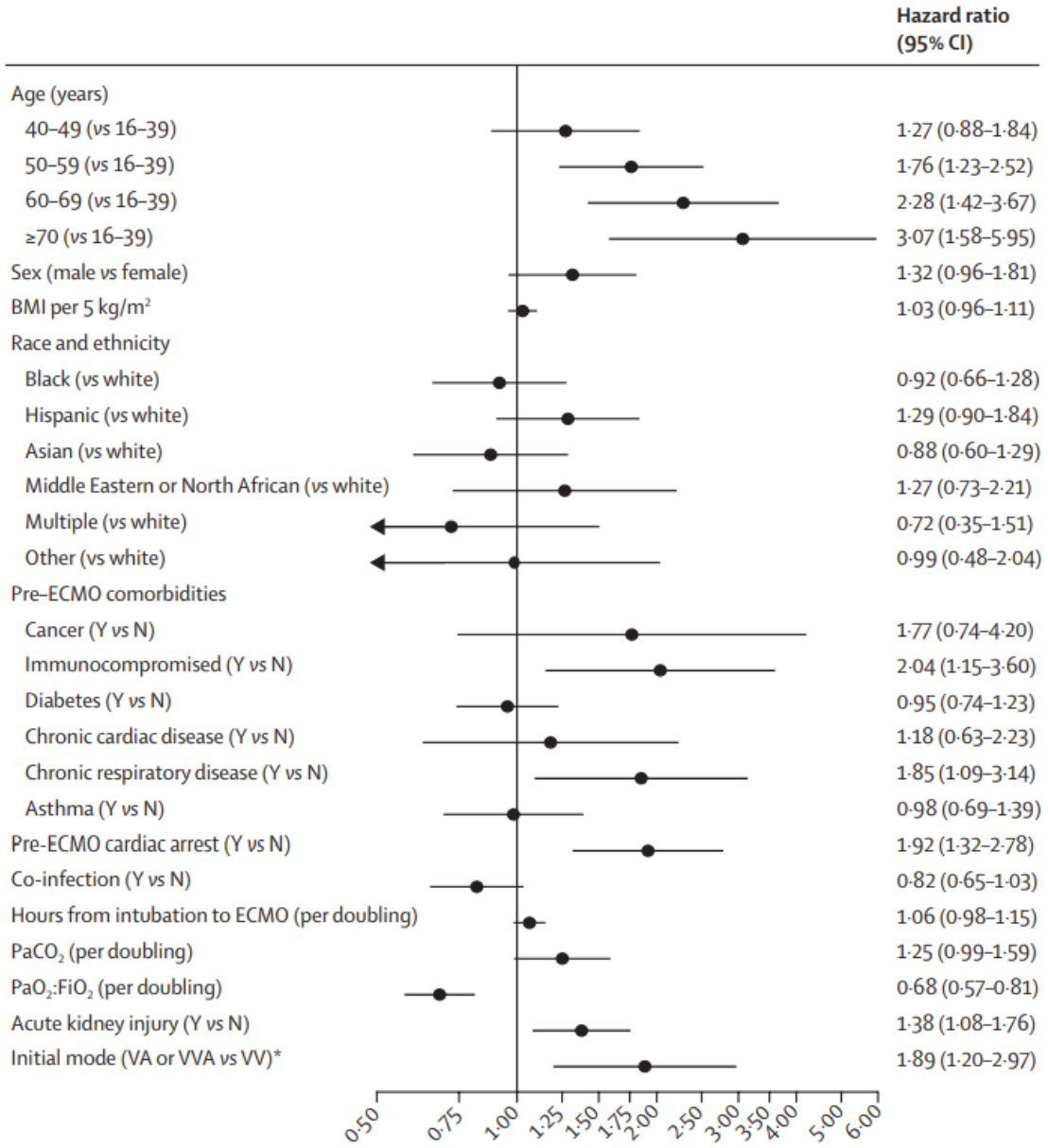
Barbaro R, et al. Lancet 2020;396:1071-78.

# ECMO for COVID-19 Infection: Outcomes

| | Full cohort (n=1035) | ARDS cohort* (n=779) |
|---|---|---|
| Patient status at study completion | | |
| Discharged alive to home or acute rehabilitation centre | 311 (30%) | 262 (34%) |
| Discharged alive to long-term acute care centre or unspecified location | 101 (10%) | 79 (10%) |
| Discharged to another hospital | 176 (17%) | 97 (12%) |
| Remain in the hospital (discharged from ICU) | 11 (1%) | 10 (1%) |
| Remain in the ICU | 56 (5%) | 40 (5%) |
| In-hospital death | 380 (37%) | 291 (37%) |
| Tracheostomy† | 444 (44%) | 353 (47%) |

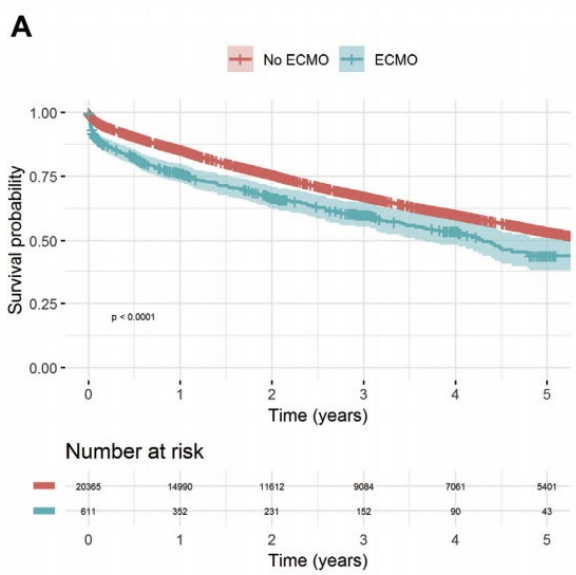


# ECMO for COVID-19 Infection: Risk Factors for Mortality

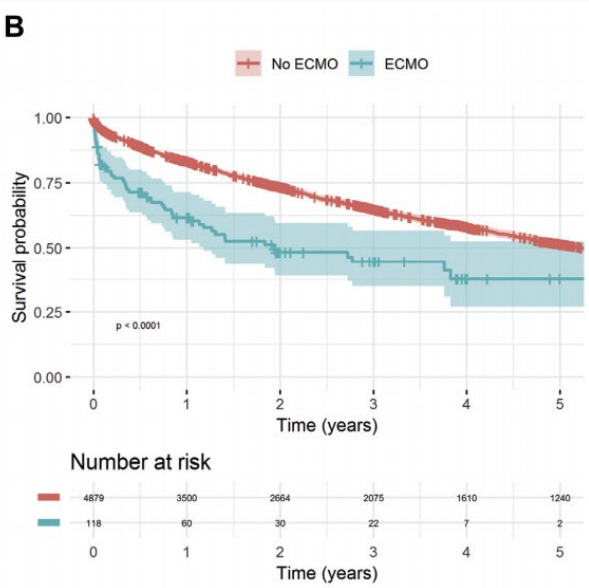


# ECMO Outcomes By Center Volume

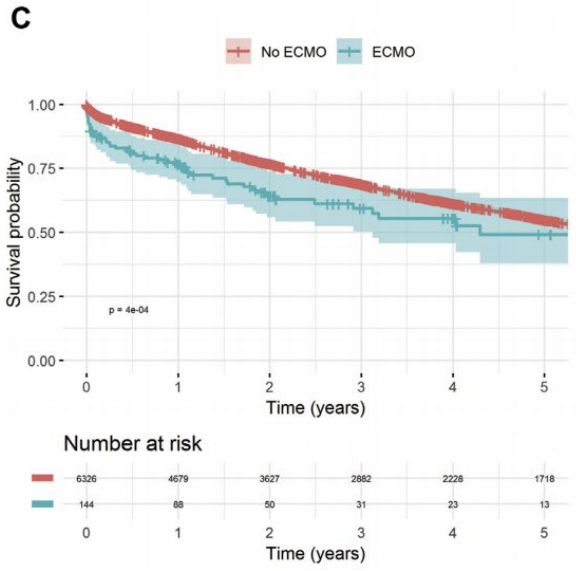
**Overall**



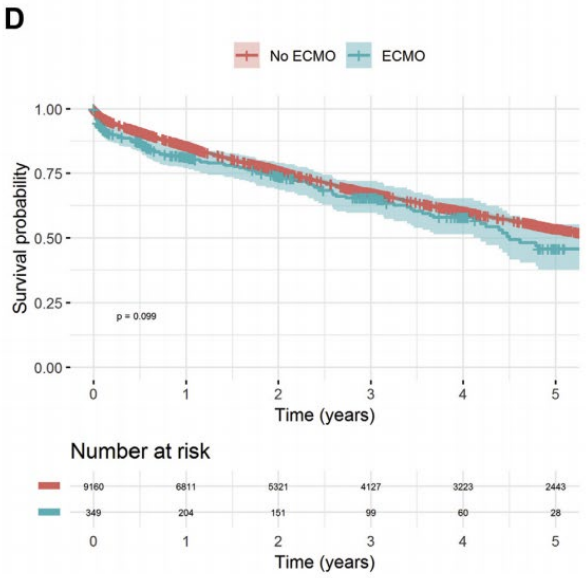

**Low (<25)**




**Moderate (25-49)**




**High (>50)**




Halpern AL, et al. Ann Thorac Surg. 2019;108(2):350-7.

# Timing of Recovery from COVID-19

| | Overall (n = 300) | Survivor 30 days post admission (n = 143; 47.7%) | Nonsurvivor 30 days post admission (n = 157; 52.3%) | Relative mortality risk[€] (95% CI) | p-value[¥] |
|---|---|---|---|---|---|
| Therapy: | | | | | |
| Mechanical ventilation—No. (%) | 274 (91.3) | 121 (84.6) | 153 (97.5) | 3.63 (1.5,9.00) | <.0001 |
| *No. days—median [range]* | *9.5 [1-58]* | *11 [1-58]* | *8 [1-29]* | | |
| No mechanical ventilation (HFNC) | 26 (7.7) | 22 (15.4) | 4 (2.6) | .28 (.11,.68) | <.0001 |
| ECMO | 2 (.6) | 2 (1.4) | 0 (0) | | |
| NM blockade use | 131 (43.7) | 40 (28.0) | 91 (58.0) | 1.78 (1.43,2.22) | <.0001 |
| NM blockade use in MV patients | 131/274 (47.8) | 40/121 (33.1) | 91/153 (59.5) | 1.60 (1.29,1.99) | <.0001 |
| *No. days—median [range]* | *2 [1-20]* | *3 [1-20]* | *2 [1-13]* | | |
| Prone positioning—No. (%) | 174 (58.0) | 75 (52.4) | 99 (63.1) | 1.24 (0.98,1.55) | .06 |
| *No. days—median [range]* | *3 [1-31]* | *3 [1-31]* | *3 [1-16]* | | |

Chand S, et al. J Intensive Care Med 2020;35(10):963-970.

# Timing of Recovery from COVID-19

| | Overall (n = 300) | Survivor 30 days post admission (n = 143; 47.7%) | Non-survivor 30 days post admission (n = 157; 52.3%) | Relative mortality risk[€] (95% CI) | p-value[¥] |
|---|---|---|---|---|---|
| ARDS—No. (%) | | | | | |
| Not present | 25 (8.3) | 21 (14.9) | 4 (2.5) | *reference* | <.0001 |
| Mild | 13 (4.3) | 11 (7.8) | 2 (1.3) | .96 (.20,4.6) | .96 |
| Moderate | 106 (35.3) | 51 (36.2) | 55 (34.6) | 3.18 (1.3,8.0) | .01 |
| Severe | 156 (52.0) | 58 (41.1) | 98 (61.6) | 3.89 (1.6,9.6) | .003 |
| Acute kidney injury (AKI) | | | | | |
| AKI at admission or during ICU—No. (%) | 230 (76.7) | 93 (65.0) | 138 (87.9) | 2.17 (1.46,3.23) | <.0001 |
| Development of AKI during ICU | 108 (36.0) | 50 (35.0) | 58 (37.0) | 1.04 (0.83,1.3) | .72 |
| Renal replacement therapy | 133 (44.3) | 51 (35.7) | 82 (52.2) | 1.37 (1.11,1.7) | .004 |
| In patients with AKI (n = 230) | 117/230 (50.9) | 47/93 (50.5) | 70/137 (51.1) | 1.01 (.74,1.39) | .93 |
| Died in hospital—No. (%) | 157 (52.3) | 0 (0) | 157 (100) | | |
| Discharged from ICU—No. (%) | 141 (47.0) | 141 (98.6) | 0 (0) | | |
| *Total hospital LOS, days—median [range]* | *15 [1-58]* | *25 [2-58]* | *11 [1-30]* | | |
| 0-5 days—No. (%) | 28 (9.3) | 8 (5.6) | 20 (12.7) | | |
| 6-10 days | 69 (23.0) | 13 (9.1) | 56 (35.7) | | |
| 11-15 days | 60 (20.0) | 24 (16.8) | 36 (22.9) | | |
| 16-20 days | 36 (12.0) | 13 (9.1) | 23 (14.7) | | |
| 21-25 days | 27 (9.0) | 16 (11.2) | 11 (7.0) | | |
| 26-30 Days | 26 (8.7) | 15 (10.5) | 11 (7.0) | | |
| >30 days | 54 (18.0) | 54 (37.8) | 0 (0) | | |

# Radiographic Follow-Up of Patients with COVID-19

| | |
|---|---|
| Age, yr | 46.6 ± 13.9 (14–70) |
| Male/female | 21/30 |
| Smoking | 3 (5.9) |
| Comorbidity | 8 (15.9) |
| Diabetes | 4 (7.8) |
| Hypertension | 7 (13.7) |
| Coronary heart disease | 1 (2) |
| Pregnancy | 1 (2) |
| Symptoms 4 wk after discharge | |
| Cough | 8 (15.7) |
| Sputum | 2 (3.9) |
| Throat discomfort | 3 (5.9) |

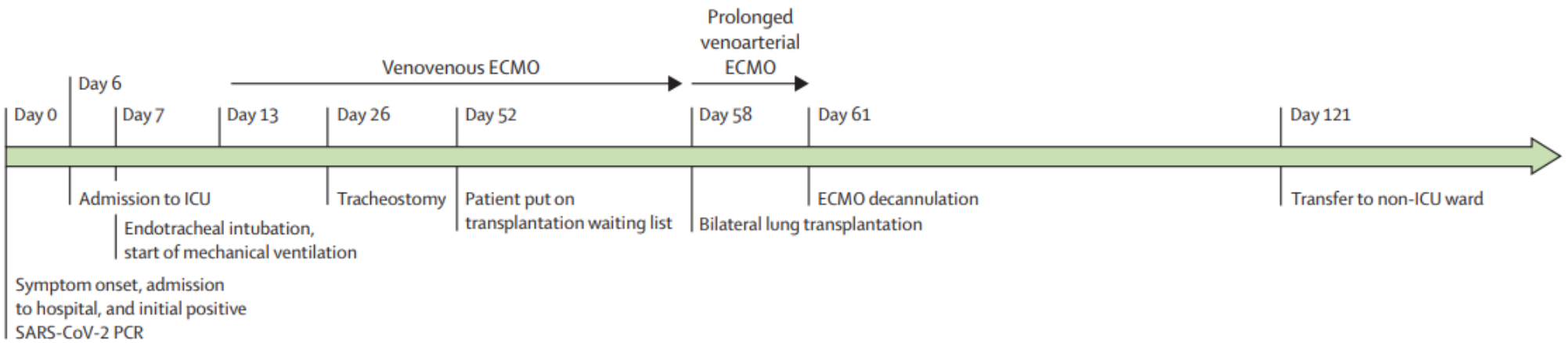
| | Last CT Scan before Discharge [*n* (%)] | First Follow-Up CT Scan after Discharge [*n* (%)] | Second Follow-Up CT Scan after Discharge [*n* (%)] |
|---|---|---|---|
| GGO | 9 (17.7) | 5 (9.8) | 5 (9.8) |
| Multiple GGOs | 41 (80.4) | 32 (62.8) | 12 (23.5) |
| Diffuse GGO | 1 (2.0) | 1 (2.0) | 0 (0) |
| Consolidation | 25 (49.0) | 4 (7.8) | 1 (2.0) |
| Interlobular septal thickening | 41 (80.4) | 25 (49.0) | 18 (35.3) |
| Subpleural lines | 15 (29.4) | 11 (21.6) | 4 (7.8) |
| Irregular lines | 21 (41.2) | 16 (31.4) | 8 (15.7) |
| Bronchiectasis | 17 (33.3) | 6 (11.8) | 2 (3.9) |
| Reticular pattern | 2 (3.9) | 1 (2.0) | 0 (0) |

65% of discharged patients had full resolution of radiographic findings 4-weeks post discharge

Liu C, et al. Ann Am Thorac Soc 2020;17:1231-1237

# Lung transplantation for COVID-19-associated acute respiratory distress syndrome in a PCR-positive patient

**A**



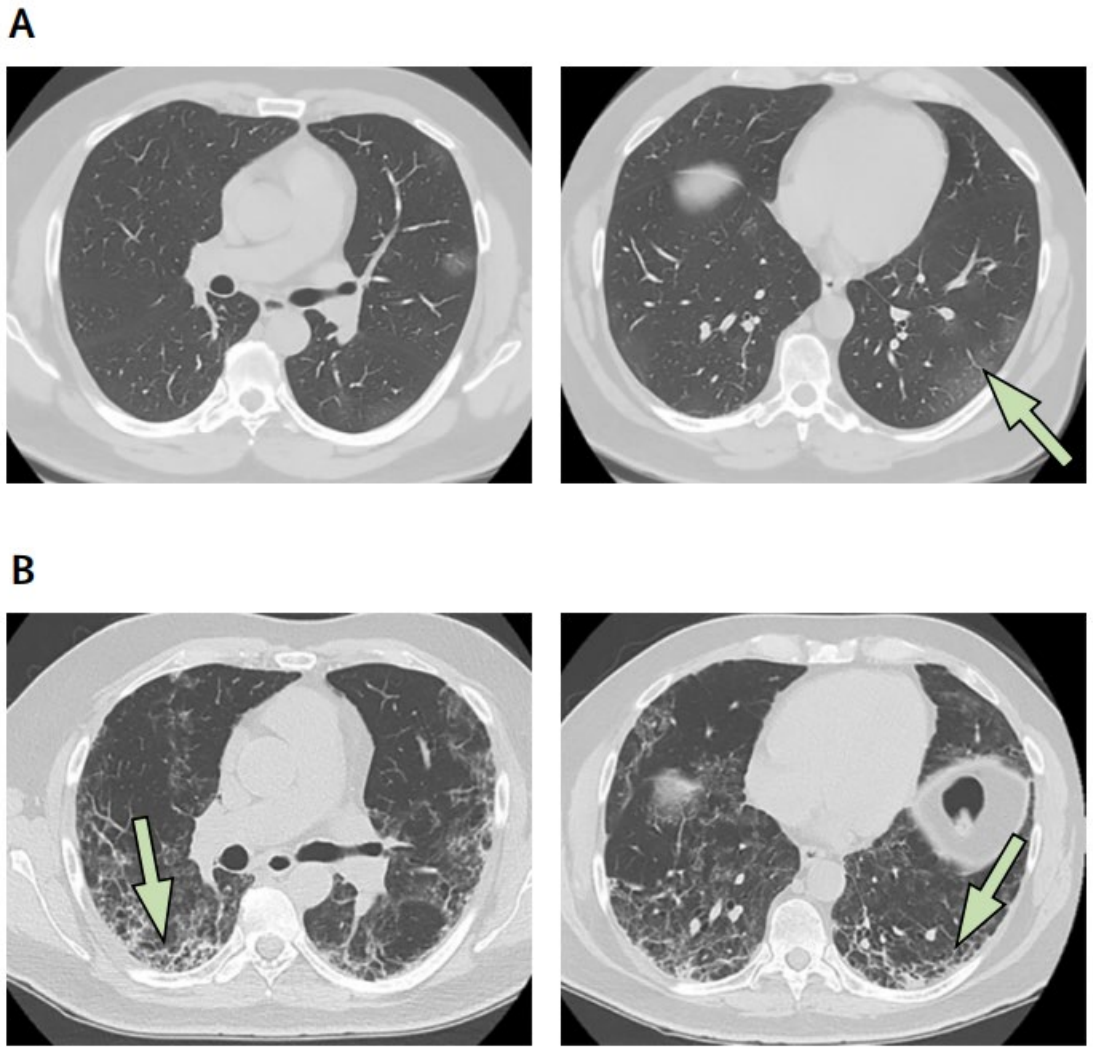

**B**

| Days since initial positive SARS-CoV-2 PCR | 0 | 17 | 23 | 29 | 31 | 36 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 | 65 | 66 | 67 | 68 | 69 | 70 | 71 | 72 | 73 | 74 | 75 | 76 | 88 | 95 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nasopharyngeal swab | + | + | + | + | + | + | + | | | | | | | | | | | + | | − | + | | − | | + | | + | | − | | − | | − | | − | | − |
| Bronchoalveolar lavage | | | | | | | | | | | | + | | | | | | − | | | − | | | + | | + | − | | | | | | | | − | − | |
| Ct value | 27 | 21 | 23 | 32 | 32 | 29 | 39 | | | | | 34 | | | | | | 33 | | 0 | 36 | | 0 | 36 | 39 | 39 | 39 | | 0 | | 0 | | 0 | 0 | 0 | 0 | 0 |
| Vero cell culture | | | | | | | – | | | | | | | | | | | | | | | | | – | | | | | | | | | | | | |

Transplantation

Lang C, et al. Lancet Respir Med 2020;8:1057-60.

# Pulmonary Fibrosis from COVID-19?




Spagnolo P, et al. Lancet Respir Med 2020;8:750-52.

# UNOS Diagnosis Codes

- The following codes for lung transplant candidates will be available on October 28th
  - COVID-19: ARDS
  - COVID-19: Pulmonary fibrosis

https://unos.org/news/covid-19-organ-failure-in-candidate-listings-in-unet-coming-soon/

# ISHLT Recommendations

- Lung transplantation will be appropriate for a small minority of patients with COVID-19
- Proceed with listing for otherwise healthy patient with COVID-19 related respiratory failure in carefully selected cases:
  - At least 28 days since onset of severe lung injury
  - Negative SARS-CoV-2 PCR test separated at least 24-48 hours
  - Presence of single organ failure
  - Nutritional status and rehabilitation potential of patient
  - Other listing criteria based on center policies are met

https://ishlt.org/ishlt/media/documents/SARS-CoV-2_Guidance-for-Cardiothoracic-Transplant-and-VAD-centers.pdf

# Closing Thoughts

- Lung transplant likely has only a small role in COVID-associated ARDS
  - Too sick
    - Comorbidities, age, multiorgan dysfunction, poor rehab potential
  - Recovery
    - What is a sufficient amount of time to allow for recovery?
      - 4-6 weeks? Longer?
  - Is a negative PCR necessary?
  - Should be limited to large volume centers with sufficient bridging experience
  - Guidance should evolve with experience
- Need for delayed transplant for progressive fibrosis is unclear
- Overall need will be impacted by infection prevention measures