COVID-19 induced lung damage necessitating lung transplantation

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NMLUNG

Northwestern Medicine®

Science TM, Dec 2020

THE LANCET
Respiratory Medicine
Volume 9, Issue 5, May 2021, Pages 487-497

Articles

Early outcomes after lung transplantation for severe COVID-19: a series of the first consecutive cases from four countries

Lancet RM, Mar 2021

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Article | Published: 11 January 2021

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Circuits between infected macrophages and T cells in SARS-CoV-2 pneumonia

Rogan G et al, ***Nature***, Jan 2021

COVID-19 – Best understood as respiratory illness

Geleris J et al, NEJM 2020

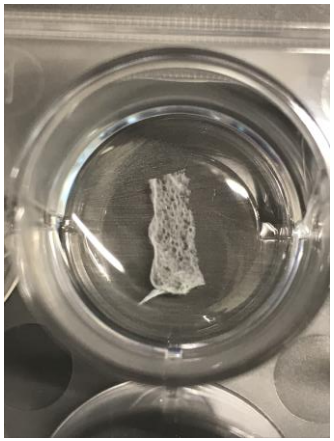
6-10% progress to ARDS and require ventilation

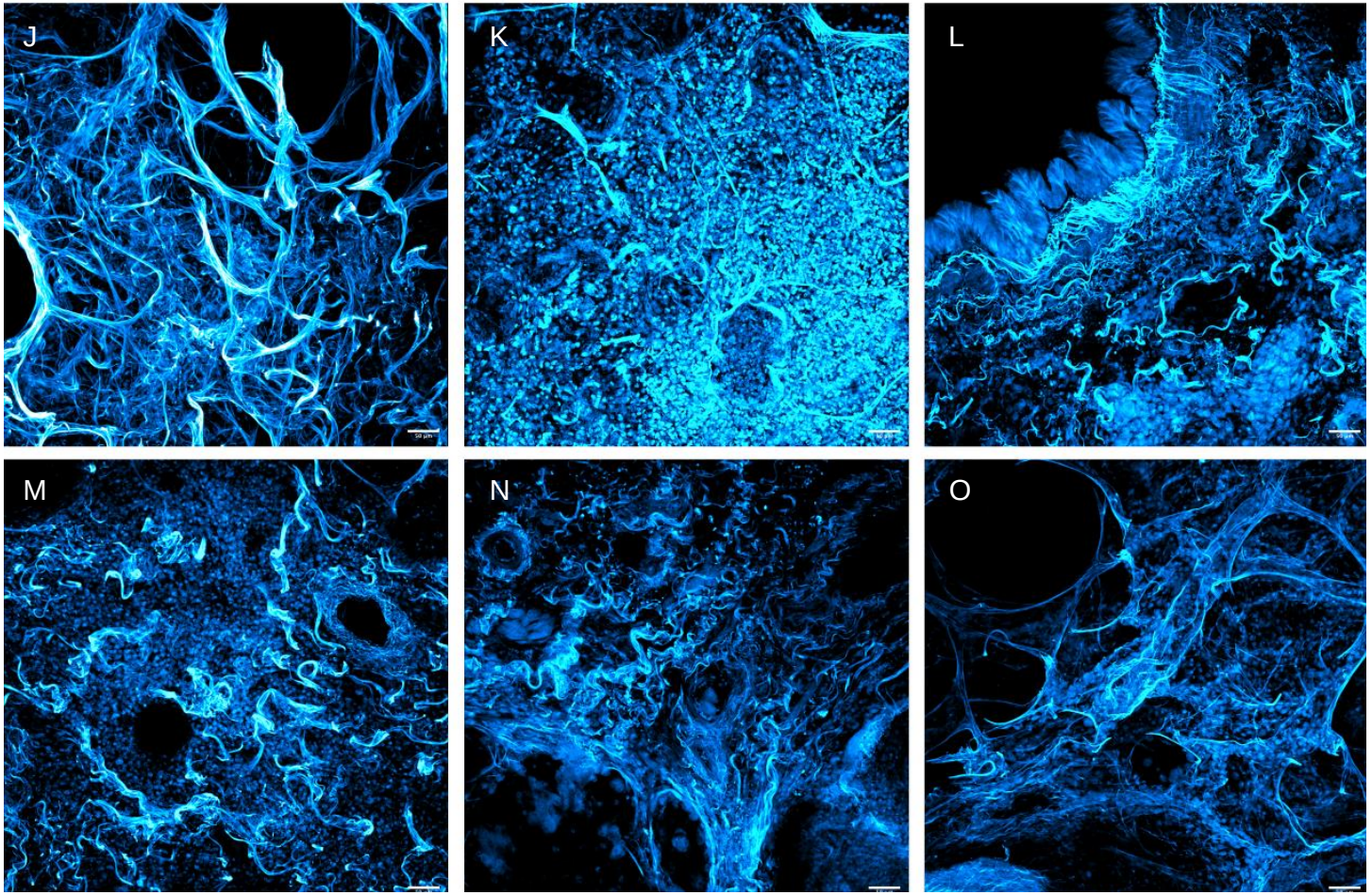
Richardson S et al, JAMA 2020

Mortality with severe COVID-19 ARDS > 40%

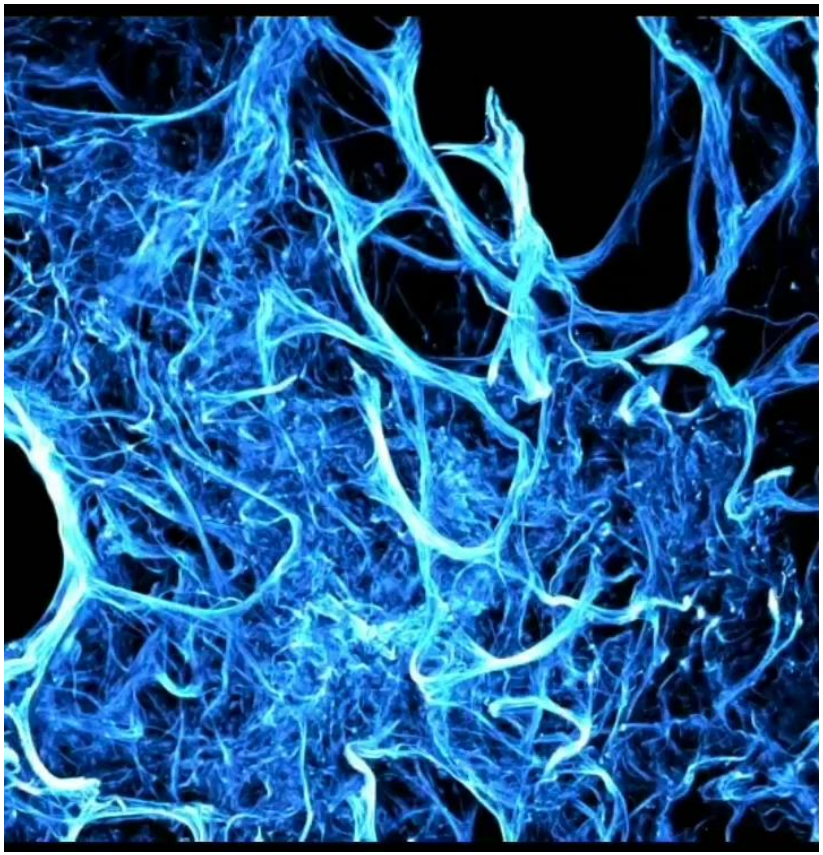
Group RC et al, NEJM 2020
Beigel JH, NEJM 2020

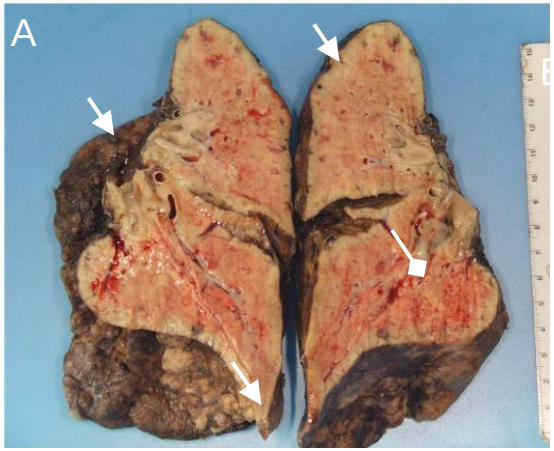
Matrix imaging reveals structural framework distortion with severe COVID-19





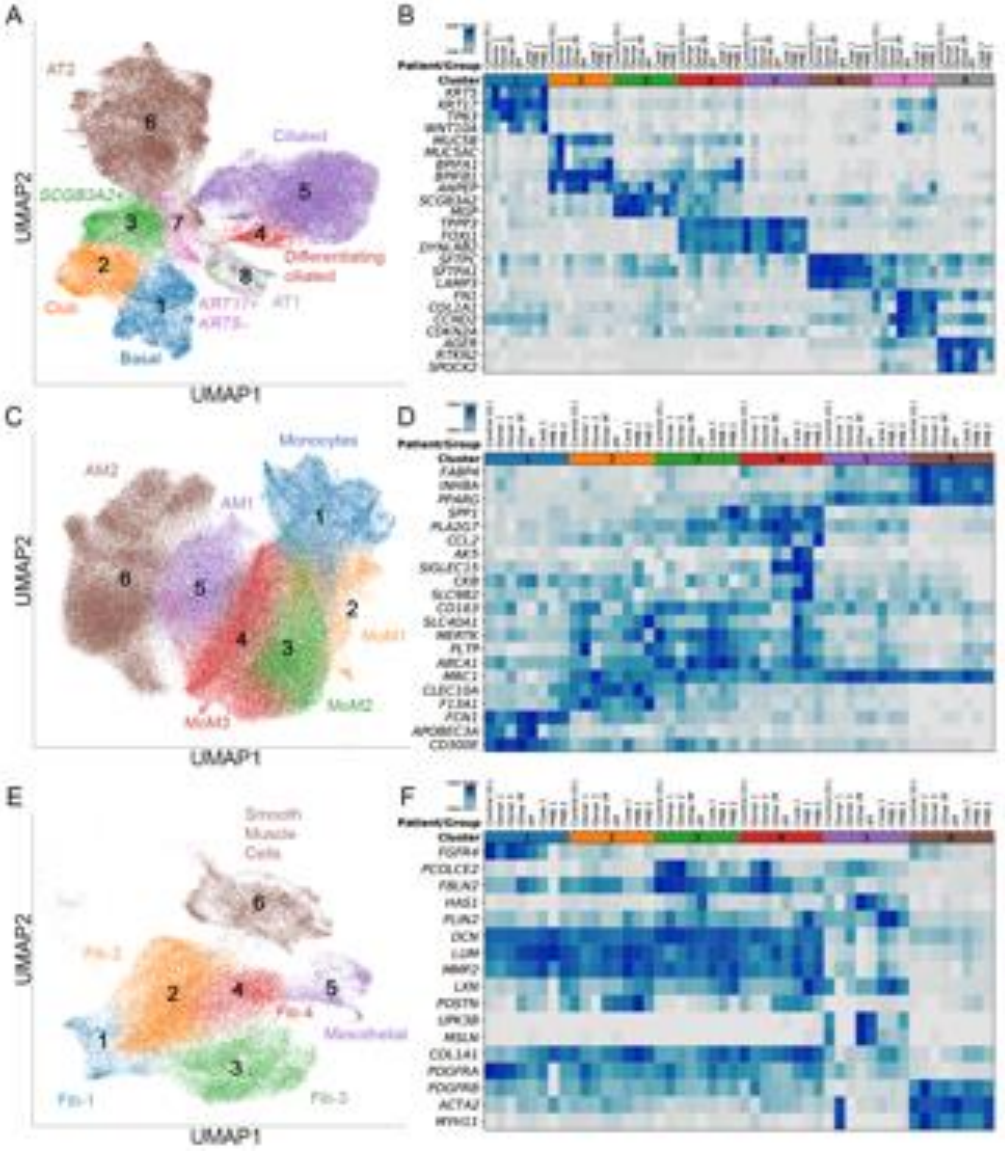
Bharat et al, STM, 2020



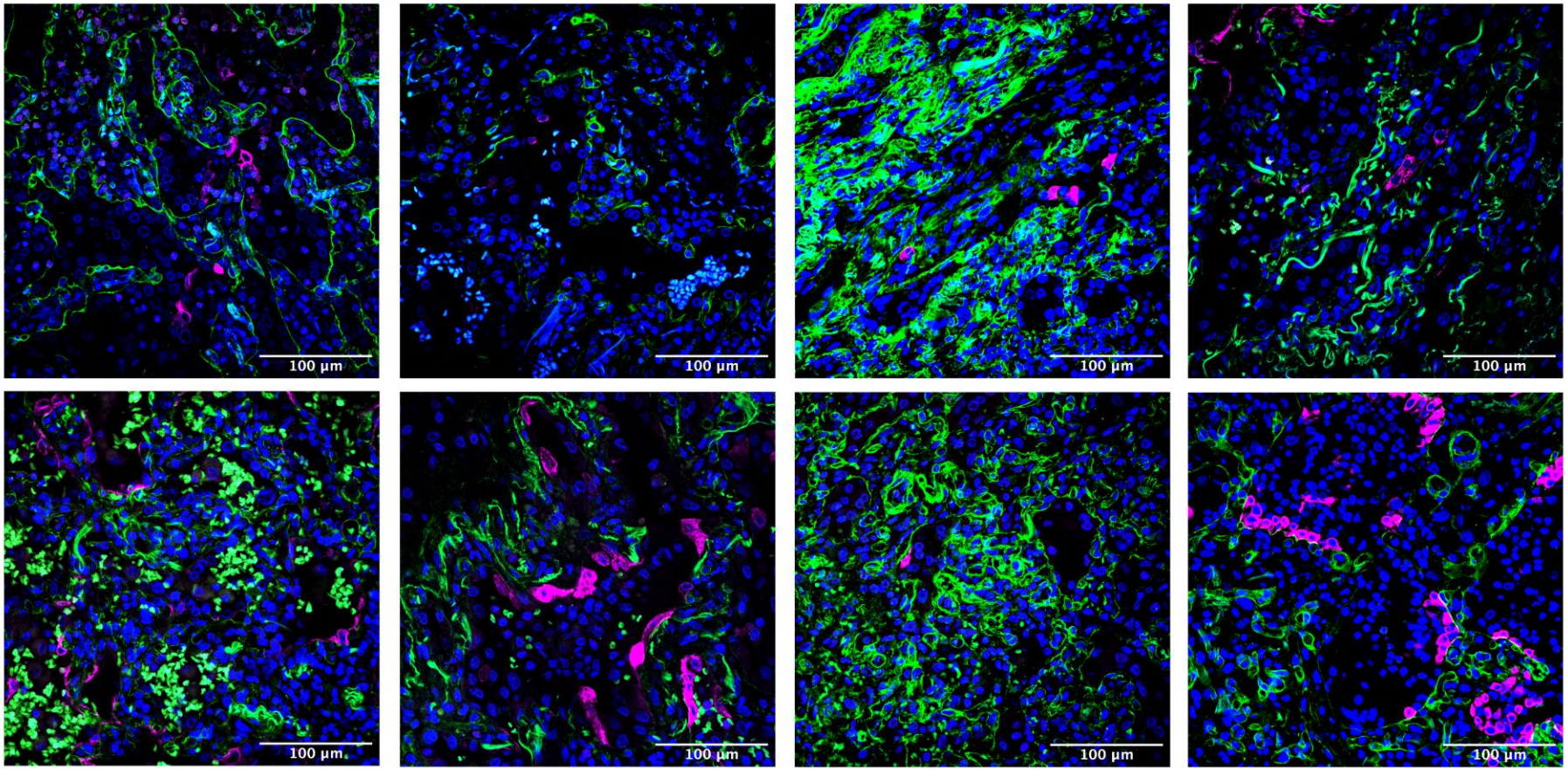


Bharat et al, ***Science TM,*** Dec 2020

Machine (transfer) learning analysis of scRNAseq in COVID-19 lungs

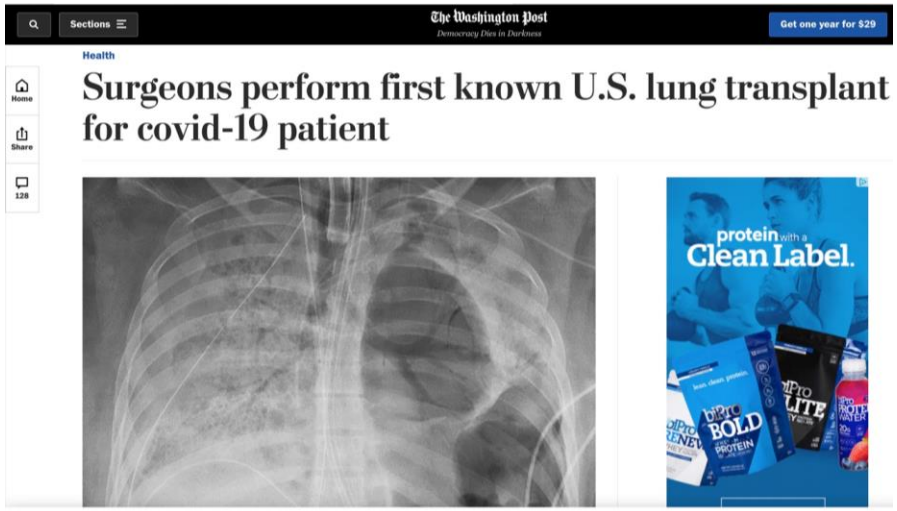


KRT17+ cells colocalized with Col1A1 fibroblasts

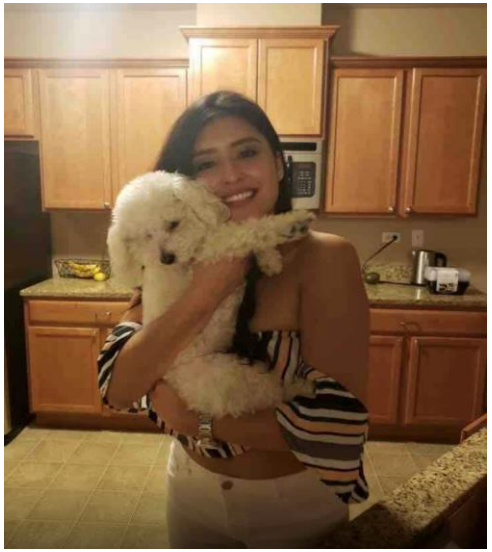


First COVID-19 Double Lung Transplant in the US

- June 5th 2020



28 YR OLD F
WELL-CONTROLLED NEUROMYELITIS OPTICA



With permission

Intubation: Day 1 of hospitalization

ECMO within 1 week

Serratia pneumonia ~3 weeks with necrotic cavity

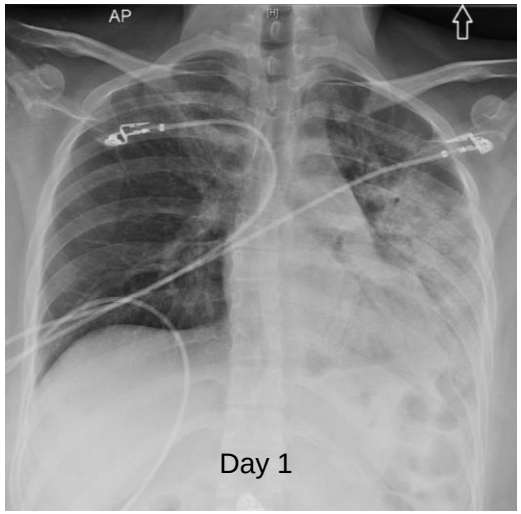
Right heart failure – Congestive hepatitis

Acute Kidney Injury

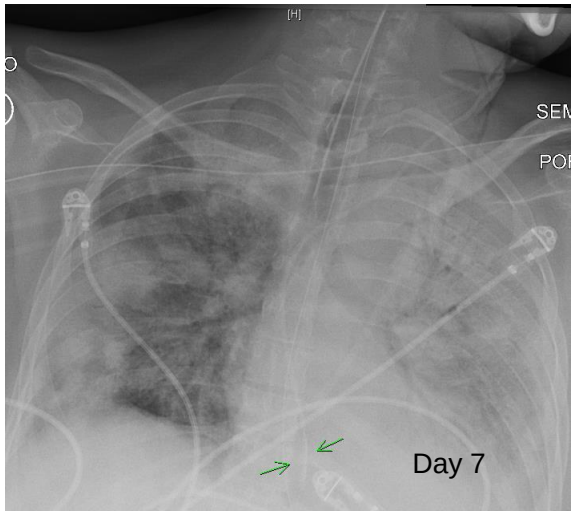
Liver laceration – emergent laparotomy and multiple blood transfusions

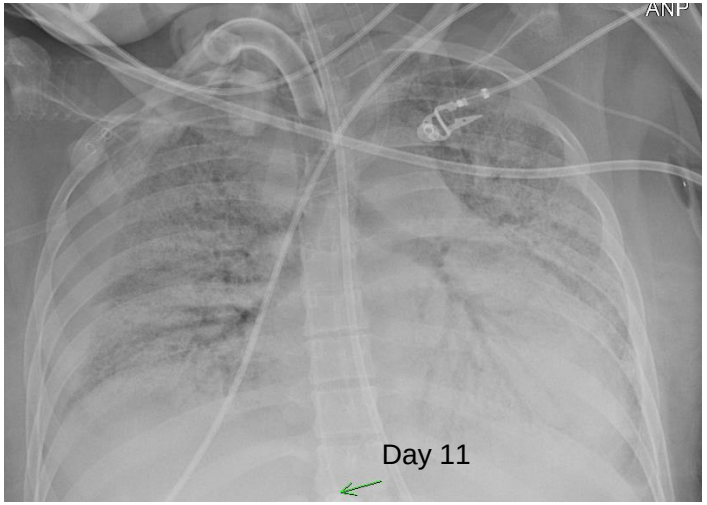
Vasodilatory shock

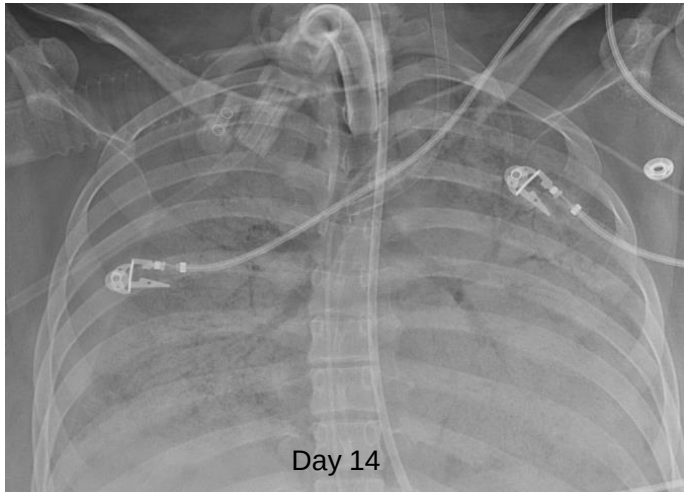
Negative COVID-19 PCR

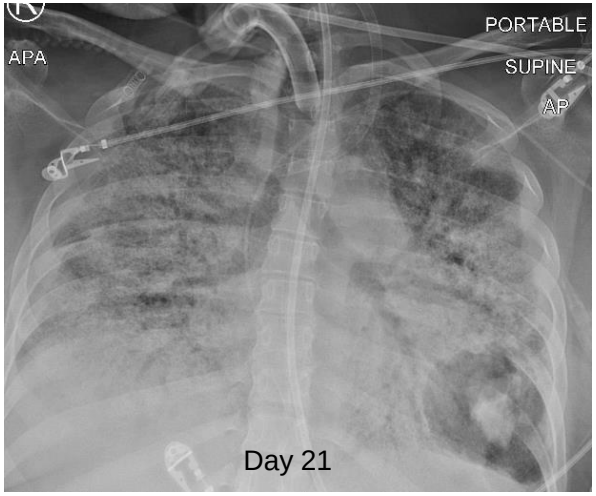


Day 1

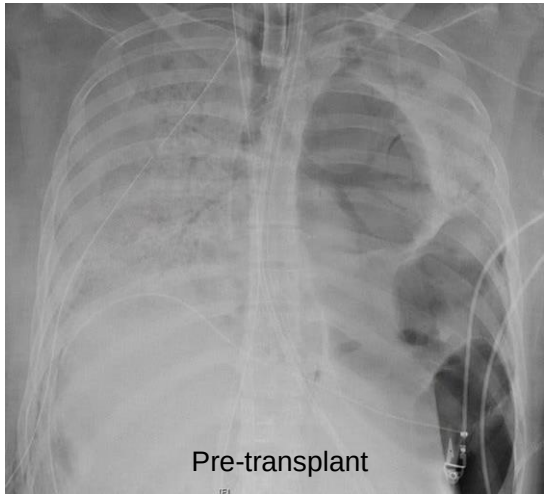

Day 7

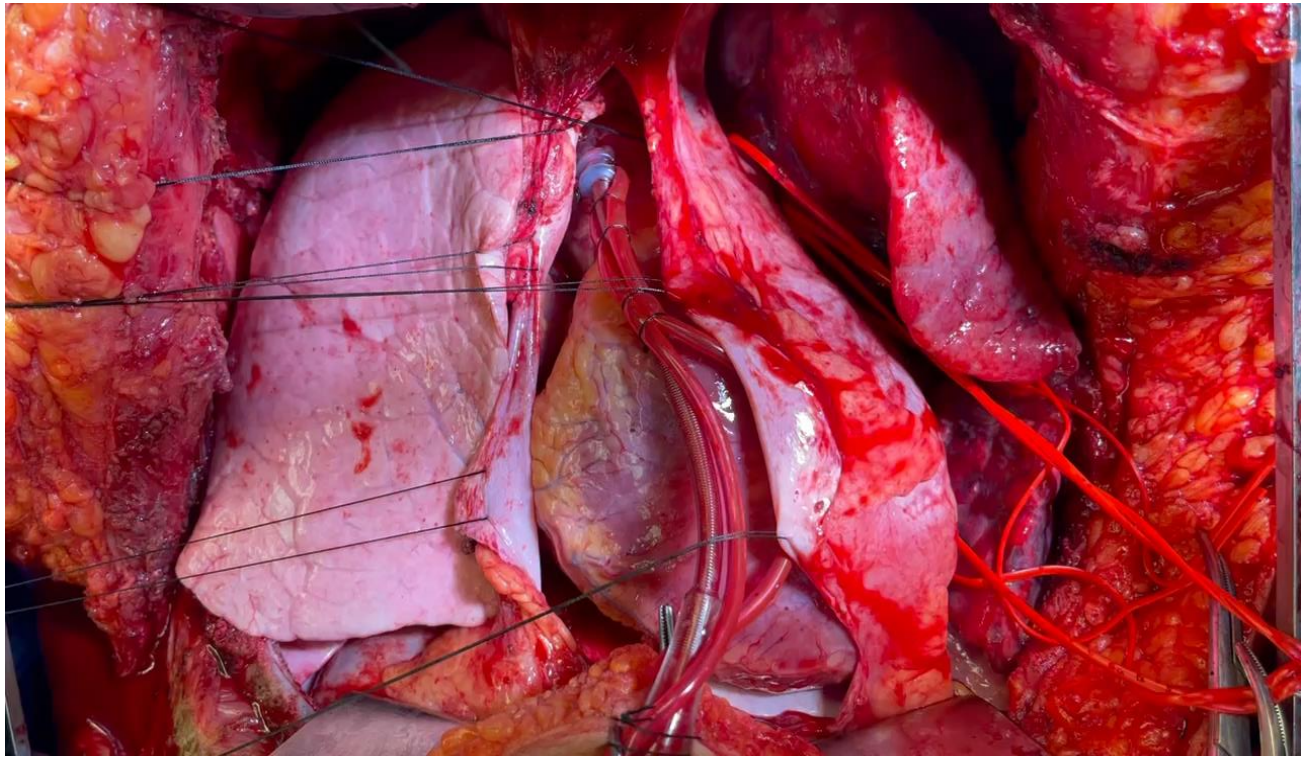

Day 11


Day 14



Day 21


Pre-transplant



Post op day 10

Post op day 17

With permission

Post-transplant outcomes

Transplants till date 31
Included in study 21

General Observations

All COVID-19 patients received double lung transplants using VA ECMO

Over 81% were ECMO bridge to transplant

No significant difference in waitlist mortality in COVID-19 and non-COVID-19 groups

No change in waitlist mortality or waitlist time in non-COVID-19 group over time

Median time from onset of severe COVID-19 ARDS to transplant 114 days

100% survival till date

No recurrence of SARS-CoV-2 or nosocomial pathogens

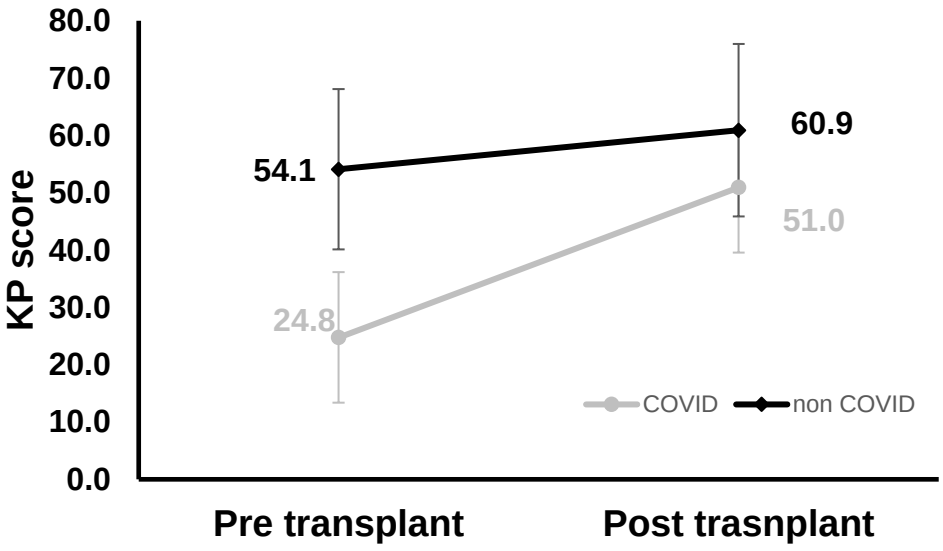
Covid-19 recipients have increased post-op complications

Variable	Overall (n=77)	Non-COVID (n=56)	COVID (n=21)	*P* value
OR time (hours)	7.8 ± 1.8	7.2 ± 1.7	9.3 ± 1.1	<0.01
Intra-op blood transfusion				
pRBC	3.3 ± 5.1	1.1 ± 1.8	9.4 ± 6	<0.01
FFP	1.1 ± 2.5	0.3 ± 1.1	3.1 ± 3.9	<0.01
Plt	0.6 ± 1.4	0.2 ± 0.8	1.8 ± 2.1	<0.01
Intraop VA ECMO time (hours)	3.2 ± 1	3.1 ± 1.1	3.4 ± 0.8	0.23
Intraop VA ECMO use	54 (70.1%)	33 (58.9%)	21 (100%)	<0.01
Ischemic time (hours)	5.1 ± 1.3	4.8 ± 1.4	5.7 ± 0.8	<0.01

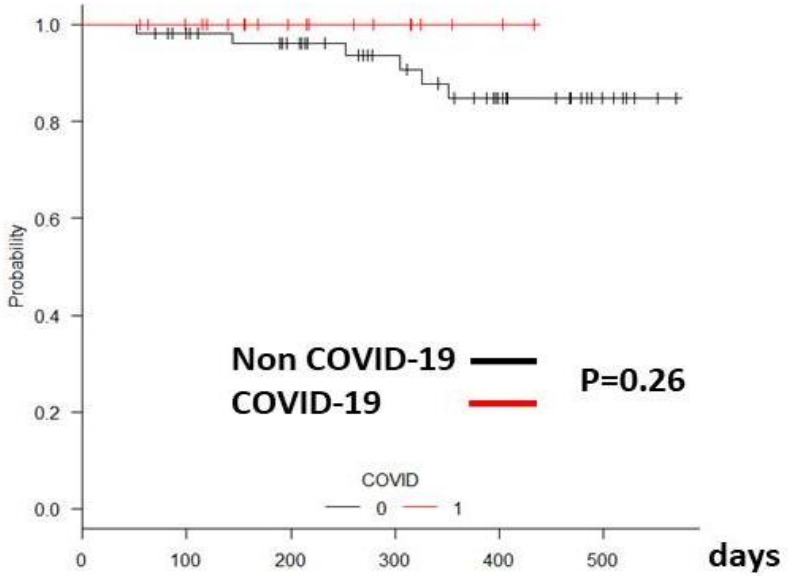
Variable	Overall (n=77)	Non-COVID (n=56)	COVID (n=21)	*P* value
Post transplant VV ECMO Use	13 (16.9%)	5 (8.9%)	8 (38.1%)	<0.01
Continuous VV ECMO Use	10 (13.0%)	2 (3.6%)	8 (38.1%)	<0.01
New Onset VV ECMO Use	3 (3.9%)	3 (5.4%)	0 (0.0%)	0.56
Post transplant VV ECMO use (days)	6.4 ± 10.9	6.7 ± 13.5	6.0 ± 5.4	0.87
AKI	37 (48.1%)	21 (37.5%)	16 (76.2%)	<0.01
Dialysis	13 (16.9%)	6 (10.7%)	7 (33.3%)	0.04
PGD	17 (22.1%)	8 (14.3%)	9 (42.9%)	0.01
ICU stay (days)	14.8 ± 12.1	12.8 ± 12.2	20.1 ± 10	0.01
Post discharge Acute rejection	22 (28.5%)	22 (39.2%)	0 (0%)	<0.01
Post transplant ventilator (days)	6.4 ± 9.6	4.6 ± 9.2	11.3 ± 9.1	0.01
Pleural drainage (days)	16.9 ± 10.8	14.8 ± 9.8	22.6 ± 11.4	0.01
Hospital stay (days)	27.4 ± 29.5	25.1 ± 32.2	33.6 ± 20.3	0.17

Post-transplant outcomes

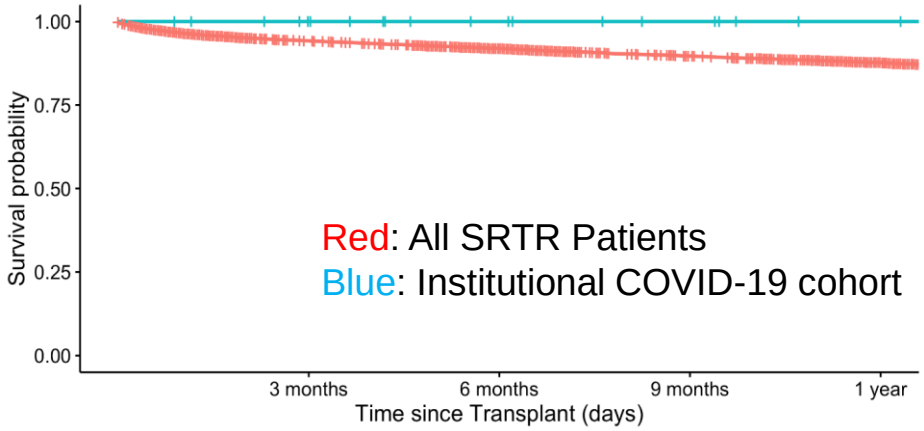
Performance status



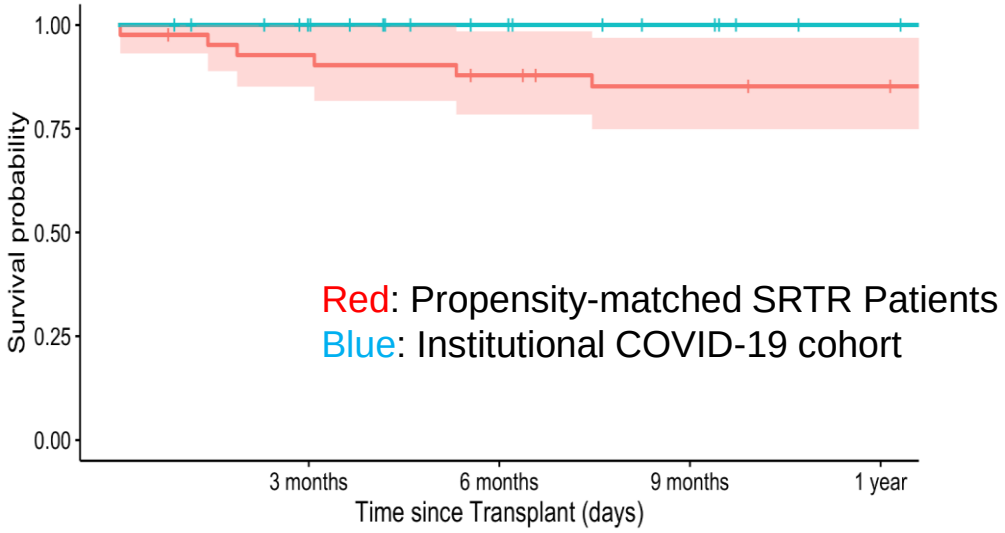
Overall survival



Recipients with COVID-19 have superior post-transplant outcomes



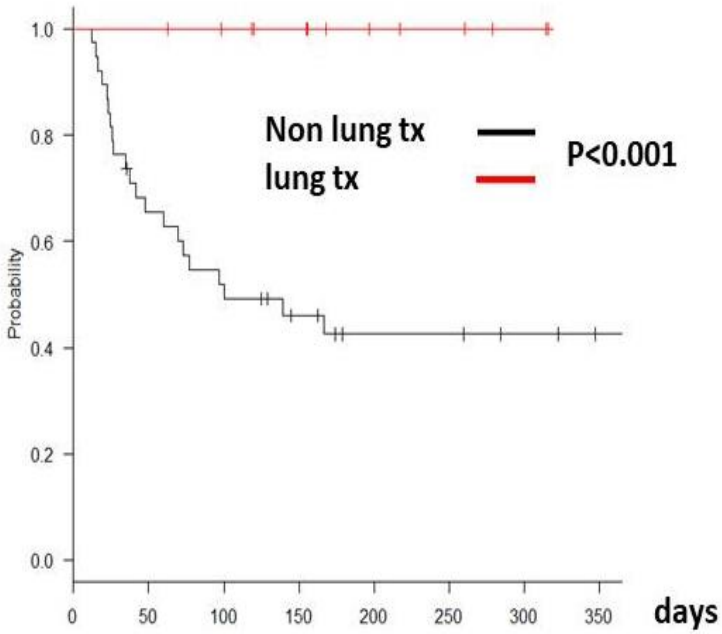
P<0.01



Survival to discharge in COVID-19 patients requiring ECMO support

Probability of weaning from ECMO

Days	overall	30 days	60 days	90 days
Probability (%)	23.3	10.3	3.8	0.0



Predictors of postoperative mortality in COVID-19 patients supported on ECMO for over 30 days using Cox multivariate analysis

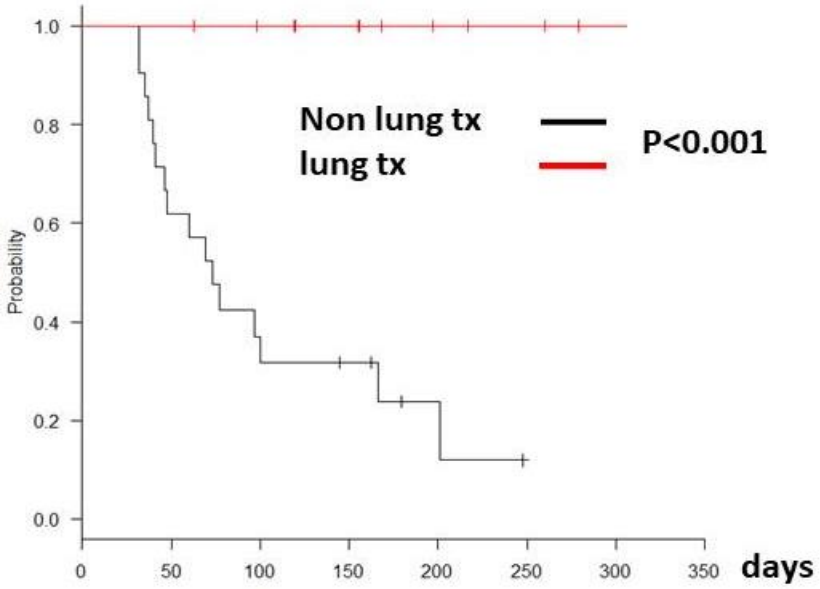
Variable	HR	*P* value	95% CI
Lung transplant	0.93	<0.01	0.87-0.97
ECMO support days	1.18	<0.001	1.10-2.07
BMI, kg/m2	1.20	<0.01	1.05-1.38
BSA, m2	108.60	0.82	0.01-228.0
Hypertension	2.69	0.59	0.87-4.16

ECMO, Extracorporeal Membrane Oxygenation; BMI, body mass index; BSA, body surface area

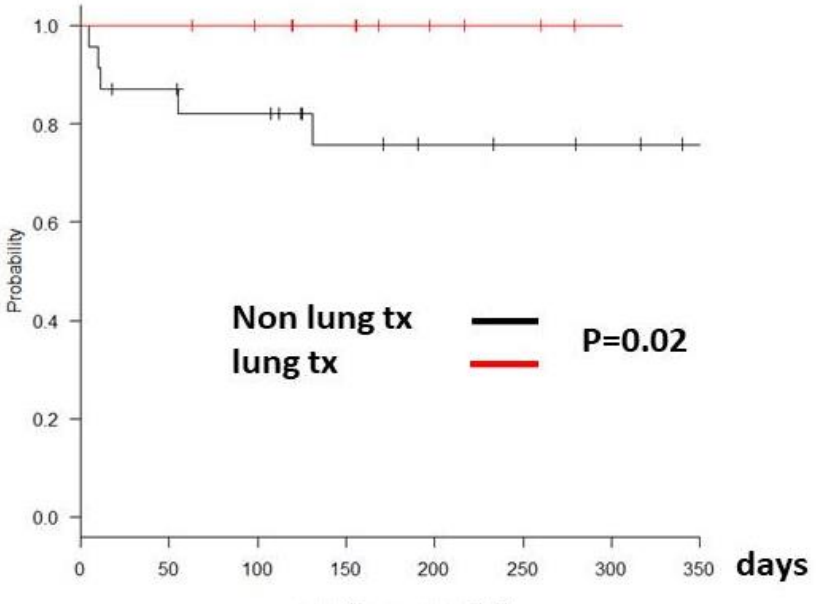
Yuden Index: likelihood of death high after 30 days of ECMO support

Discharge and post-discharge survival in patients supports on ECMO >30 days

Survival to discharge



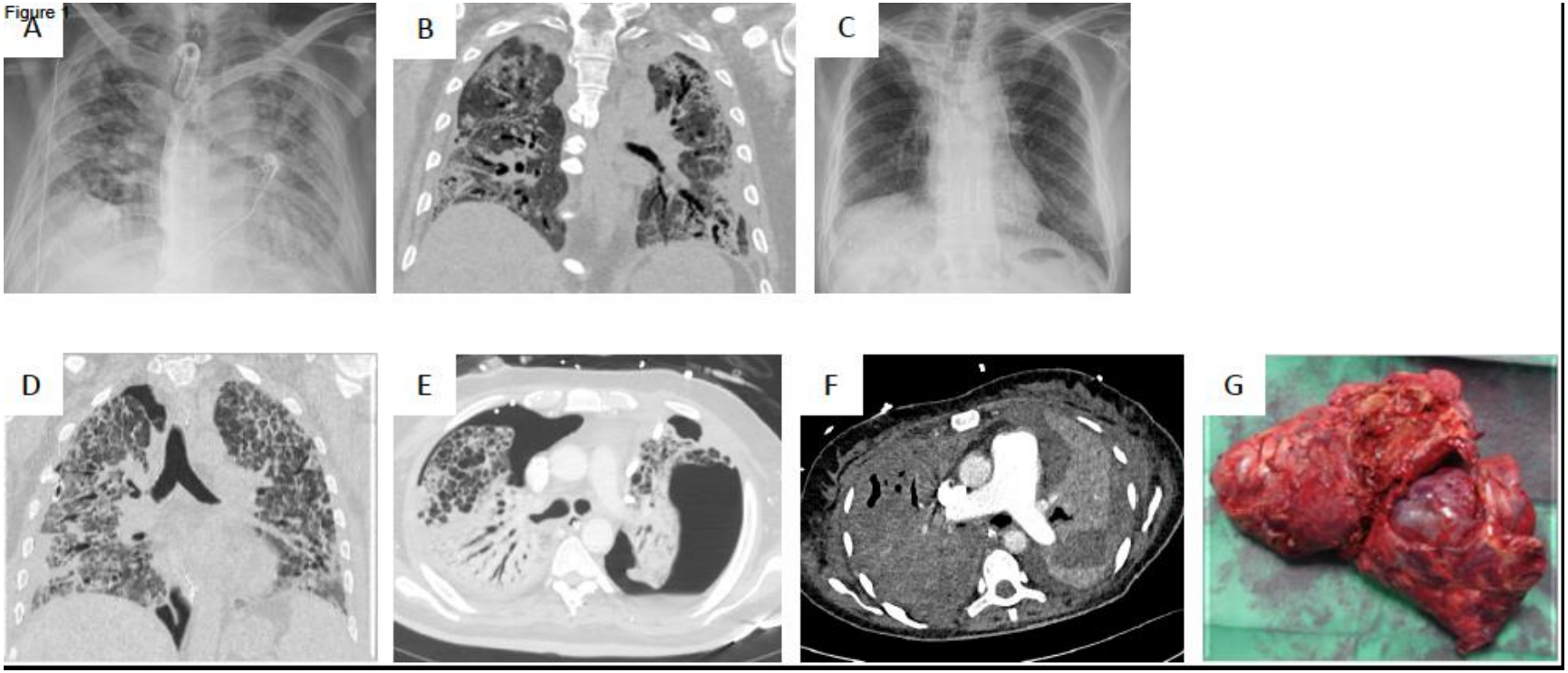
Post-discharge survival



International experience of first consecutive national transplants

U.S.
Vienna
Italy
India

Transplantation		
Time on the waiting list in days (median, IQR)		6 (4-9)
Type of incision	Clamshell	12 (100%)
Intraoperative support	VA ECMO	12 (100%)
Type of Tx	Whole lungs	11 (91.6%)
	Lobar	1 (8.3%)
Surgery time (skin to skin) in min (median, IQR)		504 (448-649)
Total ischemic time in min (median, IQR)		336 (307-460)
Number of intraOp pRBC (median, IQR)		8 (5-15)
Number of intraOp FFP (median, IQR)		4 (3-7)
Post-transplant period		
Induction therapy		9 (75%)
Postoperative prolonged ECMO		10 (83.3%)
PGD at T72hrs	PGD 0	2
	PGD 1	1
	PGD 2	2
	PGD 3	0
	PGD ungradable	7
Length of mechanical ventilation in days (median, IQR)		16 (4-21)
Length of stay in ICU in days (median, IQR)		20 (13-24)
Length of hospital stay in days (median, IQR)		37 (27-42)
Number of patients still in hospital		1 (8.3%)
Complications	AKI/CVVH	4 (33.3%)
	Bleeding requiring chest reopening	3 (25%)
	Critical illness neuropathy	3 (25%)
	Complicated pleural effusion	1 (8.3%)
	Dysexecutive syndrome	2 (16.6%)
Overall survival	Alive	11 (91.6%)
	Dead	1 (8.3%)
Follow-up after transplantation in days (median, IQR)		80 (57-119)
Karnofsky Performance Status		80 (55-85)
Need for supplemental oxygen at the time of discharge	Yes	2
	No	9



Bharat et al, ***Lancet RM,*** In Press

General Criteria

- Age <65 (in exceptionally fit individuals it can be extended to 70)
- Single organ failure (in rare cases, multi-organ transplant can be considered after discussions with the transplant team)
- Absence of malignancy or disabling comorbidities
- No drug dependence (alcohol, drugs, others), and not active smoker
- BMI within range of 17 to 32 although exceptions can be made on a case-by-case basis
- Social support (at least one reliable primary and one secondary caregiver needs to be identified)
- Insurance approval and/or establishment of financial support for transplant-related care
- Patient and caregivers agreeable to lung transplantation and be willing to relocate close to the transplant center for a period of 1 year following transplantation

Neurocognitive Status

Patient should be awake and interactive

- Exceptions can be made in selected cases after discussions with transplant team if sedation wean is associated with severe hypoxemia and hemodynamic changes.
- In such cases, evidence supporting absence of irreversible brain injury that would prevent a successful transplant outcome, through the use of physical assessment in combination with brain imaging and/or neuropsychological consultation, should be obtained. A reliable medical power of attorney who can make informed and educated decisions consistent with patient's goals is required for consent to proceed with transplant.

COVID-19 status

- Two bronchoalveolar lavage fluids PCRs should be negative, 24 hours apart. When two negative bronchoalveolar lavage fluid samples are negative, nasopharyngeal swabs are irrelevant for transplant consideration
- When patient has been separated from the ventilator and has no tracheostomy, two nasopharyngeal swabs can be obtained, 24 hours apart
- Viral cultures should be used when available to determine presence of replication competent virus in the potential transplant recipient. When possible bronchoalveolar fluid should be used and when access to bronchoalveolar fluid is not feasible, nasopharyngeal swabs can be used. Transplant can be considered when viral cultures are negative even if PCR is positive.

Determination of irreversible lung damage

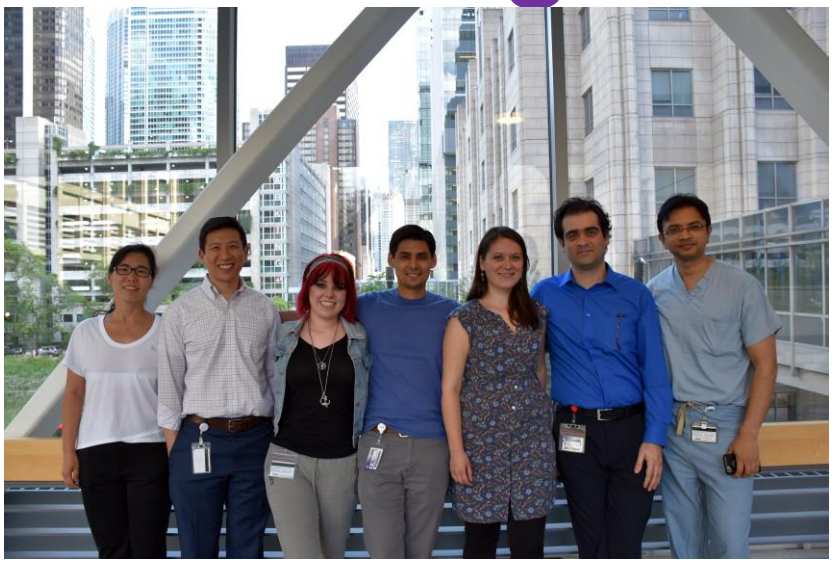
- At least 4 weeks have elapsed since the onset of acute respiratory distress syndrome (ARDS) and there is no significant improvement in lung recovery despite best medical care
- Lung recovery has been deemed unlikely according to at least two different physicians from two different specialties (surgery, critical care, and/or pulmonary medicine)
- Evaluation of lung transplantation can be considered earlier if there is development of potentially lethal pulmonary complication(s) that cannot be managed medically or through the use of ECMO and it is determined that transplant would be effective in treating the pulmonary complication(s)
- Lung transplantation should not be considered if there is continued lung improvement regardless of the time elapsed

Conclusions

- Lung transplant feasible for irrecoverable COVID-19 ARDS

- Post-transplant outcomes excellent despite early post-op complications

Acknowledgements



Funding

R01 HL487967
R01 HL747882
R01 HL823331

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