

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. as psychiatric evaluation. The ethical aspects should also be considered in this situation, with regard to the centre rate mortality on waiting list. Anyway, the potential role of LT in the acute and sub-acute/chronic settings suggests the need for maintaining LT centre active during pandemic. Finally, COVID-19, once more, imposes to share clinical experiences.

Table 1	Clinical details and relevat time-points of patients'
course	

	Patient 1	Patient 2		
Age	18	48		
Sex	М	М		
ABO group	A+	B+		
Comorbidity	None	None		
Preoperative support	MV + VV-ECMO (55 days)	MV + VV-ECMO (53 days)		
Pre-Tx colonization	Ps. Aeruginosa	КРС-Кр		
Tx date	May 18	June 8		
Nasal swab SARS-CoV-2	Negative	Negative		
Type of Tx	Bilateral	Bilateral		
Intraoperative support	VA-ECMO	VA-ECMO		
Postoperative support	VV-ECMO (1 day)	VV-ECMO (2 days)		
Compliance FKT program	Full	Absent		
Septic shock	No	3 episodes		
Last follow-up (days)	150	62		
Status	Alive	Dead		
Last FEV1	68% (3L) (Best=72%)	N/A		
Last FVC	61% (3.2L)	N/A		
Ab anti-HLA	Negative	N/A		
ТВВ	RA1-BX-RC0	N/A		

(329)

Poor Outcomes of COVID-19 in Lung Transplant Recipients. Cohort Study in a Single Center

S.M. Amor,¹ B.D. Fox,² A. Grubstein,³ D. Rosengarden,¹ Y. Shostak,¹ D. Shitenberg,¹ and M.R. Kramer.¹ Pulmonary Division, Rabin Medical Center, Petah Tikva, Israel; ²Pulmonary Division, Shamir Medical Center, Tzrifin, Israel; and the ³Radiology Institue, Rabin Medical Center, Petah Tikva, Israel.

Purpose: The world SARS-CoV-2 pandemic has affected global health, including the health of lung transplant recipients. There is very little data reported on the outcomes of SARS-CoV-2 on this gruop of patients

Methods: Retrospective cohort study approved of all LTx recipients with symptoms consistent with COVID-19 investigated with naso-pharyngeal swabs and reverse PCR for SARS-COV-2. Postive test for SARS-COV-2 Inserted to our cohort and investigated their files. We also conducted pooled analysis of published cases of covid 19 cases of lung transplant recipients

Results: We identified eleven cases of COVID-19 among a cohort of 348 LTx recipients. All but two patients were hospitalized. Seven patients required intensive care and six died (55% mortality). Non-survivors had lower baseline FEV1 than survivors and worse and/or deteriorating chest radiographic scores during admission. No effect of medical therapy including steroids and remdesivir could be determined. This mortality rate compared poorly general hospitalized COVID-19 patients at our institution (13%) and national mortality rate of 0.3% in the general population. Incidence of COVID-19 was similar to the general population (0.3%). In a pooled analysis of published cases, we determined mortality of 28% across different reports of lung transplant patients with COVID-19.

Conclusion: COVID-19 disease is very severe in lung transplant recipients. In the absence of effective therapy and vaccination, transplant physicians should concentrate their efforts on prevention of disease and encourage meticulous preventative behavior by recipients under their care.

no Pt	Diagnosis time (days)	Hospati- zation (days)	Final status	Respiratory thearpy	Covid therapy	Steroids	Compil cation:
R1	3	30	Survived	Nasl Canula	none	PO	CVA
R2	0	3	Survived	Nasal Canula	anti IL2	PO	none
R3	0	7	died	Mechnical Ventilation	Remdesvir	IV	AKI,AL
R4	0	9	died	Mechnical Ventilation	Remdesvir	IV	AKI,AL
R5	0	18	died	Mechnical Ventilation	Remdesvir	IV	AKI,AL
R6	0	20	died	Mechnical Ventilation	Remdesvir	IV	AKI,AL
R7	4	10	died	Mechnical Ventilation	Remdesvir	IV	AKI,AL
R8	0	7	died	Mechnical Ventilation	Remdesvir	IV	AKI,AL
R9	0	0	Home	None	none	none	none
R10	3	0	Home	None	none	none	none
R11	1	4	Addmited	ECMO	Remdesvir	IV	AKI,AI

Study	Events	Total				P	roportion	95%-CI
Fox, Israel	6	11	4		*		0.55	[0.23; 0.83]
Verleden, Belgium	1	10 -					0.10	[0.00; 0.45]
Aversa, USA	11	32	_		-		0.34	0.19:0.53
Myers, USA	2	8 -	- 8	_			0.25	[0.03: 0.65]
Case Reports	1	10						[0.00; 0.45]
Random effects mode	1	71					0.28	[0.15; 0.45]
Heterogeneity: 12 = 30%,	r ² = 0.1981	p=0.17	-	1	1			
			0.2	0.4	0.6	0.8		

(330)

Lung Allograft Dysfunction in a COVID-19 Transplanted Patient is Associated with a Peculiar Immunopathological Phenotype

V. Vaira,¹ G. Croci,² A. Palleschi,³ L. Rosso,⁴ D. Trabattoni,⁵ M. Biasin,⁵ L.C. Morlacchi,⁶ V. Rossetti,⁷ F. Blasi,⁷ M. Nosotti,⁸ M. Clerici,⁹ and S. Ferrero.¹ Division of Pathology, Fondazione IRCCS Ca' Granda -Ospedale Maggiore Policlinico, Milan, Italy; ²Division of Pathology, Division of Pathology, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy; ³Division of Thoracic Surgery and Lung Transplantation, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy; ⁴Thoracic Surgery and Lung Transplantation, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy; ⁵Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, Milan, Italy; ⁶Internal Medicine Department, Respiratory Unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; ⁷Internal Medicine Department, Respiratory Unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy; ⁸Unit of Thoracic Surgery and Lung Transplantation, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy; and the ⁹Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy.

Purpose: Lung transplantation (LT) after severe SARS-CoV-2 infection is emerging as a life-saving medical procedure for selected patients who experience acute respiratory distress syndrome (ARDS). We present the first immunopathological evaluation of a lung allograft rejection in a patient who underwent LT because of irreversible ARDS related to COVID-19.

Methods: Two male patients with irreversible ARDS caused by COVID-19 underwent bilateral LT at our Institution. A surveillance transbronchial biopsy (TBB) was performed 2 months after LT in the first patient (Pt#1), while the

second patient (Pt#2) died because of allograft rejection at day 62 post LT and explanted lungs were retrieved. CT imaging of the lungs was performed three days before death. Morphological examination was performed by H&E, whereas the immunophenotyping was performed by immunohistochemistry.

Results: Imaging and morphological examination of Pt#2 lungs indicated the presence of a graft dysfunction with features of a restrictive, widespread usual interstitial pneumonia-like syndrome (Fig. 1A, B). The immunophenotyping showed that B-lymphocytes (CD20-positive) were nearly absent, CD8-T-cells were not particularly expanded (mean positive cells within the lung stroma=13.8%; Fig. 1C), and the CD4/CD8 ratio was not decreased (Fig. 1D). The T-regs (Foxp3-positive) were 6% of the overall population (Fig. 1E). Analysis of the immune checkpoint molecules PD1, Tigit, CTLA4 and PDL1 showed that the expression of PD-L1 alone was highly increased in vases and in alveolar cells of rejected lungs, whereas it was nearly undetectable in the TBB from Pt#1 (Fig. 1F, G).

Conclusion: PDL1 expression in vases was previously documented as a sign of indirect ARDS. Together with our preliminary data, we can hypothesize that PDL1 may play a role in tissue effacement and graft failure, possibly indicating poor allograft prognosis.



(331)

Immunosuppressive Treatment Does Not Prevent Humoral and Cellular Virus-Specific Immunity in Heart or Lung Recipients with SARS-CoV-2 Pneumonia

<u>E. Seminari,</u>¹ T. Abbate,² E. Arbustini,³ B. Cattadori,¹ A. Di Matteo,¹ E. Gabanti,⁴ F. Meloni,⁵ C. Pellegrini,⁶ A. Turco,⁷ F. Zavaglio,⁴ and D. Lilleri.⁴ ¹Infectious Disease, IRCCS S.Matteo Foundation, Pavia, Italy; ²Respiratory Diseases, IRCCS S.Matteo Foundation, Pavia, Italy; ³Genetics of cardiomyopathies, IRCCS S.Matteo Foundation, Pavia, Italy; ⁴Virology, IRCCS S.Matteo Foundation, Pavia, Italy; ⁶Cardiothoracic Surgery, IRCCS S.Matteo Foundation, University, Pavia, Italy; ⁶Cardiothoracic Surgery, IRCCS S.Matteo Foundation, University, Pavia, Italy; and the ⁷Infectious Disease, Internal medicine, IRCCS S.Matteo Foundation, Pavia, Italy.

Purpose: Clinical characteristics of SARS-CoV-2 infection and virus-specific humoral and cellular response were analyzed in 4 heart (HR) and 3 lung (LR) Tx recipients in standard triple immunosuppressive regimen.

Methods: SARS-CoV-2 infection was diagnosed by real-time PCR on nasopharingeal swabs (NPS). T-cell response to structural antigens Spike (S), Envelope (E), Membrane (M) and Nucleocapsid (N) was evaluated by PBMC stimulation with overlapping peptides spanning the entire viral proteins and subsequent detection of cell activation markers CD137 and CD25. Serum IgG antibody to S and N, and IgA antibody to S were determined by ELISA.

Results: Three patients developed SARS-CoV-2 infection early (<3 months) and four patients late (>3 years) after Tx. One HR was asymptomatic, one LR presented only gastrointestinal symptoms, and five patients developed dyspnea with radiologic signs of interstitial pneumonia (in one HR ICU admittance was necessary. All patients recovered from SARS-CoV-2 infection, with viral clearance from NPS within 3 weeks. However, two HR (one early and one late HR) died at 6 and 4 months after infection because of multi-organ failure and sudden death. Both deaths were considered as unrelated to SARS-CoV2 infection. Patients who had no lung involvement did not develop specific antibody response, while all the other five patients developed IgG and IgA antibodies to S, and IgG antibody to N, within 2 months after infection. All the symptomatic patients developed a detectable CD4+ T-cell response to two or more antigens. Four patients were subsequently examined >3 months after infection, showing the persistence of IgG and IgA antibodies to S and a decline of IgG antibody to N, while CD4+ T-cell response to N was maintained. Timing of Tx did not affect the occurrence of virus specific immunity.

Conclusion: Although this series is small, the data indicate that immunosuppression does not prevent the development of a specific humoral and cellular anti-SARS-CoV-2 response, more likely in patients who have experienced clinically relevant pneumonia. These preliminary data encourage the maintenance of regular follow-up to monitor the persistence of immune response and the potential occurrence of SARS-CoV-2-related sequelae in heart and lung recipients.

(332)

Rapid ECMO Training for Nurses in Response to the COVID-19 Pandemic <u>B. Toy,</u>¹ A. Emmarco,¹ L. Lester,² M. Lohan-Mullens,³ E. Ottoson,³ T. Garofalo,³ M. Saputo,³ N. Moazami,⁴ Z. Kon,⁴ and D. Smith.⁴ ¹Transplant Institute, NYU Langone Health, New York, NY; ²NYU Grossman School of Medicine, NYU Langone Health, New York, NY; ³Nursing, NYU Langone Health, New York, NY; and the ⁴Cardiothoracic Surgery, NYU Langone Health, New York, NY.

Purpose: From March 17th to April 29th, our ECMO Program placed 30 adult patients on venovenous extracorporeal membrane oxygenation (VV-ECMO) for management of coronavirus disease 2019 (COVID-19). This acute increase in volume placed a strain on our available ECMO-competent nursing staff. Although perfusionists function as our ECMO specialists, our critical care nurses provide continuous circuit monitoring and respond to emergencies. Because of the need to increase the number of ECMO-competent nurses, on March 27th a focused, two-hour COVID-ECMO training course was implemented.

Methods: We retrospectively reviewed the number of ECMO care hours provided by our nursing staff and separated the nursing staff into two cohorts. Group A consisted of nurses who had undergone ECMO training prior to the pandemic (n=126). Group B consisted of nurses whose initial ECMO training occurred during the pandemic (N=145). We then compared the number of nursing hours provided by each cohort before and after training.

Results: From March 27^{th} to May 4^{th} , 145 nurses completed training, increasing our total number of ECMO-competent nurses from 126 to 271 (115% increase). From March 17^{th} to June 30^{th} , 20,677 ECMO care hours were provided. Pre-training, all 634 care hours were 100% provided by Group A nurses. Post-training, 20,043 care hours were provided, consisting of 39% Group A nursing coverage and 61% Group B nursing coverage. There were no differences in nursing related ECMO-emergencies between the two groups. At the conclusion of the surge, 28 out of 30 (93%) patients survived ECMO and 26 out of 29 patients (90%) survived to hospital discharge. One patient has a pending hospital disposition.

Conclusion: Rapid implementation of an abbreviated ECMO education program for nurses is feasible. It met the time-sensitive needs of the COVID-19 pandemic and provided safe nursing coverage to patients requiring ECMO.