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data on its association with clinically relevant non-rejection complications post-OHT exists. This study aims to assess the relationship of GEP testing to infection and malignancy in OHT recipients.

Methods: 128 adults with OHT and GEP testing from 2016-2019 were retrospectively evaluated for demographics, GEP scores and clinical outcomes at our institution. The primary outcome was composite infection and malignancy treated post-OHT and GEP testing. Descriptive statistics are reported. A mixed effect discrete time hazard logistic regression model was used for repeated measurements.

Results: 128 OHT adults (mean age of 60 ± 12 years) had GEP testing (median 32 [29, 34] per patient) sampled after median 16 [12, 22] months post-OHT. Most were Caucasian (81%) males (71%), who had chronic kidney disease (81%), hyperlipidemia (77%), and diabetes (40%). The overall incidence of acute rejection was 2.3% and of composite infection and malignancy was 8.6%. The odds ratio for composite infection and malignancy for the lowest score in a patient follow-up was 0.90 [95% CI 0.82-0.98], $p=0.01$. In patients with a GEP score of ≤ 25 vs >25 , the composite outcome was 48% vs 26%, $p=0.03$. A higher GEP score correlated with a lower risk of composite outcome: For every one unit and five units increase in the GEP score, the relative risk was 0.90 [95% CI 0.81-1.01, $p=0.06$] and 0.54 [95% CI 0.32-0.92, $p=0.02$], respectively.

Conclusion: The overall incidence of infection and malignancy was $<10\%$. A lower GEP score post-OHT is associated with a higher risk of infection and malignancy. As well as for acute rejection, GEP testing may have the potential to prognosticate risk for infection and malignancy. This association along with an examination of allomap score variability with these clinical outcomes will need to be validated in future analyses.

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A Multicenter Prospective Registry Study of Lung Transplant Recipients Hospitalized with COVID-19

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Purpose: Outcomes of lung transplant recipients (LTR) hospitalized for COVID-19 and comparisons to non-lung solid organ transplant recipients (SOTR) are incompletely described.

Methods: Using a multicenter prospective registry of SOTR, we examined 28-day outcomes (mortality [primary outcome], intensive care unit (ICU) admission, mechanical ventilation, and bacterial pneumonia) among both LTR and non-lung SOTR hospitalized with laboratory-confirmed COVID-19 diagnosed between March 1, 2020 and September 21, 2020. Data were analyzed using Stata (StataCorp, College Station, TX); chi-square tests were used to compare categorical variables and multivariable logistic regression was used to assess risk factors for mortality.

Results: The cohort included 72 LTR and 392 non-lung SOTR (Table 1). Overall, 28-day mortality trended higher in LTR vs. non-lung SOTR (27.8% vs. 19.9%, $P=0.136$). Other 28-day outcomes were similar between LTR and non-lung SOTR: ICU admission (45.8% vs. 39.1%, $P=0.28$), mechanical ventilation (32.9% vs. 31.1%, $P=0.78$), and bacterial pneumonia (15.3% vs. 8.2%, $P=0.063$). Congestive heart failure, diabetes, age >65 years, and obesity (BMI ≥ 30) were independently associated with mortality in non-lung SOTR, but not in LTR (Table 2).

Conclusion: In this large prospective cohort comparing lung and non-lung SOTR hospitalized for COVID-19, there were high but not significantly different rates of short-term morbidity and mortality. Baseline comorbidities appeared to drive mortality in non-lung SOTR but not LTR. Further studies are needed to identify risk factors for mortality among LTR.

Table 1 Characteristics and outcomes of hospitalized lung and non-lung SOTxR with COVID-19

Characteristics, n (%)	Lung (n=72)	Non-lung (n=352)	P-value	Comments
Age in years, mean (SD)	59 (12.8)	56.4 (14.2)		
Male	38 (52.8)	225 (64.0)	0.076	
Lung transplant	72 (100.0)	0 (0.0)		includes 3 heart-lung and 1 lung-liver recipients; 21 (29.2%) received a single lung transplant
Heart transplant	-	47 (13.1)		includes 5 heart-kidney and 1 heart-kidney-small bowel recipients
Liver transplant	-	47 (13.1)		includes 11 liver-kidney recipients
Kidney or kidney-pancreas transplant	-	255 (72.4)		includes 6 kidney-pancreas recipients
Other transplanted organ	-	3 (0.852)		includes 2 small bowel and 1 vascular composite allograft recipients
Hypertension	39 (54.9)	285 (81.0)	$<0.001^*$	
Congestive heart failure	5 (7.0)	34 (9.7)	0.49	
Diabetes mellitus	36 (50.7)	194 (55.1)	0.50	
CKD or ESRD	38 (52.8)	160 (45.5)	0.26	
Chronic lung allograft dysfunction	9 (12.5)	-		
Chronic lung disease	-	34 (9.7)		
Obesity (BMI ≥ 30)	19 (27.1)	121 (34.9)	0.21	
Outcomes at 28 days, n (%)				
Death	20 (27.8)	70 (19.9)	0.14	
Intensive care	33 (45.8)	136 (39.1)	0.28	
Mechanical ventilation	23 (32.9)	108 (31.1)	0.78	
Bacterial pneumonia	11 (15.3)	29 (8.2)	0.06	

Table 2 Risk factors for 28-day mortality: lung vs. non-lung recipients

	Lung, OR (95% CI)	Non-lung OR (95% CI)
Age > 65 years	2.02 (0.70-5.86)	3.09 (1.80-5.31)*
Male	0.36 (0.12-1.07)	1.67 (0.93-2.97)
Single lung transplant	2.72 (0.92-8.12)	-
Comorbidities		
Hypertension	1.0 (0.35-2.81)	1.52 (0.73-3.15)
Congestive heart failure	0.62 (0.06-5.90)	5.75 (2.75-12.01)*
CKD or ESRD	1.13 (0.40-3.19)	1.09 (0.65-1.84)
Diabetes Mellitus	0.96 (0.34-2.70)	2.20 (1.26-3.87)*
Obesity (BMI ≥ 30)	1.89 (0.61-5.90)	1.71 (1.0-2.91)*

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Cell-Free DNA Tissue Damage Mapping in Transplant Patients Infected with COVID-19

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Purpose: Patients with COVID-19 show variable clinical course; transplant patients often show worse outcomes. The effect of COVID-19 on the allograft and the sources of tissue injury that contribute to such poor outcomes are poorly defined. This study leverages cell-free DNA (cfDNA) to measure allograft injury as donor-derived cfDNA (ddcfDNA) and injury from different tissue types using tissue-specific DNA methylomic signatures.

Methods: 14 consecutive COVID-19 transplant patients (8 Kidney, 3 Lung, 1 Heart, 1 Liver, and one multi-organ transplant patients) and 30 healthy controls were included. Plasma nuclear cfDNA (ncfDNA) and mitochondrial cfDNA (mtcfDNA) level were measured via digital droplet PCR, and ddcfDNA using AlloSure (CareDx). cfDNA whole-genome bisulfite sequencing was performed to identify cfDNA tissues of origin leveraging tissue specific DNA methylomes and deconvolution algorithm.

Results: 75% of the COVID-19 transplant patients showed high ddcfDNA level compared to published quiescent values, including all lung, 50% of the kidney, liver and multi-organ transplant patients (8.5, 4.4, 30 and 16-X fold change, respectively). Total ncfDNA and mtcfDNA were 15X and 310X higher in COVID-19 transplant patients compared to controls, respectively; < 0.0001. The predominant tissues contributing to cfDNA were hematopoietic cells (80%) (Figure). More importantly, COVID-19 transplant patients showed 10 to 100 fold higher tissue specific cfDNA derived from monocyte, neutrophil, erythroblast, vascular endothelium, adipocyte, hepatocyte, kidney, heart and lung compared to controls. Analysis comparing cfDNA in transplant and non-transplant COVID-19 patients is on-going.

Conclusion: The allograft undergoes significant injury following COVID-19. Further, cfDNA from multiple tissue types is significantly higher in COVID-19 transplant patients. Future studies in a larger cohorts of transplant and non-transplant patients are needed to elucidate why transplant patients show worse COVID-19 outcomes.

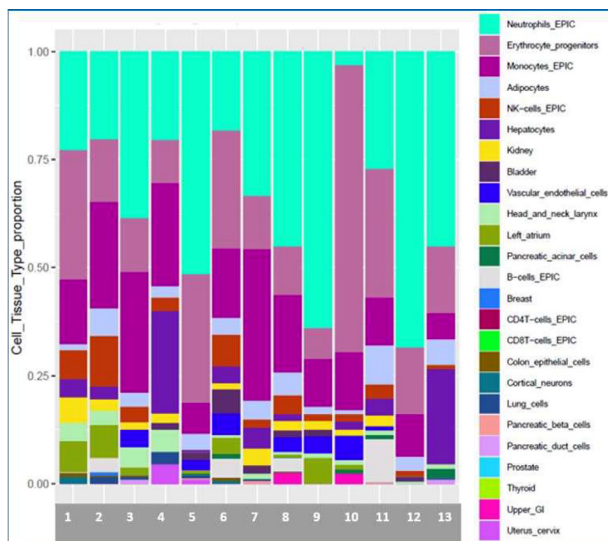


Figure. Tissue-specific cfDNA methylation profiling of 13 COVID-19 transplant patients.

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Impact of COVID-19 on Lung Transplantation in Australia

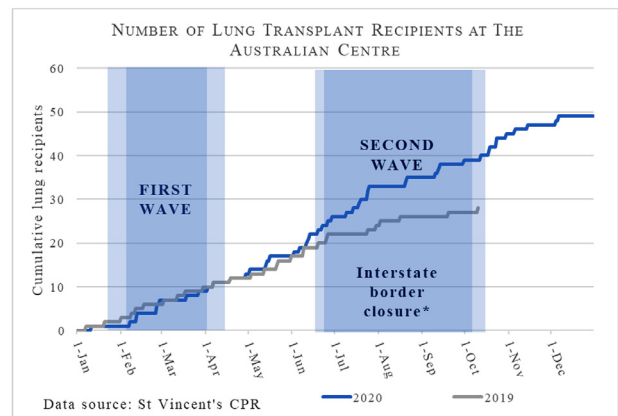
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Purpose: The impact of COVID 19 on lung donors and lung transplant recipients in Australia has not been studied. This study followed the impact of COVID 19 in the initial Australian COVID 19 surge.

Methods: This was a retrospective cohort study which examined data from the centre's local CPRS transplant database, Australia and New Zealand Organ Donation Registry and hospital medical records from 01st Jan 2017 to 31st August 2020. Organ donation patterns, cause of donor deaths, recipient characteristics and transplant surgery volumes were monitored.

Results: Over the 8 months, from 1st of January to 31st August, there were 26 lung transplants in 2020 compared to 35 in the same period in 2019 at the centre. Suicide and overdose became 2.65 times more likely as causes of donor death at the centre and 1.60 times more likely nationally. Heart attack and stroke became less likely causes of donor death. Lung transplant recipients were more likely to have a diagnosis of pulmonary fibrosis, but had on average improved measures of pre-surgical frailty and improved operative outcomes. The exception to this was ICU time and ventilatory time, which increased on average. MOCA scores improved on average, suggestive of better mental acuity. Indicators of mental health were worse in the 2020 cohort, based on the average dmi10 depression screening score.

Conclusion: There was a 69.23% decline in volume of organ transplantation as of August 2020. With the initial surge of cases the transplant volumes decreased dramatically, however with "lockdown" and control of "COVID cases" the lung transplant rates increased. The Victorian outbreak from August further diminished rates of transplant due to travel restrictions, however the NSW based unit managed to maintain lung transplant levels with local donors and minor interstate referrals. An increase in physical robustness corresponds to increased referral and uptake of "prehabilitation" by waitlisted patients.



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COVID-19 Related Stress among Lung Transplant Recipients

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Purpose: Over 43 million COVID-19 cases and 1 million deaths have been reported globally and rates continue to climb. During pandemics people exhibit stress that may be disproportionately felt by LTR due to immunosuppression and comorbidity that increase their risk for poor COVID-related outcomes. Transplant providers have an important role in addressing the physical and emotional impact of COVID, yet COVID-related stress has not been assessed in LTR. The aims of this project, conducted in Oct 2020, were to quantify COVID-related stress, stressors and correlates.