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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.

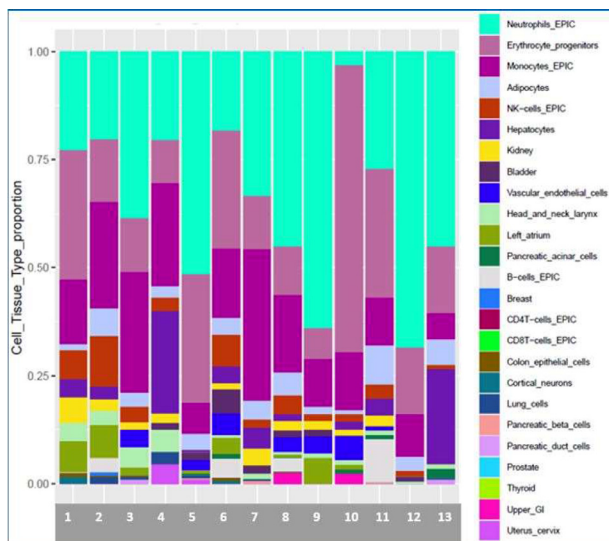


Figure. Tissue-specific cfDNA methylation profiling of 13 COVID-19 transplant patients.

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**Impact of COVID-19 on Lung Transplantation in Australia**

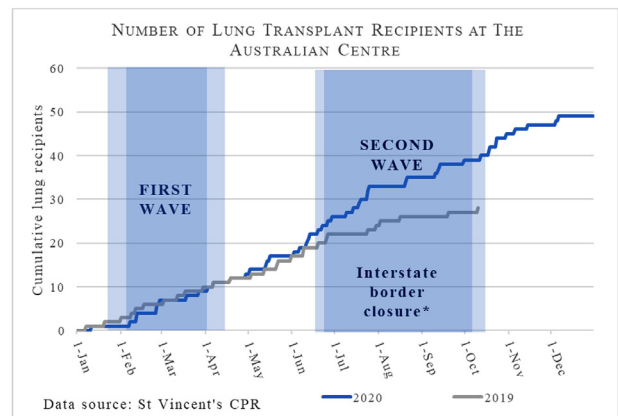
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**Purpose:** The impact of COVID 19 on lung donors and lung transplant recipients in Australia has not been studied. This study followed the impact of COVID 19 in the initial Australian COVID 19 surge.

**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 01<sup>st</sup> Jan 2017 to 31<sup>st</sup> August 2020. Organ donation patterns, cause of donor deaths, recipient characteristics and transplant surgery volumes were monitored.

**Results:** Over the 8 months, from 1<sup>st</sup> of January to 31<sup>st</sup> 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.