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.

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BRIEF COMMUNICATION

COVID-19 diagnosis and testing in pediatric heart transplant recipients

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Pediatric heart transplant recipients have been expected to be at higher risk of adverse events from developing COVID-19 infection. COVID-19 RNA PCR and antibody testing has been performed in our cohort of patients since March 15, 2020 and outcomes were reviewed. COVID-19 infection in our population of pediatric heart transplant recipients is common (21%), despite recommendations to avoid contact with others. Asymptomatic COVID-19 infection is common as well (55%). Despite the frequency of infection, COVID-19 is well tolerated in this population (5% admission from home; 0% mortality). A suppressed immune system does not significantly inhibit an antibody response in pediatric heart transplant recipients (>70% antibody seroconversion) and appears to persist, similar to those without transplantation (>90 days). Routine testing for COVID-19 via PCR and antibody testing enhances the ability to detect COVID-19 infection in asymptomatic patients and may help reduce unintended transmission to more susceptible individuals.
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Brief communication

Pediatric heart transplant recipients have been expected to be at higher risk of adverse events from developing COVID-19 infection due to having a suppressed immune system. Few reports in this population have been published to date. [1,2] According to hospital policy, symptomatic patients, those undergoing anesthesia, and those being admitted to our hospital for any other reason have been tested with COVID-19 RNA PCR since March 15, 2020. To aid in exposure prevention of other clinic patients and staff to those recently infected with COVID-19, routine COVID-19 antibody screening (IgG and IgM) has been performed prior to outpatient office visits (every three months) in all pediatric heart transplant patients since August 24, 2020. Confirmatory COVID-19 RNA PCR was performed on all patients with positive COVID-19 antibodies without a known history of COVID-19 infection to distinguish between current infection and prior infection. COVID-19 antibody testing was also performed at transplant listing and every three months after transplant in those transplanted within one year of the start of the pandemic. No alterations to testing were made based on intensity of induction therapy. Subjects were receiving our center's standard immunosuppression regimens during the study period, which consisted of tacrolimus with mycophenolate or tacrolimus with an mTOR inhibitor. These studies were all performed as part of routine post-transplant care, therefore IRB approval was not obtained for this report.

After 1 year of the COVID-19 pandemic, 94 children having received a heart transplant at Loma Linda University Children's Hospital have undergone testing for COVID-19 infection between March 15, 2020 and March 15, 2021. One-hundred-forty-six tests for COVID-19 antibodies and

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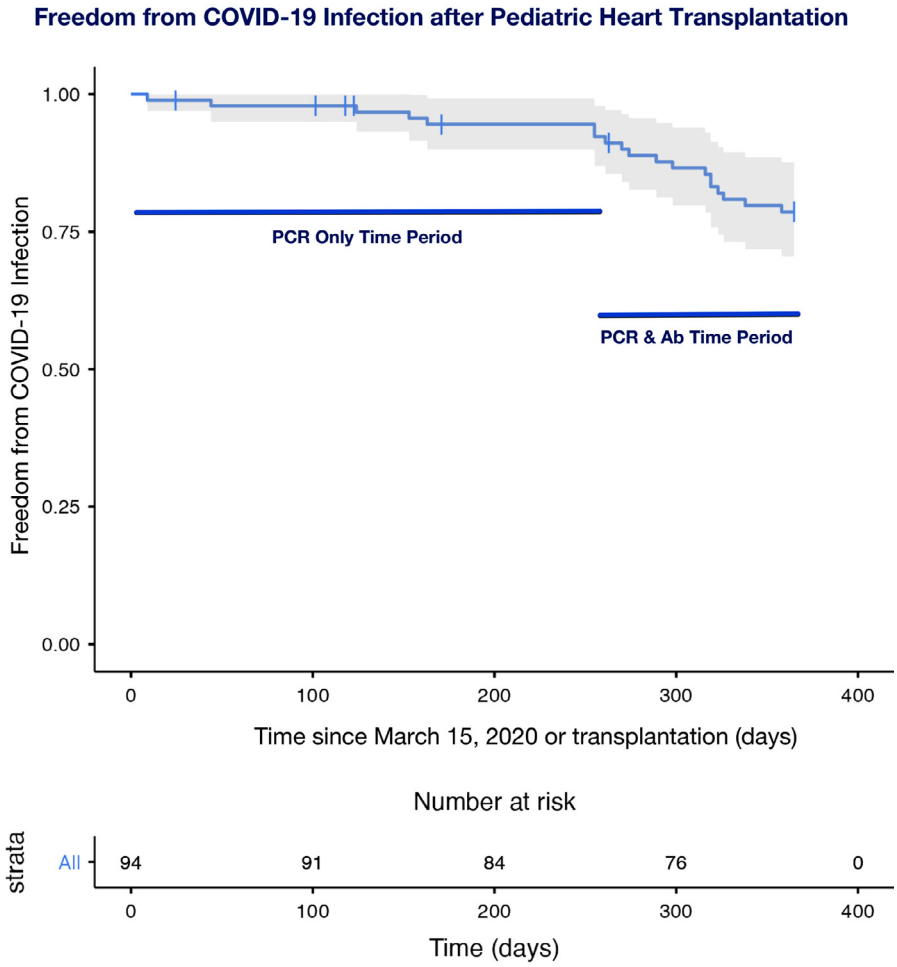

Figure 1 Freedom from COVID-19 infection as diagnosed by PCR or antibody testing in a single-center population of pediatric heart transplant recipients. Day 0 is March 15, 2020 for those transplanted prior to this date and the date of transplantation for those transplanted after this date.

265 COVID-19 RNA PCR tests were performed on our patients. Twenty-one percent of pediatric heart transplant recipients (20/94, 21.3%) have received a diagnosis of COVID-19 via either PCR or antibody screening during this time period (Figure 1). The median age at diagnosis was 12.9 years (IQR 9.3 - 16.8 years). The median time since heart transplant was 9.6 years (IQR 6.6 -13.0 years).

Forty-five percent (9/20, 45%) of patients were diagnosed after developing symptoms, confirmed by PCR. Fifty-five percent (11/20, 55%) of patients were asymptomatic at diagnosis. Ten percent (2/20, 10%) were diagnosed by PCR without symptoms. Forty-five percent (9/20, 45%) were diagnosed by routine antibody testing without symptoms. A total of 55% (11/20) of patients were diagnosed by PCR. Of these children, seven (7/11, 64%) had antibody testing after diagnosis by PCR. Of those diagnosed by PCR with subsequent antibody testing, 5 children had antibody (IgG) conversion (5/7, 71%). Of those having antibody testing at or after COVID-19 diagnosis, 14 (14/16, 88%) had positive antibody (IgG) testing. Two (2/9, 22%) symptomatic children required admission for COVID-19 disease. One had shortness of breath and required 1 day of hospitalization. One child was already admitted to the hospital for treatment of cryptococcal meningitis and developed shortness of breath and tested positive for COVID-19. One asymptomatic child already admitted to the hospital, nine days post-transplant, tested positive for COVID-19 prior to heart catheterization testing. He remained asymptomatic and tested negative 2 days after diagnosis. No changes to immunosuppression or COVID-19 directed therapies were given. No mortalities occurred due to COVID-19 infection.

COVID-19 RNA PCR was positive in 1.5% (4/265) of tests in asymptomatic patients, while 6.2% (9/146 tests) had positive antibody testing. Of those with positive PCR testing, the average time of PCR positivity was 38 days (min 2, max 60 days). Of those with positive antibody testing, the average time of IgG positivity was 93 days (min 30 days, max 180 days), while the average time of IgM positivity was 88 days (min 30 days, max 180 days). Most patients remained both IgG and IgM positive at the time of this letter, making the true length of antibody positivity unknown.

Our results show that COVID-19 infection is common (21%) in pediatric heart transplant recipients despite

recommendations to avoid contact with others. This is likely an underestimation of true disease prevalence in this population. Asymptomatic COVID-19 infection is common as well (55%). Despite the frequency of infection, COVID-19 is well tolerated in this population (5% admission from home; 0% mortality). Additionally, a suppressed immune system, does not significantly inhibit an antibody response in pediatric heart transplant recipients (>70% antibody seroconversion) and appears to persist, similar to those without transplantation (>90 days). [3] Routine testing for COVID-19 via PCR and antibody testing enhances the ability to detect COVID-19 infection in asymptomatic patients and may help reduce unintended transmission to more susceptible individuals. Larger scale data collection, like that being undertaken by the Pediatric Heart Transplant Society, will likely expand on these findings.

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