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The impact of COVID-19 infection on heart transplant function

Micaela MacKay[1*], Jeremy C. Tomcho[2] and Wissam Khalife[2]

Abstract

Background Heart transplant recipients are a subset of immunocompromised patients at particularly high risk of morbidity and mortality from COVID-19. Acute effects of the viral infection have been well-described in the literature but the chronic effects persisting after recovery from infection have not. The aim of this study is to determine the impact of COVID-19 on heart transplant function both during and after recovery from acute infection.

Methods We retrospectively analyzed the data of 32 heart transplant recipients at the University of Texas Medical Branch (UTMB). Echocardiograms of patients with documented COVID-19 infection were analyzed at three time points including pre-infection, peri-infection, and post-infection. Echocardiograms of patients without history of infection were analyzed as control. Left Ventricular Ejection Fraction (LVEF) and presence or absence of valvular insufficiency were collected from echocardiograms to assess systolic and valvular function.

Results 2 out of 10 COVID-19 positive heart transplant recipients had decreases in LVEF below 20% during the peri-infection period, and one of these patients passed away from complications of infection. Despite this, mean LVEF was not significantly different at peri-infection ($p = .3$, 95% CI − 11.5 to 27.6) or post-infection ($p = .6$, 95% CI − 3.6 to 5.8) time points when compared to pre-infection. A statistically significant increase in valvular dysfunction was found among COVID-19 positive patients without documented history of valvular dysfunction on pre-infection echocardiograms ($p = .01$, 95% CI 19.3% to 96.4%). COVID-19 negative heart transplant recipients did not experience statistically significant changes in LVEF 1, 2, or 3 years after baseline echocardiogram.

Conclusion COVID-19 may induce myocardial dysfunction resulting in decreased systolic function and valvular dysfunction among heart transplant recipients. Severity of systolic dysfunction may be a useful prognostic indicator among this patient population. More research must be conducted to fully elucidate the effects of COVID-19 infection on heart transplant recipients.

Keywords Cardiology, Transplant, COVID-19, Immunosuppression

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Background

Coronavirus disease 2019 (COVID-19) has spread to nearly every country in the world and caused over six million fatalities (Novel coronavirus (COVID-19) 2020). Despite advancements in prevention and treatment, incidence of the disease is still relatively high—3 million new cases were reported globally from March 13, 2023 to April 9, 2023 (Weekly epidemiological update on COVID-19 2023). Healthy patients with intact immunity typically are asymptomatic or experience mild infection with symptoms such as cough, myalgias, fatigue, and headache. Conversely, solid-organ transplant recipients and other immunocompromised populations eradicate infection less rapidly which results in prolonged viral shedding and the emergence of resistive variants (Immunocompromised 2023). Severe infection is common among heart transplant recipients leading to hospitalization rates as high as 75% and short-term mortality rates as high as 25% among this population (Diaz-Arocutipa et al. 2021; Bottio et al. 2021). In addition to immunosuppression therapy resulting in a blunted immune response, heart transplant recipients have high rates of comorbid conditions such as cardiovascular disease and hypertension. These comorbidities have been associated with poor prognosis and high mortality risk (Chakinala et al. 2021).

Complications related to nearly every organ system have been described in the setting of severe COVID-19 infection. Cardiac complications are common and include myocarditis, arrhythmias, cardiomyopathy, and stress-induced demand ischemia resulting in a Type 2 myocardial infarction (Heart Problems and after COVID-19 2023). Myocarditis involves pathological immune responses which induce structural and functional abnormalities in cardiomyocytes (Sagar et al. 2011). Viral infection is the most common cause of myocarditis in the United States. Prior to the COVID-19 pandemic, the most frequently identified genomes in heart tissue of patients with acute myocarditis were parvovirus B19, human herpes virus 6, and enteroviruses. COVID-19 may become a leading cause of myocarditis, however, as occurrence of myocarditis inpatient encounters were 42% higher in 2020 during the COVID-19 pandemic than in 2019 (Boehmer et al. 2021). The CDC estimates that patients with COVID-19 infection are at 16 times higher risk of developing myocarditis than those without. COVID-19 damages myocardium in the acute phase of infection by two primary mechanisms. First, COVID-19 infection non-selectively damages myocardial tissue through processes including cytokine-induced systemic inflammation and hypoxemia (Zaccone et al. 2021). The second mechanism involves binding of the virus to angiotensin converting enzyme-2 (ACE-2), a receptor expressed in cardiomyocytes. Binding of this receptor allows COVID-19 to enter these cells and damage myocardium directly.

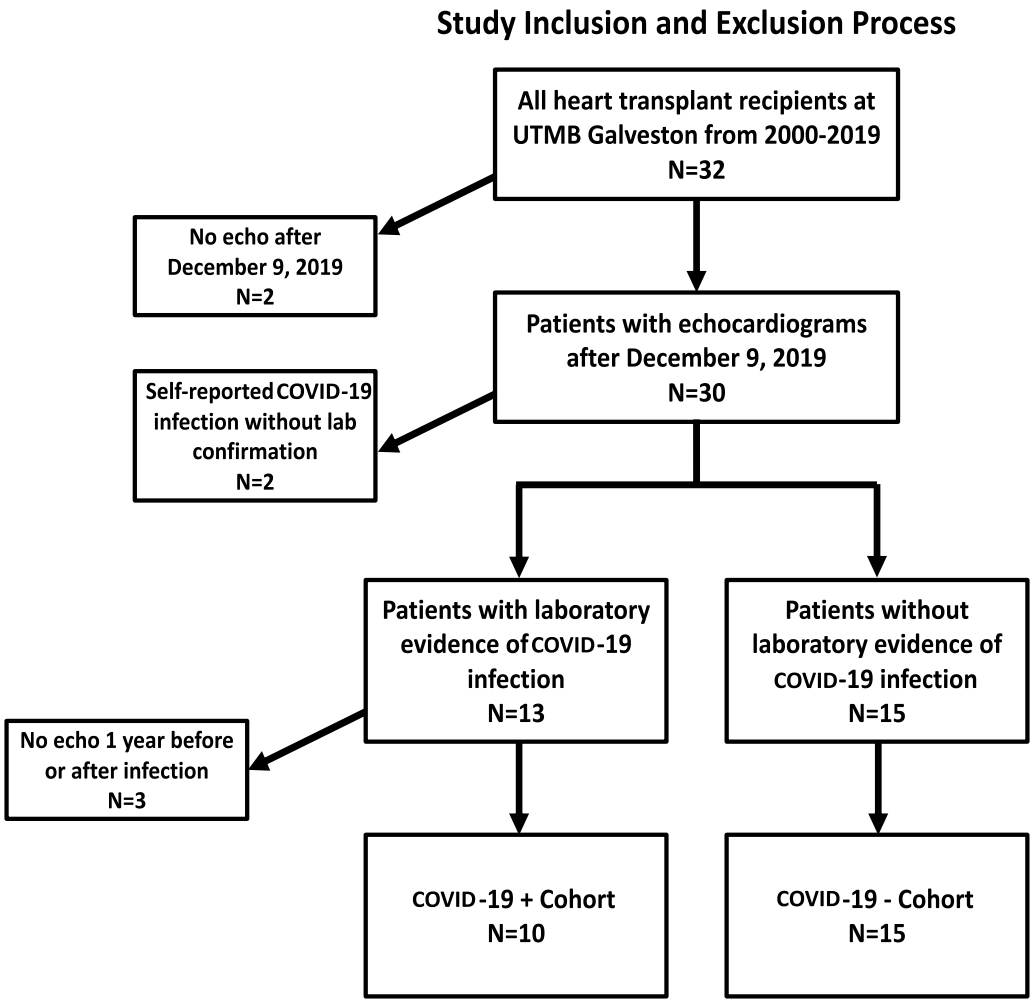
In addition to the well-described effects of acute COVID-19 infection on myocardial tissue, studies have found evidence of viral-induced damage persisting beyond the acute infectious period. Evidence of cardiac involvement on imaging has been found to persist months after infection among more than half of patients with COVID-19 (Puntmann et al. 2020). The mechanism by which COVID-19 causes persistent cardiac damage is poorly understood, but theories include viral reservoirs in the heart evoking chronic inflammation and destructive autoantibodies caused by molecular mimicry (Proal and VanElzakker 2021). As many studies have found evidence of COVID-19 causing chronic damage to the heart among healthy patients, further investigation on this topic specific to immunocompromised populations is necessitated.

The aim of this study is to analyze the effects of COVID-19 infection on heart transplant function, specifically LVEF and valvular function, during both the acute infectious period and after resolution of infection. We retrospectively review the outcomes of 32 heart transplant recipients at the University of Texas Medical Branch (UTMB). This study contributes information which has not yet been well described in the literature and may assist providers in their clinical decision making when taking care of this high-risk population.

Methods

Study design

Our study is a retrospective chart review analysis of heart transplant recipients at the University of Texas Medical Branch in Galveston, TX. IRB approval was obtained (IRB #22-0259). After obtaining the official list from transplant coordinators within our institution, we analyzed the charts of all 32 patients with a history of heart transplant from 2000 to 2019.



Data collection

The UTMB electronic medical record was utilized for chart review. For all 32 heart transplant recipients, baseline characteristics and pertinent past medical history were collected. Baseline characteristics included age, sex, race, COVID-19 vaccination status, and date of heart transplant operation. Pertinent past medical history included hypertension, hyperlipidemia, diabetes mellitus, and chronic kidney disease. Smoking history was collected as this could impact pulmonary function and severity of COVID-19 infection. Patients were divided into two cohorts—those with a documented history of COVID-19 infection and those without. Patients were included in the COVID-19 positive cohort if they had positive COVID-19 diagnostic tests including either SARS-CoV-2 RNA rapid tests, Nucleic Acid Amplification Tests (NAAT), or both. Patients with self-reported history of COVID-19 infection without laboratory evidence were excluded (n = 2). 13 of 32 heart transplant recipients had laboratory evidence of COVID-19 infection and were included in analysis. Date of positive test was documented and compared with date of transplantation to ensure that infection occurred after the patient had received their transplanted heart. COVID-19 testing was not conducted on a predetermined, routine basis at our institution among this population and rather was conducted when patients were symptomatic. Routine COVID-19 testing was conducted among all patients admitted to the hospital for inpatient care or for cardiac catheterization. For these reasons, not all patients had laboratory testing available at multiple time points.

Transplant function was assessed utilizing LVEF and valvular function documented on echocardiograms. To assess the impact of infection on transplant function, data collection for COVID-19 positive patients was divided into three time periods including pre-infection (baseline), peri-infection, and post-infection. The baseline or pre-infection time period began one year prior to infection and ended one month prior to positive COVID-19 diagnostic test and was considered to represent the function of the transplant prior to infection. The first documented infection among all heart transplant recipients at UTMB Galveston occurred on December 9, 2020. The peri-infection period ranged from one month before to one month after the positive test. If patients had multiple positive tests during the same infection, the peri-infection period began one month prior to the first positive test and ended one month after the final positive test. The post-infection period began one month after the positive test and included all data to present day. COVID-19 positive patients had to have undergone echocardiograms in both the pre-infection period and post-infection period to qualify for inclusion in our analysis. Although peri-infection echocardiograms were collected and analyzed, patients without peri-infection echocardiograms were not excluded as this was a relatively short period and many patients did not have echocardiograms during this time. Of the 13 patients with laboratory evidence of COVID-19 infection, two were excluded as they did not have echocardiograms conducted within one year prior to infection (pre-infection period) and one was excluded as they did not have an echocardiogram conducted after infection (post-infection period). Thus, the COVID-19 positive cohort included ten heart transplant recipients.

Patients without laboratory evidence or self-reported history of COVID-19 infection were included in our COVID-19 negative control cohort. This cohort initially included 17 patients. As we aimed to compare transplant function among the control cohort with the COVID-19 positive cohort as accurately as possible, we analyzed echocardiograms conducted during similar time periods. As the first infection among the COVID-19 positive cohort was documented on December 9, 2020 and the pre-infection period for this patient began on December 9, 2019, all data collection for the COVID-19 negative cohort began on December 9, 2019. This ensured that COVID-19 negative patients were analyzed during the COVID-19 pandemic, similarly to COVID-19 positive patients. All echocardiograms beginning on this date up to present day were collected and analyzed, and patients were excluded from analysis if they did not have echocardiograms conducted after this date (n = 2). Our COVID-19 negative cohort ultimately included 15 patients.

Statistical analysis

Mean difference in LVEF within cohorts was analyzed for significance utilizing a Paired t-Test method. This test was used for both COVID-19 positive and negative cohorts. A comparison of proportions calculator was used to determine the significance of valvular insufficiency rates.

Results

Baseline characteristics	COVID + (n = 10)	COVID − (n = 15)
Age		
Mean	56.4	56.5
18–40	10% (n = 1)	13% (n = 2)
41–60	50% (n = 5)	40% (n = 6)
61 +	40°% (n = 4)	47% (n = 7)
Race		
Caucasian	20% (n = 2)	73% (n = 11)
African American	80% (n = 8)	20% (n = 3)
Hispanic	0% (n = 0)	7% (n = 1)
Sex		
Male	90% (n = 9)	73% (n = 11)
Female	10% (n = 1)	27% (n = 4)
Comorbid conditions		
Hypertension	90% (n = 9)	100% (n = 15)
Hyperlipidemia	70% (n = 7)	60% (n = 9)
Diabetes Mellitus	60% (n = 6)	47% (n = 7)
CKD Stage 2 + /renal transplant	60% (n = 6)	73% (n = 11)
Former/current tobacco use	60% (n = 6)	60% (n = 9)

Demographics and mortality

Of 32 patients who underwent heart transplantation at UTMB Galveston from 2000–2019, 10 of these with documented history of COVID-19 infection met inclusion criteria. Our COVID-19 positive cohort had a mean age of 56.4 and was largely comprised of African American males (90% male, 80% African American). The other 20% of patients were Caucasian and no Hispanic patients were represented in this group. 15 patients without history of COVID-19 infection qualified for analysis. Mean age of COVID-19 negative patients was 56.5 and these patients were also mostly male (73%). Race characteristics of the COVID-19 negative cohort were 73% Caucasian, 20%

African American, and 7% Hispanic (n = 11, 3, and 1 respectively). The mortality rate was 10% (n = 1) among COVID-19 positive patients and 13% (n = 2) among COVID-19 negative patients. The average time since date of transplant was 10.9 years among COVID-19 negative and 9.4 years among COVID-19 positive patients.

Vaccination rates

Heart transplant recipients at UTMB Galveston had impressive vaccination rates against COVID-19. Only 12% of the 25 patients (n = 3) in our analysis had no documented vaccination history against COVID-19. Three doses of the Pfizer-BioNTech COVID-19 mRNA vaccination is considered a completed vaccination series. 90% of COVID-19 positive patients were vaccinated at the time of analysis with 50% having completed the full series and 40% having two documented doses. 87% of COVID-19 negative patients had documented vaccination—53% completed the vaccination series and 33% had either one or two doses.

COVID-19 positive cohort

Among the COVID-19 positive cohort, average Left Ventricular Ejection Fraction (LVEF) prior to infection, or baseline LVEF, was 57% (n = 10, SD 6.7). Most of these patients had multiple echocardiograms documented during the pre-infection period (1–12 months prior to infection) and all available ejection fractions documented during this time were averaged to calculate each patient's baseline LVEF. Most of these patients had clinically normal LVEFs at baseline—100% of baseline LVEFs were > 40% and only 20% (n = 2) were < 50%. 50% (n = 5) of patients had peri-infection echocardiograms documented from one month before to one month after infection. Average LVEF during the peri-infection period decreased to 46% (n = 5, SD 16.1), but this decrease was not statistically significant when compared to average pre-infection LVEF ($p = 0.3$, 95% CI − 11.5 to 27.6). There was significant variability in recorded LVEFs during the peri-infection period and two patients experienced significant decreases in previously normal LVEFs. Of these two patients, one had recorded LVEFs as low as 5–10% and the other as low as 15–20%. One of these patients passed away

Change in left ventricular ejection fraction (LVEF) among COVID-19 positive cohort

	Pre-infection: 1 to 12 months before infection		Peri-infection: 1 month before to 1 month after infection		Post-infection: 1 month after infection to most recent echo					
					Echo #1:		Echo #2:		Echo #3:	
Patient #	# of Echos	Average LVEF (range)	# of Echos	Average LVEF (range)	Months*	LVEF	Months*	LVEF	Months*	LVEF
1	1	62.5% (60–65%)	0	NA	6–12	55–60%				
2	4	57.5% (55–60%)	2	60% (55–65%)	6–12	55–60%	6–12	55–60%	18–24	25–30%
3	5	60.5% (55–65%)	1	62.5% (60–65%)	1–6	55–60%	1–6	60–65%	6–12	60–65%
4	3	59.2% (50–65%)	0	NA	1–6	55–60%	12–18	55–60%		
5	5	60.5% (55–65%)	10	30.8% (5- > 65%)	1–6	45–50%	1–6	40–45%		
6	1	62.5% (60–65%)	0	NA	1–6	60–65%				
7	3	60.8% (55–70%)	0	NA	6–12	55–60%				
8	1	57.5% (55–60%)	0	NA	1–6	55–60%	12–18	55–60%		
9	2	42.5% (40–45%)	1	47.5% (45–50%)	1–6	50–55%	6–12	40–45%	6–12	55–60%
10	1	47.5% (45–50%)	2	27.5% (15–40%)	1–6	55–60%	6–12	50–55%		

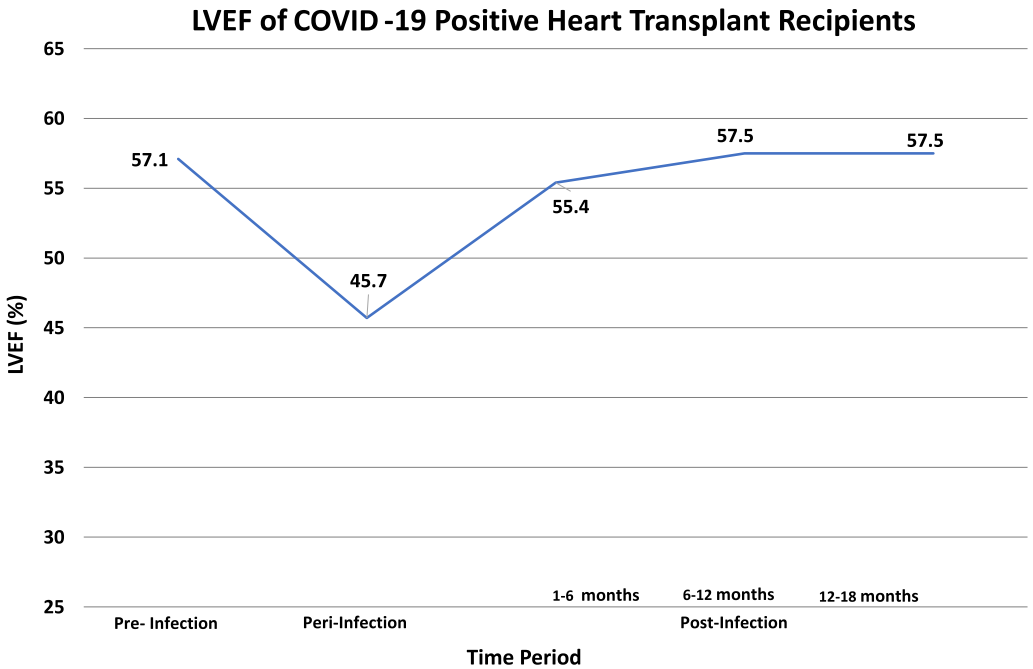
*Number of months elapsed since COVID-19 infection (time from positive test to echocardiogram)

from COVID-19 related complications while the other patient's LVEF recovered to 50–55% at ten months post-infection. The other three patients with peri-infection echocardiograms available experienced clinically insignificant changes in LVEF during this time period. All ten COVID-19 patients had.

post-infection echocardiograms available from one to twelve months after infection. Mean LVEF at the first post-infection echocardiogram at an average of 4.5 months after infection (range 1 month to 11 months) was 56% (n = 10, SD 12.2). The difference between mean LVEF prior to infection and mean LVEF at first post-infection was not statistically significant ($p = 0.6$, 95% CI − 3.6 to 5.8). 50% of patients had two echocardiograms available during the post-infection period, one 1–6 months post-infection and one 6–18 months post infection. These patients all maintained LVEFs ranging from 50–65% from 6 to 18 months post-infection at the second echocardiogram and actually demonstrated an increase in mean LVEF from 53% at baseline to 58% at their second post-infection echocardiogram, although this increase was not statistically significant ($p = 0.2$, 95% CI − 12.3 to 4.1).

Among patients who tested positive for COVID-19, most (60%) received REGEN-COV monoclonal antibody therapy. This infusion was FDA approved as post-exposure prophylaxis for patients at high risk for severe infection on August 10, 2021 (FDA authorizes REGEN-COV 2023). Two of the patients in our cohort who did not receive the infusion tested positive for infection in 2020, prior to FDA approval. The remaining two patients were not treated with the monoclonal antibody due to not fulfilling protocol (according to the medical records) or for an unknown reason. The two patients not treated were the same two patients who experienced significant decline in systolic function during the peri-infection period, with LVEFs of 5–10% and 15–20%.

Valvular function was collected from echocardiograms and analyzed. Valvular dysfunction was considered significant when it was documented in the echocardiogram report as either "mild", "moderate", or "severe". Documentation of "trace" valvular dysfunction was not considered significant. Prior to infection with COVID-19, half of the patients within our cohort (n = 5) had evidence of valvular dysfunction. A statistically significant increase in valvular dysfunction was found among COVID-19 positive patients without documented history of valvular dysfunction on pre-infection echocardiograms ($p = 0.01$, 95% CI 19.3% to 96.4%).



Four of five patients with no documented evidence of valvular dysfunction pre-infection developed valvular dysfunction on echocardiograms conducted during the post-infection period (range 3 months-15 months after positive test). These cases of valvular insufficiency included mild to moderate pulmonic insufficiency, mild mitral regurgitation, and mild tricuspid regurgitation. Among those patients with pre-existing valvular insufficiency, no significant worsening of valvular function was noted on post-infection echocardiograms.

Valvular function among COVID-19 positive cohort

Patient #	Pre-infection: 1 to 12 months before infection	Post-infection: 1 month after infection to most recent echo
1	Normal	Normal
2	Mild TR	Mild TR
3	Normal	Mild- Mod PI + Mild MR
4	Normal	Mild TR
5	Mild- Mod TR, Mild AI, Mild MR	Mild MR + Mild TR
6	Normal	Mild PR
7	Mild-Mod TR	Mod TR
8	Mild TR + Mild MR	Normal
9	Mild MR, Mild-Mod TR, Mild PR, Mod Pulm HTN	Mild MR + Mild-Mod TR
10	Normal	Mild MR + Mild TR

Mod moderate, *TR* tricuspid regurgitation, *MR* mitral regurgitation, *PI*: pulmonic insufficiency, *PR*: pulmonic regurgitation, *AI*: aortic insufficiency, *Pulm HTN* pulmonary hypertension

COVID-19 negative cohort

The average baseline LVEF among COVID-19 negative patients was 58% at echocardiograms conducted from December 2019 to May 2021. 9 of 15 COVID-19 negative patients had echocardiograms available from 1 to 12 months after baseline echocardiograms, and there was no statistically significant change in LVEF among these patients ($p=0.9$, 95% CI − 9.4 to 10.7). 12 of 15 patients had documented echocardiograms 1–2 years after baseline, these patients also experienced no significant change in mean LVEF ($p=0.2$, 95% CI from − 2.3 to 9.6). Lastly, 8 COVID-19 negative patients had echocardiograms 2–3 years after baseline echocardiogram. LVEF did not change among these patients during this time period in comparison to baseline ($p=0.1$, 95% CI − 3.0 to 16.1). Only two of these patients had decreases in previously normal baseline LVEFs to below 40% at time points greater than one year after baseline echocardiogram. Of these, one returned to a normal LVEF while the other remained significantly below their baseline LVEF at 17.5% at most recent echocardiogram.

Discussion

Our study found no statistically significant difference in mean Left Ventricular Ejection Fraction (LVEF) among COVID-19 positive patients during the post-infection period at an average of 4.5 months (range 1–11 months) when compared to pre-infection LVEF. Although 20% (n = 2) of COVID-19 positive heart transplant recipients presented with severe systolic dysfunction during the peri-infection period, the decrease in mean peri-infection LVEF was not statistically significant. These two patients had normal LVEFs at baseline which decreased below 20% during acute infection. One of these patients died from COVID-19 related complications. Of five patients in the COVID-19 positive cohort without previously documented valvular dysfunction, four (80%) developed mild to moderate mitral, tricuspid, or pulmonic dysfunction post-infection. No statistically significant change in LVEF was found among our cohort of 15 heart transplant recipients without history of COVID-19 infection at time points less than one year, 1–2 years, or 2–3 years in comparison to baseline.

Two patients of ten within our COVID-19 positive cohort experienced significant decreases in LVEF during the peri-infection period from one month before to one month after infection. Of these two patients, one patient passed away due to infection-related complications. Both patients were among the minority of COVID-19 positive patients who did not receive the monoclonal antibody infusion, suggesting potential efficacy of monoclonal antibody prophylaxis for prevention of systolic dysfunction induced by severe infection. Our findings suggest a correlation between COVID-19 induced systolic dysfunction and disease severity. Literature supports the use of LVEF as an indicator of disease course and prognosis for patients with or without history of heart transplant. Studies indicate that significant decreases in LVEF are associated with increased mortality rates. One study found that 27% of patients who experienced a decrease in LVEF of at least 10% after infection with COVID-19 died (Morin et al. 2021). Results such as these and the findings of our analysis indicate that COVID-19- induced systolic dysfunction may be correlated with increased risk of mortality. Although COVID-19 mRNA vaccination-induced myocarditis has been documented in the literature and cannot be completely excluded as a potential contributing factor to the decrease in systolic function among our cohort of patients, this complication is very unlikely. According to the US Centers for Disease Control and Prevention, rates of such a reaction to the COVID-19 mRNA vaccinations are estimated to be 12.6 cases per million doses of second-dose mRNA vaccine among studied populations (Bozkurt et al. 2021). The rarity of this complication in addition to the chronology

of events among our patients (decrease in LVEF shortly after COVID-19 infection) points to the infection itself as the cause of systolic dysfunction.

Pre-existing cardiovascular disease and hypertension are independent risk factors for severe COVID-19 infection. Patients with these conditions have increased rates of severe pneumonia, intensive care unit admission, and death once infected (Chakinala et al. 2021). These patients are also more likely to experience myocardial injury due to COVID-19 infection. Elevated troponin levels, indicative of myocardial injury, have been noted in 10% of patients hospitalized with COVID-19 infection. In contrast, elevated troponin levels have been noted in much higher percentages (25–35%) of severely ill patients with co-morbid cardiovascular disease. Heart transplant recipients have high rates of cardiovascular disease and hypertension. 96% of heart transplant recipients in our analysis (24 our of 25) had pre-existing hypertension. The high rates of pre-existing cardiovascular disease and hypertension among this population may contribute to increased disease severity, represented by the 20% of our COVID-19 positive patients who presented with severe infection.

80% of COVID-19 positive patients in our study without valvular insufficiency prior to infection developed evidence of pulmonic insufficiency or tricuspid regurgitation after infection. As mentioned previously, myocardial damage induced by the virus is more common among patients with pre-existing cardiovascular disease or hypertension. COVID-19 induced myocardial injury and impairment of right ventricle (RV) strain are independent predictors of poor prognosis (Martha et al. 2021). COVID-19 infection can cause pulmonary hyperinflation and hypercapnia leading to right heart failure, a known complication of severe pulmonary diseases. This pulmonary-induced right heart failure, or Cor Pulmonale, frequently causes tricuspid valve dysfunction. Studies have found that tricuspid annular plane systolic excursion (TAPSE), a measure of right ventricular and tricuspid valve function, is negatively impacted by COVID-19 infection. Right heart dysfunction from COVID-19 is correlated with increased mortality and may be indicative of disease severity. Despite our small sample size limiting the power of our findings, our study may suggest that COVID-19 infection increases the risk of tricuspid and pulmonic insufficiency. More investigation must be conducted on these findings, but close monitoring of this patient population post-infection is crucial.

Limitations

As with any retrospective chart-review study, our study has limitations. Despite all heart transplant recipients at UTMB Galveston being included in our analysis, our sample was small which limits power and generalizability of our results. More studies, both retrospective and prospective, at centers with larger populations of heart transplant recipients are necessitated to fully understand the impact of COVID-19 infection on this patient population. Heart transplant recipients have high rates of comorbidities which could affect outcomes. Our study was unable to control for these comorbidities meaning imaging collected both prior to and after infection with COVID-19 could have been impacted by comorbid disease. Lastly, heart transplant function was assessed utilizing echocardiograms read by various cardiologists. There may be discrepancies between echocardiogram reads between different cardiologists which we were unable to control for as this study was retrospective.

Conclusions

COVID-19 positive heart transplant recipients did not experience statistically significant decreases in LVEF during the peri- or post-infection periods. 20% of COVID-19 positive patients experienced severe infection with significant decreases in LVEF, one of these patients passed away. A significant increase in rates of valvular dysfunction was found after infection with COVID-19 among heart transplant recipients without prior evidence of valvular insufficiency. Although our population sizes were limited, our findings support those of existing literature which state that COVID-19 may negatively impact heart transplant function both during and after the acute infectious period. More studies are necessitated to determine the chronic effect of COVID-19 infection on heart transplant function. Heart transplant recipients require regular monitoring to prevent life-threatening complications due to infection.

Abbreviations

LVEF	Left ventricular ejection fraction
COVID-19	Coronavirus disease 2019
CDC	Center for Disease Control
ACE-2	Angiotensin converting enzyme-2
UTMB	University of Texas Medical Branch
IRB	Institutional Review Board
NAAT	Nucleic acid amplification
RV	Right ventricle
TAPSE	Tricuspid annular plane systolic excursion

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Author contributions

All authors contributed to conception, design, analysis, and/or interpretation of the data. MM and WK conceived and designed the analysis. MM collected the data. MM, with the assistance of a UTMB- employed statistician, analyzed the data. MM authored the manuscript under the supervision of and with guidance from WK and JCT. WK and JCT revised the manuscript.

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Availability of data and materials
In accordance with HIPAA policy, data utilized in analysis for this project will remain confidential and will not be shared. Deidentified data can be obtained upon request.

Declarations

Ethics approval and consent to participate
IRB approval was obtained for this retrospective analysis (IRB #22-0259). Informed consent was not required as patient care was unaffected and there was no divergence from standard of care. No animals were involved in this research.

Consent for publication
Not applicable.

Competing interests
The authors of this manuscript including MM, WK, and JT, have no financial or non-financial conflicts of interest to disclose.

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