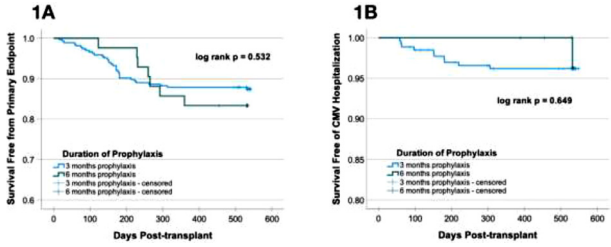
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Methods: Retrospective analysis of 321 intermediate risk (CMV R+) HTx recipients from 6 U.S. centers between 2010-2018 treated with universal prophylaxis with valganciclovir for either 3 months (n = 277) or 6 months (n = 44). The primary endpoint was the development of CMV viremia or end-organ disease resulting in the escalation of anti-CMV therapy. The secondary endpoint was hospitalization for CMV-related infection.
Results: Of the 321 patients in the analysis, 13.4% (n = 43) developed CMV viremia or end-organ infection requiring escalation of anti-CMV therapy, and 3.4% (n = 11) were hospitalized for CMV infection. Overall, there was no significant difference in the primary endpoint in patients treated with 3 months of valganciclovir compared to 6 months (12.6% vs. 18.2%, p = 0.316; Figure 1A). There was a trend toward reduction in CMV hospitalization in the 6-month treatment group (Figure 1B), but this did not achieve statistical significance (3.6% vs. 2.3%, p = 0.651), potentially due to a low number of events.
Conclusion: We found no difference in the risk of CMV viremia or hospitalization for CMV using either a 3-month or 6-month regimen for prophylaxis in HTx recipients at intermediate risk for CMV (R+).



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The Risk of Leukopenia with Universal vs. Preemptive Prophylaxis Strategies in Heart Transplant Recipients at Intermediate Risk for CMV Complications

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Purpose: Heart transplant recipients with prior exposure to CMV (R+) are considered intermediate risk for CMV-related complications, and current guidelines allow for either universal prophylaxis or a pre-emptive approach to prophylaxis. Some centers prefer a preemptive approach to mitigate the cost and risks of prophylaxis, most notably the risk of leukopenia. In the present study, we evaluate the risks of leukopenia with each prophylaxis approach.
Methods: Retrospective analysis of 440 intermediate risk (CMV R+) HTx recipients from 6 U.S. centers between 2010-2018, treated with either universal prophylaxis (73%, n = 323) or preemptive therapy (27%, n = 117). The primary endpoint was the development of leukopenia (WBC < 3.5) in the first 6 months post-transplant. The secondary endpoint was the use of gmCSF to treat severe leukopenia.
Results: Of the 440 patients in the analysis, 177 (40%) developed leukopenia (WBC < 3.5) within the first 6 months. Of those developing leukopenia, the mean WBC nadir was 2.1 +/- 0.7. Overall, there was no significant differnce in the risk of leukopenia in the universal prophylaxis group compared to the preemptive prophylaxis group (42.7% vs. 33.3%, p = 0.076). Additionally, there was no difference in the need for gmCSF between the groups (2.9% vs. 5.3%, p = 0.236). In those developing leukopenia in each group, there was no difference in the mean WBC nadir (2.2 +/- 0.7 vs. 2.1 +/- 0.7, p = 0.743).
Conclusion: Leukopenia occurs in 40% of heart transplant recipients. Although CMV prophylaxis has been associated with leukopenia, there is no difference in this risk when comparing a universal vs. preemptive prophylaxis strategy for CMV.

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Universal CMV Prophylaxis Mitigates the Risks of Basiliximab Induction in Heart Transplant Recipients at Intermediate Risk (R+) for Post-Transplant CMV Complications

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Purpose: Induction therapy with either thymoglobulin or basiliximab is used in approximately 50% of patients at the time of heart transplant. While the use of thymoglobulin has been reported to increase the risk of CMV reactivation, it remains unclear if this risk is also seen with basiliximab. In the present analysis, we compared post-transplant CMV outcomes in patients receiving basiliximab vs. no induction in a multicenter, retrospective analysis. We also assess the effects of universal prophylaxis on any attendant risk.
Methods: Retrospective analysis of 439 intermediate risk (CMV R+) HTx recipients from 6 U.S. centers between 2010-2018 treated with either basiliximab induction (63%, n = 276) or no induction (37%, n = 163). The primary endpoint was the development of CMV viremia or end-organ disease resulting in the escalation of anti-CMV therapy. The secondary endpoint was hospitalization for CMV-related infection.
Results: Of 439 patients in the analysis, 18.9% (n = 83) developed CMV viremia or end-organ infection requiring escalation of anti-CMV therapy, and 5.7% (n = 25) were hospitalized for CMV infection. Patients who received induction with basiliximab were more likely to meet the primary endpoint (22.8% vs. 12.3%, p = 0.006) and had a trend towards higher risk for CMV hospitalization (7.2% vs. 3.1%, p = 0.068) in the overall group. However, in patients receiving universal CMV prophylaxis, there was no difference in the primary (14.7% vs. 13.1%, p = 0.672) or secondary endpoint (4.1% vs. 3.3%, p = 0.687) when basiliximab was used compared to no induction. Alternatively, 36% of patients receiving basiliximab induction reached the primary endpoint when a preemptive therapy approach to prophylaxis was used (vs. 0% in no induction, p = 0.021).
Conclusion: Although basiliximab induction increases the risk of CMV viremia/end organ damage and CMV-related hospitalizations, this risk is eliminated when a universal CMV prophylaxis strategy is used.

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Six-Month Outcomes of Heart Transplant Recipients Infected by COVID-19

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Purpose: COVID-19 infection might be associated with higher mortality risk for transplanted patients, as a result of their multiple co-morbidities and their immunosuppressed status. We sought to describe the six-month outcomes of heart transplant (HT) recipients infected by COVID-19.
Methods: We retrospectively analyzed clinical and echocardiographic data from all HT recipients infected with COVID-19 between March and April 2020. All patients were followed for a minimum of 6 months or until death.
Results: Twenty-eight HT patients were studied, median age was 64 (range 59-69) and 22 were male. Co-morbidities included obesity (25%), diabetes (61%), HTN (71%), CKD (68 %) and chronic lung disease (36%). Eight patients died (29%) (non-survivors) and 20 survived (survivors) COVID-19 infection. All patients who survived the initial hospitalization period remained alive at 6 months (figure 1). There was no difference in the prevalence of co-morbidities between survivors and non-survivors. Survivors had lower peak ferritin (2185 ± 793 vs 18023 ± 16724, p= 0.04) and procalcitonin (0.8 ± 0.3 vs 104 ± 31, p<0.005). Baseline allograft function was similar between survivors and non-survivors and it remained unchanged at 6 months for the survivors' group (LVEF baseline: 58 ± 1% vs LVEF 6 m 61 ± 3%). Renal function returned to baseline in 85% of survivors at 6 months after hospitalization. Mycophenolate mofetil was held during the acute infection and was resumed after discharge. At 6 months follow-up, all patients returned to their baseline

immunosuppression regimen, have no further symptoms of COVID-19 and there have been no subsequent rejection events.

Conclusion: COVID-19 infection is associated with a high fatality rate (29%) among HT recipients, however, HT recipients that survive the acute COVID-19 infection have preserved allograft function and end-organ function has returned to baseline at 6 months follow-up.

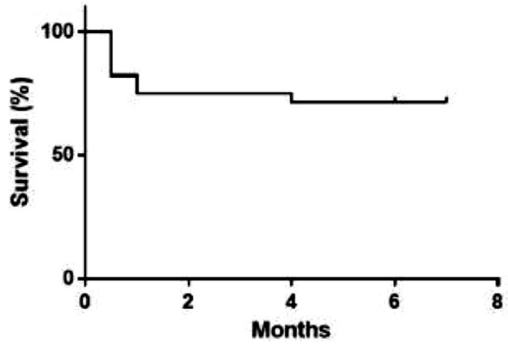

Figure 1. Survival curve of heart transplant recipients infected by COVID-19.

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Non-Association of Infectious Exposure and Seasonality with Cardiac Graft Rejection

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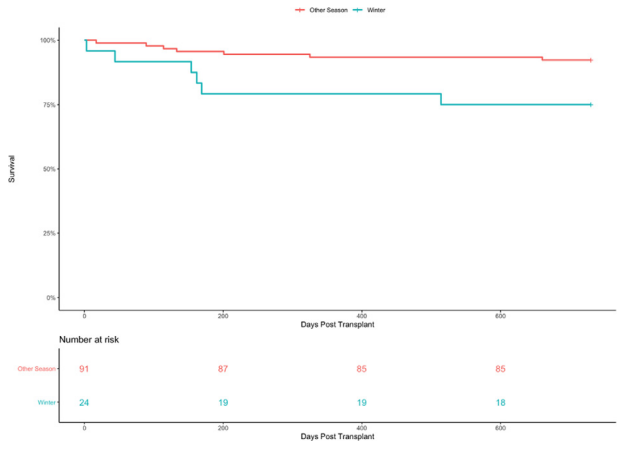
Purpose: Graft rejection remains a significant complication following cardiac transplantation. As infection results in elevated immune system activity, we hypothesized that acute rejection events would be more common following infectious exposures and during the winter respiratory virus season.

Methods: Patients were included who underwent cardiac transplantation at our center in the Midwest, between January 1st, 2014 and December 31st, 2017. The composite endpoint consisted of antibody mediated rejection (AMR), donor specific antibodies (DSA), heart failure readmissions, and death within two years. Infectious events collected during readmissions included a primary infectious diagnosis, positive respiratory virus panel, and other diagnosed or treated infections excluding BK, CMV, and EBV.

Results: We analyzed 115 patients meeting inclusion criteria. The primary composite endpoint was met by 69 patients (60%). Pre-transplant PRA Class 1 was associated with the composite endpoint (HR 1.03, 95% CI 1.003-1.05, p<0.05). Overall, 85 patients (73.9%) had an infectious event. Twenty two of 69 patients (32%) meeting the composite endpoint had an infectious event within 6 months prior to the endpoint. Incidence of the composite endpoint and secondary endpoints did not vary by season (p>0.05). However, patients transplanted during winter - defined as January to March - had worse survival when compared to a composite of other seasons (2-year survival: 75% vs 88.7%, p=0.014) (Figure 1). Freedom from the composite endpoint was not associated with whether a patient had an infectious event (p>0.05).

Conclusion: Our study did not show any association between infectious exposure and rejection following cardiac transplantation. However, this analysis was likely underpowered to determine this association and national studies are needed.



(262) *Reprinted from the April 2020 meeting issue by approval*

Factors Associated with Neutropenia Post-Heart Transplantation

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Purpose: Neutropenia is a serious complication following heart transplantation (OHT) however risk factors for its development and its association with outcomes is not well described. We sought to study the prevalence of neutropenia, risk factors associated with its development and its impact on infection, rejection and survival.

Methods: A retrospective single center analysis of adult OHT recipients from July 2004 to December 2017 was performed. Demographic, laboratory, medication, infection, rejection and survival data were collected for 1 year post-OHT. Baseline lab measurements were collected within the 24 hours before OHT. Neutropenia was defined as absolute neutrophil count ≤ 1000 mm3. Cox proportional hazards models explored associations with time to first neutropenia. Associations of neutropenia, analyzed as a time-dependent covariate, with secondary outcomes of time to infection, rejection or death were also examined.

Results: Of 278 OHT recipients, 84 (30%) developed neutropenia within a median of 142 days (81-228 days) after transplant. More than half (56%) of those with neutropenia were treated with GCSF. Most infections were CMV disease whether they occurred before (14/22, 64%) or after (8/9, 89%) neutropenia or in the absence of neutropenia (20/40, 50%). Factors associated with increased risk of neutropenia are in Table 1. Neutropenia was not significantly associated with secondary outcomes of infection (N=9), rejection (N=10) or death (N=4), however numbers were small.

Conclusion: Neutropenia is a fairly common occurrence after adult OHT. Infection was associated with subsequent neutropenia, however no statistically significant differences in outcomes (infection, rejection, death) were found between neutropenic and non-neutropenic patients in this small study. It remains to be determined if medication changes in response to neutropenia impact patient outcomes.

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Associations of Risk factors with Outcome of Neutropenia

	Unadjusted Hazard Ratio (HR)	95% Confidence Interval (CI)	Adjusted HR	95% CI
Lower Baseline WBC per unit /mm3	1.10	1.01-1.21	1.12	1.11-1.24
Pre-transplant Left Ventricuar Assist Device	1.63	1.01-2.66	1.63	1.001-2.66
Baseline eGFR <60 mL/min/1.73m2	1.56	1.02-2.39	N/A	
High Risk CMV Serostatus (D+/R-)	1.87	1.21-2.88	1.86	1.19-2.88
Length of Transplant Hospital Stay (per week)	1.05	1.01-1.10	N/A	
Valganciclovir at Time of Hospital Discharge	2.14	1.35-3.38	N/A	
Previous CMV infection - time dependent	8.40	4.52-15.6	7.34	3.92-13.7

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Location, Location, Location - Does Epitope Matching Matter in Pediatric Heart Transplantation?

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Purpose: Recent data in adult solid organ transplantation suggest that epitope-based human leukocyte antigen (HLA) matching may permit better risk assessment of *de novo* donor−specific antibody (dnDSA) development