1744. CMV Infection and Management Among Pediatric Solid-Organ Transplant Recipients

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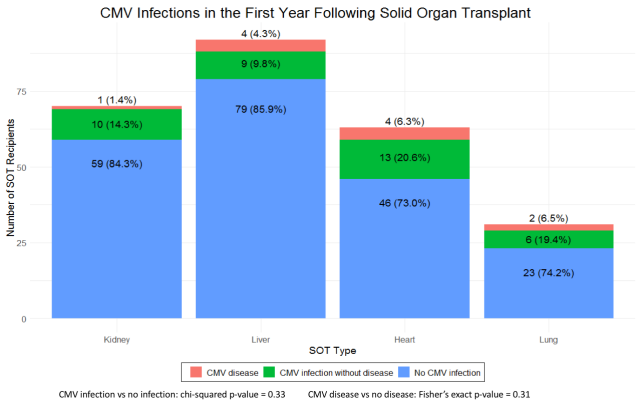
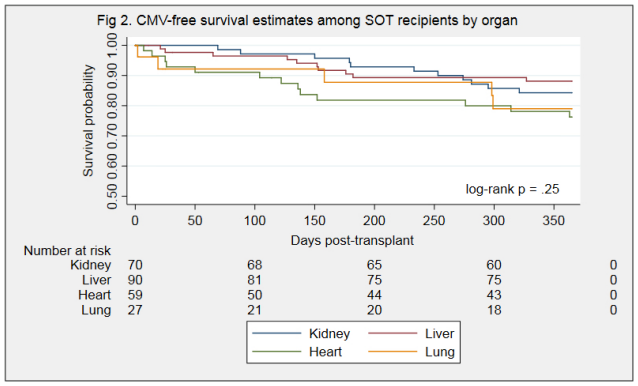
Background. Our institution provides universal CMV prophylaxis (PPX) for all high (D+/R-) and medium risk (R+) solid-organ transplant (SOT) recipients. We sought to evaluate this practice by assessing CMV infection and disease within the first year of SOT.

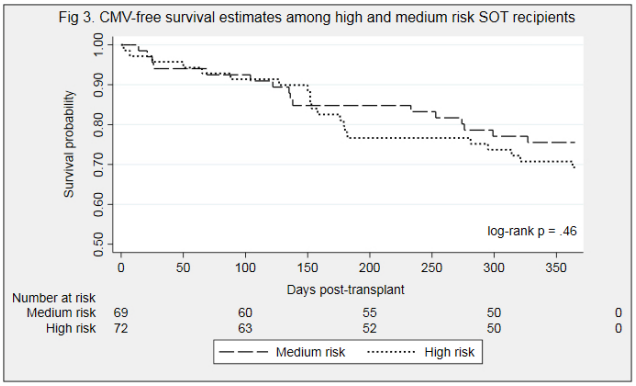
Methods. Retrospective cohort study of all children undergoing first SOT at Children's Hospital of Philadelphia from January 2012 to October 2017. We identified recipients with CMV infection (detection of CMV DNA in body fluid/tissue with or without symptoms) and disease (symptomatic or tissue-invasive infection) in the first year after SOT. We calculated the rate of CMV infection and compared CMV-free survival based on SOT type and CMV risk using log-rank tests.

Results. 244 children received 246 SOTs: 90 liver, 70 kidney, 59 heart, 27 lung. In total, 39 children (16%) had 49 CMV infections in the first year after SOT, including 29% of high (n = 21/72) and 23% of medium risk recipients (n = 16/69). The fraction of each organ type with CMV infection was similar (Figure 1, P = 0.33). Among high and medium risk recipients, all of whom received PPX, the incidence rate of CMV infection in the first year post-SOT was similar: 10.1 vs. 7.8/10,000 days (P = 0.22). There were no differences in CMV-free survival by organ (Figure 2, log-rank P = 0.25) or between high and medium risk recipients (Figure 3, log-rank P = 0.46). In total, 22% (n = 10/45) of CMV infections in high/medium risk patients occurred while on PPX; half were in the setting of reduced PPX dosing or within 2 weeks of SOT. Of the 35 CMV infections post-PPX, the median time to detection of CMV after PPX was 39 days (IQR 28–98). There were 11 cases (6 high, 5 medium risk) of CMV disease: 6 CMV syndrome, 2 hepatitis, 2 pneumonitis, 1 GI disease. Valganciclovir was more often used for treatment of asymptomatic infections than for CMV disease (79% vs. 33%, P = 0.03). All-cause mortality in the first year post-SOT was similar among those with and without CMV infections (7.7 vs. 6.3%, P = 0.76) and among those with and without CMV disease (9.1 vs. 5.2%, P = 0.57).

Conclusion. CMV infection was common in high and medium risk SOT recipients in the first year following SOT, and most infections occurred off of PPX. Our data suggest that the highest risk period for CMV infection is in the first months after PPX, and that monitoring may be most useful after PPX has been stopped or when PPX doses are reduced.







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1745. Retrospective Cohort Analysis to Determine the Incidence of CMV Infection and Disease in Allogeneic Hematopoietic Cell Transplant Recipients at an Academic Children's Hospital

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Background. Data on cytomegalovirus (CMV) infection and disease by donor (D)/recipient (R) status or prophylaxis regimen in pediatric hematopoietic cell transplant (HCT) recipients are limited. There is an absence of data on adverse events (AE) attributable to prophylaxis.

Methods. A single-center cohort (N = 352) of allogeneic HCT episodes between January 2004 and June 2017 was assembled. Exclusion criteria were CMV PCR positivity 30 days before HCT, lack of CMV surveillance (<2 blood PCRs in the 30 days post HCT), or unknown D/R CMV status. CMV prophylaxis was recommended for CMV D+ or R+ patients with ≥1 of the following factors: T-cell depletion, cord blood product, or exposure to distal alemtuzumab. The CMV prophylaxis regimen was standard-dose acyclovir from day −7 to +7, then foscarnet to engraftment, and then valganciclovir to day +100 (acyc → fos → valgan). If a patient did not meet criteria for CMV prophylaxis but was HSV IgG positive then standard-dose acyclovir was given from day −7 to the end of study follow-up (SD-acyc). All remaining patients did not receive antiviral prophylaxis. Outcomes of CMV infection and CMV disease by day +180 were captured. AEs attributable to antiviral prophylaxis were also identified. An AE was attributed to an antiviral prophylaxis medication if the dose was reduced or stopped. AEs were only reported in HCT episodes with complete medical records (n = 221).

Results. The CMV infection rate was 26.7%, with a median time to detection of 23.5 days (range: 4–146). CMV infection was common in D+/R+ (58.9%) and D−/R+ (34.6%) patients. Just under 11% of CMV infections progressed to disease (Figures 1 and 2). Breakthrough CMV infection occurred in 49.1% of patients despite acyc → fos → valgan (Figure 3) at a median of 11 days from HCT (range: 4–132). The attributable AE rate was 13.4% and 36.8% for SD-acyc and acyc → fos → valgan, respectively (Figure 4).

Conclusion. CMV infection was common in D+/R+ and D−/R+ patients, and a substantial proportion progressed to disease. Breakthrough infection persisted despite acyc → fos → valgan prophylaxis and AEs attributable to this regimen were common. CMV infection in R+ patients was frequent even in the absence of additional risk factors. Studies of novel prophylaxis approaches are needed and should include R+ patients regardless of other factors.

Figure 1. CMV infection and disease rates, in pediatric allogeneic HCT recipients under CMV surveillance.

		Donor/Recipient CMV Serology Status			
	All (n=352)	D-/R- (n=117)	D+/R- (n=58)	D-/R+ (n=104)	D+/R+ (n=73)
CMV infection, n (%)	94 (26.7)	4 (3.4)	11 (19.0)	36 (34.6)	43 (58.9)
Time from transplant to reactivation in days, median (range)	*23.5 (4–146)*	*32 (4–47)*	*20 (4–48)*	*26.5 (4–146)*	*22 (4–111)*
Specimen where CMV first detected, n (%)					
Blood	*91 (96.8)*	*4 (100)*	*11 (100)*	*34 (94.4)*	*42 (97.7)*
Bronchoalveolar lavage	*2 (2.1)*	*0 (0)*	*0 (0)*	*1 (2.8)*	*1 (2.3)*
Stool	*1 (1.1)*	*0 (0)*	*0 (0)*	*1 (2.8)*	*0 (0)*
Progression to CMV disease, n (%)	*10 (10.6)*	*1 (25.0)*	*2 (18.2)*	*1 (2.8)*	*6 (14.0)*
CMV disease type first detected					
Gastrointestinal disease	*2*	*1*	*0*	*1*	*0*
Gastrointestinal disease AND hepatitis	*1*	*0*	*1*	*0*	*0*
Hepatitis	*1*	*0*	*0*	*0*	*1*
Pneumonitis	*6*	*0*	*1*	*0*	*5*

CMV: Cytomegalovirus; HCT: hematopoiietc cell transplantation; D: donor; R: recipient