High Proportion of Symptomatic CMV Infection Despite Optimal Practice of a Preemptive CMV Strategy for Recipients of Solid Organ Transplantation (SOT) and Hematopoietic Stem Cell Transplantation (HSCT)

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Objectives: The preemptive strategy for CMV infection in transplant recipients aims to prevent CMV disease by screening for and treating emerging infections. Current guidelines recommend weekly screening to secure early diagnosis. An implicit failure criterion of the strategy is if the recipient is already symptomatic at diagnosis of infection. The rate and risk factors for failure of a preemptive strategy is unclear in the literature but examined here in a large, unselected cohort of SOT and HSCT recipients.

Method: Consecutive SOT and HSCT transplanted between 2003-23/10/2014 with a first CMV infection within the first year of transplantation and with a pre-transplant CMV IgG serostatus of either D+/R+, D+/R- or D-/R+ were eligible for inclusion. CMV infection was defined as ≥2 consecutive samples taken within two weeks of each other at ≥270 IU/mL, or one CMV PCR ≥2,700 IU/mL. SOT recipients received 90 days prophylaxis followed by preemptive screening, HSCT recipients were managed solely pre-emptively. Patient records of the CMV infection episodes were retrospectively reviewed for presence of symptomatic CMV infection according to international definitions on CMV disease (Ljungman et al. 2002, Preiksaitis et al. 2005). Recipient characteristics were compared using descriptive statistics.

Results: Of 164 SOT and 193 HSCT presenting with first time CMV infection after transplantation, 76 (21%) had CMV-related symptoms at the time of the 1st positive CMV viral load in blood (50% with syndrome and 50% with end-organ disease). Median (IQR) of 1st positive CMV viral load was 6,764 IU/mL (950-53,100) for those with symptoms vs 990 IU/mL (450-3,060) for those without ($p<0.0001$) and the % with high-risk of CMV infection was also higher (64% vs 47%, $p=0.01$). Prevalence of symptomatic CMV infection also differed depending on viral load of the first positive CMV PCR (13% (39/289), 48% (16/33) and 71% (20/28) for <9,000, 9,000-45,000 and >45,000 IU/mL, respectively, $p<0.001$) and on time since last negative CMV PCR (16%, 19%, 22% and 28% ($p<0.001$) for <8, 8-14, 14-30 and > 30 days, respectively). For the latter, the 1st positive CMV viral load was gradually higher the longer the period since the last negative test (900, 4,140, 42,300 and 19,215 IU/mL, respectively). These figures were consistent after adjusting for type of transplantation.

Conclusion: Despite optimal practice of the preemptive strategy according to current guidelines to prevent CMV disease in transplant recipients, 16% of patients contracting CMV infection fail the strategy with 50% presenting with end-organ disease. Extending the preceding screening interval to 14 days did not affect these figures. Our data suggest additional research is warranted to improve the understanding of the factors explaining failure to the preemeptive strategy, and in particular those explaining the development of CMV-related symptoms at low CMV PCR viral load which include end-organ disease.