Impact of Cytomegalovirus Infection on Long-Term Allograft Function and Survival in Renal Transplant Recipients

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Background

• Cytomegalovirus (CMV) in solid-organ transplant recipients is known to be associated with immunomodulatory effects on the allograft, such as an increased incidence of acute rejection and graft loss .

• The incidence of CMV infection is reduced by antiviral prophylaxis, but its use is associated with the emergence late-onset CMV disease.

• While controversial, late-onset CMV disease may not be associated with indirect effects, suggesting a potential protective effect of early anti-CMV prophylaxis on graft outcome

Methods

Retrospective analysis of a cohort including all adult patients who underwent kidney transplantation at a tertiary Hospital from 2004 to 2008, and that had at least a 3-month follow-up.

All patients received three months of antiviral prophylaxis according to the CMV serostatus:

1. D+/R- and R+ serostatus received antiviral prophylaxis with valganciclovir
2. D-/R- patients received valaciclovir.

After discontinuation of prophylaxis, all patients at risk for CMV infection were preemptively followed for the development of CMV infection by PCR in blood every 2 weeks during three additional months

Statistics

The impact of CMV infection and disease on graft failure-free survival was investigated by using Kaplan-Meier survival analysis and a Cox proportional-hazards model with additional covariates age, sex, rejection, serostatus, and type of transplant.

Results

161 patients received a renal transplantation with a median follow-up of 7 years (range 6-9 years).
66% had an induction therapy with basiliximab. Maintenance therapy was tacrolimus, mycophenolate and prednisone for 87%.
On the 161 patients 81 % and 28% received respectively Valgancyclovir and valaciclovir for a median duration of 91 days (IQR 87-98).

During the first year post transplant, 59/161 (37%) patients developed CMV infection and 11/161 (6.8%) patients developed CMV disease.

Overall, 32/161 (20%) patients developed graft loss during the study follow-up. The probability of graft failure-free survival was 85.2% and 89.6% at 5 years and 67.9% and 79.7% at 10 years in patients with or without CMV infection, respectively (p=0.22 by log-rank test, **Figure 1A**).Results were similar in patients with and without CMV disease (p=0.22). Neither CMV infection (p=0.3) or CMV disease (p=0.48) were associated with a higher incidence of graft loss.
By Cox regression model, the type of donor (deceased vs. living donor) was the only significant factor (HR 2.94 [95% CI 1.32-6.56], p=0.004) for graft loss.

Creatinine levels at the last follow-up was not significantly different between patients with or without CMV infection (152 µmol/L [SD 81] vs. 155 µmol/L [SD 100], p=0.86, respectively) (**Figure 1B**).

Figure 1. A: Graft loss-free survival in patients with or without CMV infection. Log-rank test (p=0.22).

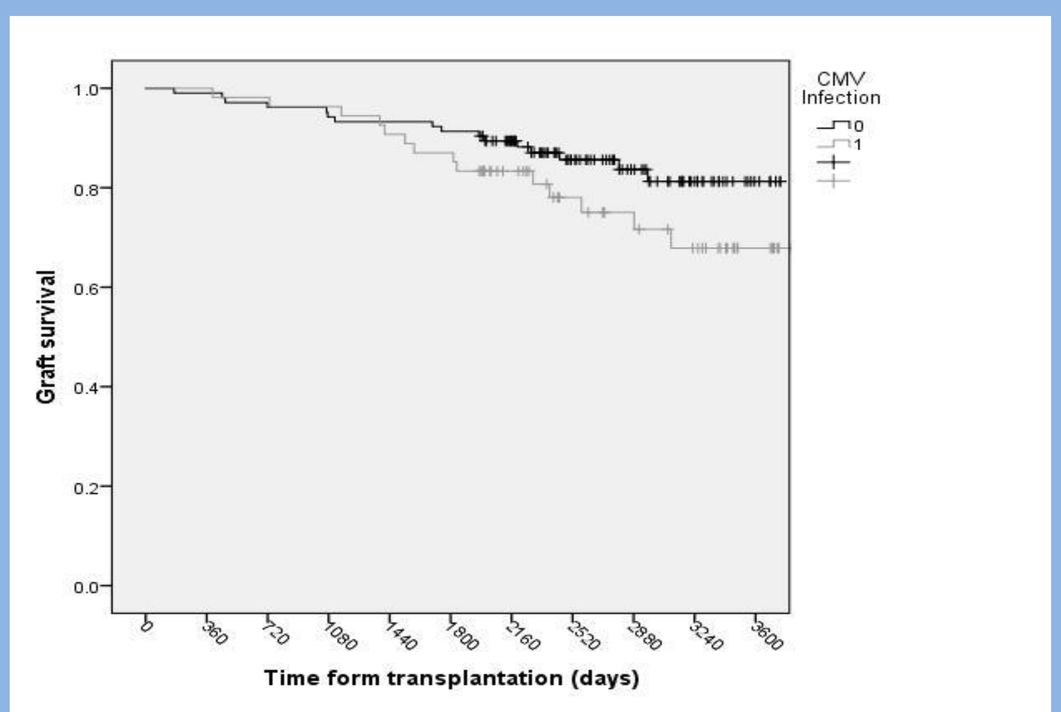
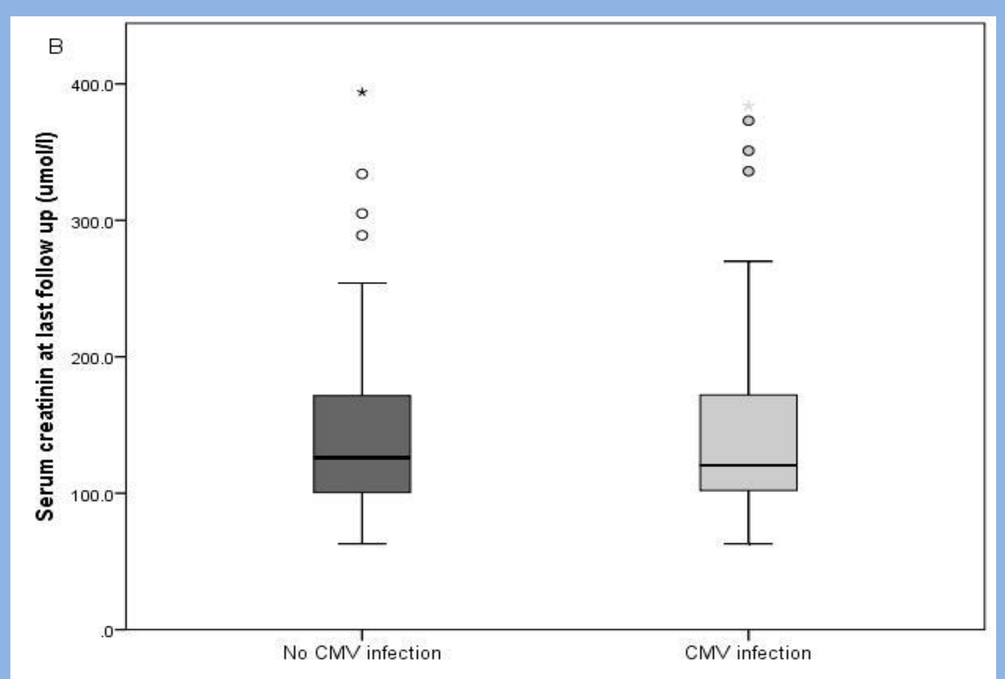


Figure 1. B: Creatinine levels (µmol/l) at the last follow-up in patients with (light gray boxplot) or without CMV infection (dark grey boxplot) (p=0.85)



Conclusion

• Late-onset CMV infection/disease in kidney transplant recipients who had received antiviral prophylaxis were not associated with impaired allograft function or survival, suggesting that late-onset CMV infection may not carry the same risks than early CMV infection.

• More long-term follow-up analyses are required to further assess this important question.

DOI: 10.3252/pso.eu.54ERA.2017