Post-transplant CMV-Infection: Therapeutic and Immunological Risk Factors

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BACKGROUND

- Post-transplantation Cytomegalovirus (CMV) infection remains a potentially serious complication to immunosuppression with risk of progression to CMV disease.
- There is currently no consensus on approach to the prevention of CMV disease.
- Pathogenesis and risk factors for CMV disease are well described, however few studies address individual combinable risk factors for predisposing CMV infection.

OBJECTIVES

- To investigate pre- and post-transplantation variables and their association with risk of CMV infection within the first 12 months of transplantation in a cohort of solid organ (Heart, Kidney, Liver, Lung) and bone marrow transplant patients.

METHODS

Patients and study design
- Consecutive patients transplanted between 2004-2007 and routinely screened for CMV infection by a minimum of 3 CMV-PCR measurements within the first 12 months of transplantation were included.
- Data was extracted from electronic health records, retrospectively.

CMV-DNA
- Detection of CMV-DNA was performed in the Department of Clinical Microbiology at Rigshospitalet. The analyses were done on EDTA-blood using the Cobas AmpliCoral monitor PCR test.

Endpoint definition
- CMV infection was defined a priori to be present if a patient had two consecutive CMV-PCR measurements above lowest limit of detection (500 copies/mL) or alternatively one CMV-PCR ≥ 3000 copies/mL.

Statistical methods
- Time to CMV-infection was investigated using Cox proportional hazards analysis; both fixed-time and time-updated variables were explored.
- The following fixed-time variables were included in the Cox models: Type of transplantation, Donor(D)/Recipient(R) CMV serostatus, gender, age, prior transplantation and year of transplantation.
- The following time-updated variables were included in the Cox models: Use of immunosuppressive drugs and use of anti-CMV drugs.
- Subgroup analyses were performed on patients who had a solid organ transplantation and among patients with known Donor/Recipient CMV serostatus.

RESULTS

Baseline characteristics
- In total 377 patients were included in the study.
- The Baseline characteristics for all patients are shown in Table 1.
- There were a total of 111 patients with CMV-infection endpoints, the distribution between the type of transplantation and time to CMV-infection is shown in Figure 1.
- The risk of CMV-infection was higher for all types of solid organ transplantations compared with bone marrow transplantation (Figure 2).
- In subgroup analysis of solid organ transplantation the highest risk of CMV-infection was seen in transplantations where the donor was CMV serostatus positive (Figure 3).
- The risk of CMV-infection was increased when patients were using immunosuppressive drugs and it was reduced when patients were using anti-CMV drugs (Figure 4).
- Among patients given and patients not given anti-CMV chemoprophylaxis, comparable numbers developed CMV-infection (Figure 5).

SUMMARY

- The risk of CMV-infection was higher among recipients of all forms of solid organ transplantation compared with bone marrow transplantation.
- In solid organ transplantation the risk of CMV-infection was highest for CMV serostatus combination D+/R-.
- When the recipient was CMV serostatus positive the risk of CMV-infection was 80% higher if the donor was CMV serostatus positive versus negative.
- The risk of CMV-infection was increased while using immunosuppressive drugs.
- Anti-CMV drugs reduced the risk of CMV-infection by 70% while actively used, but appears to merely postpone the onset of this event rather than preventing it.

CONCLUSION

- Use of anti-CMV chemoprophylaxis may possibly be restricted to donor CMV serostatus positive transplantations where the risk of CMV-infection is highest.
- In these cases the duration of anti-CMV chemoprophylaxis should possibly be extended beyond the current standard of care.
- Preemptive treatment may possibly be the optimal intervention in donor CMV serostatus negative transplantations where the risk of CMV-infection is lower.
- Effects and risks from stratification of anti-CMV intervention as outlined above should be evaluated in future clinical trials.