

The Risk of Cytomegalovirus Infection and Recurrence Among Solid Organ Transplant Recipients

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BACKGROUND

- Cytomegalovirus (CMV) infection continues to be one of the most important pathogens affecting solid organ transplant (SOT) recipients.
- Several risk factors have been identified for CMV infection post transplant but less is known about the risk of recurrent CMV.

AIM

- To identify risk factors associated with CMV infection and recurrence following SOT.

OUTCOMES

- First CMV infection:** The first of two-consecutive plasma CMV PCR ≥ 273 IU/mL taken ≤ 14 days of each other, or one CMV PCR ≥ 2730 IU/mL in the year after transplant.
- Recurrent CMV:** A second diagnosis of CMV infection within 6 months of clearing and stopping treatment for the first CMV infection. Clearance of CMV was defined as the first date of two consecutive negative CMV PCR tests.

METHODS

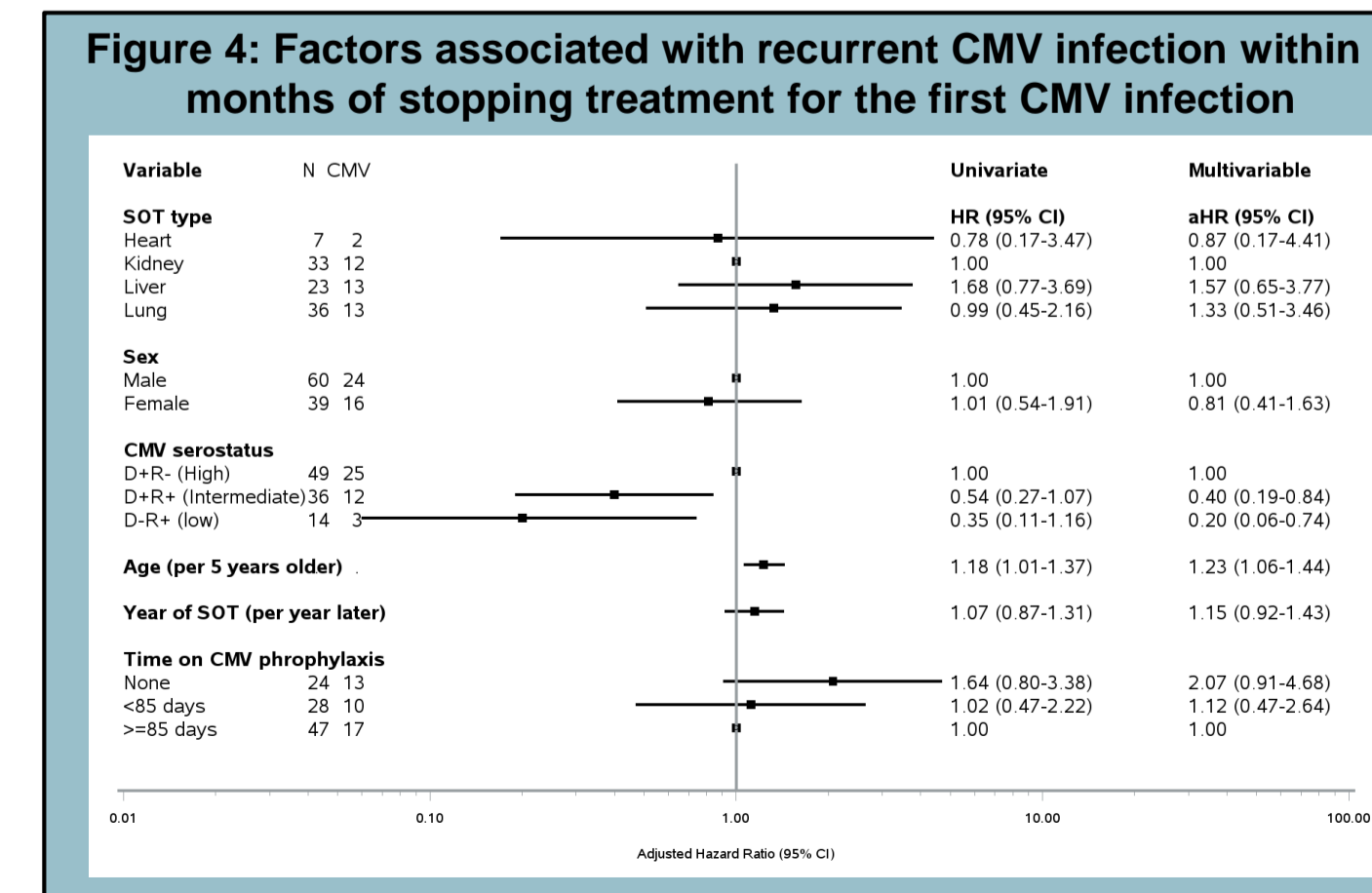
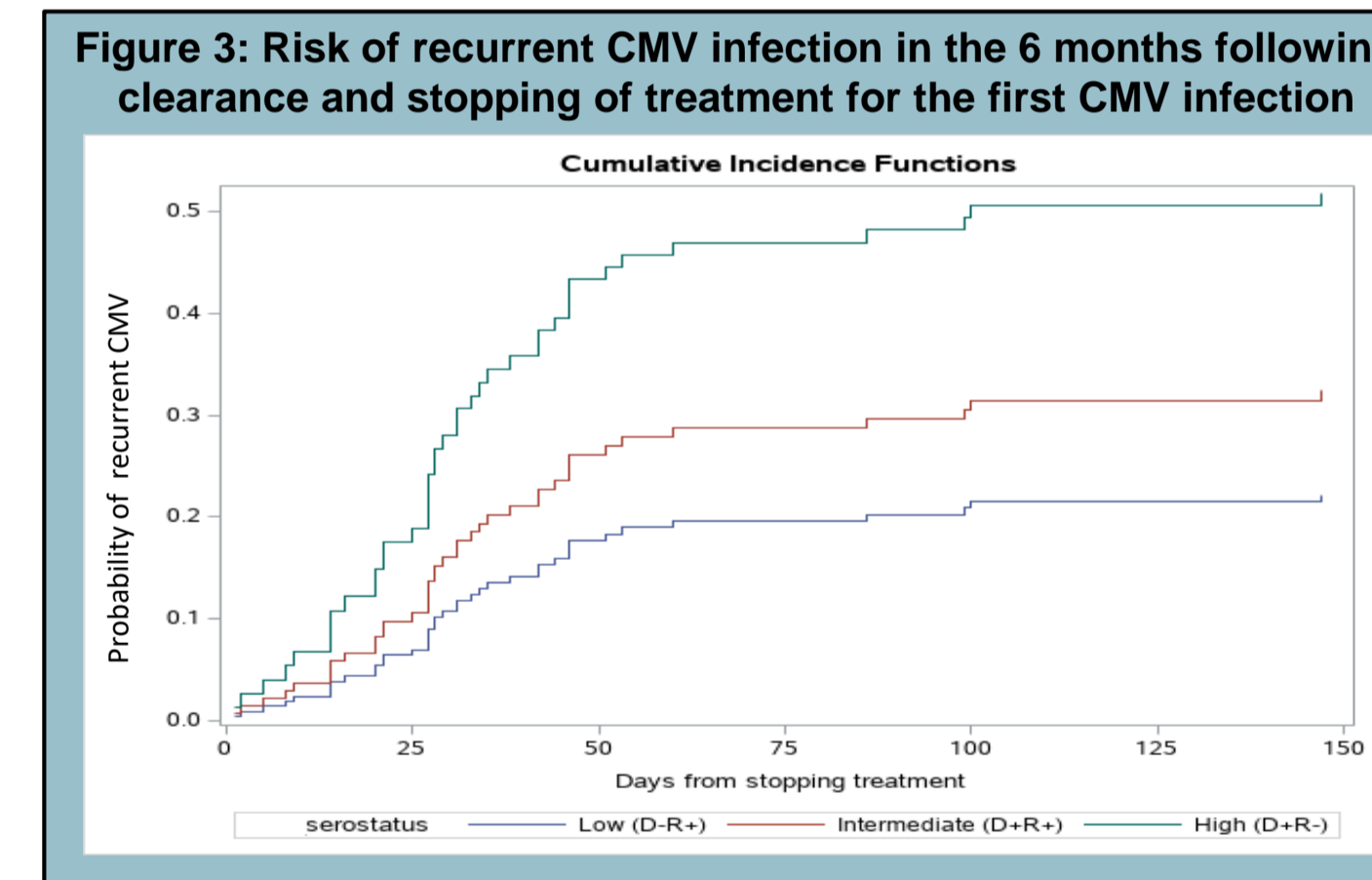
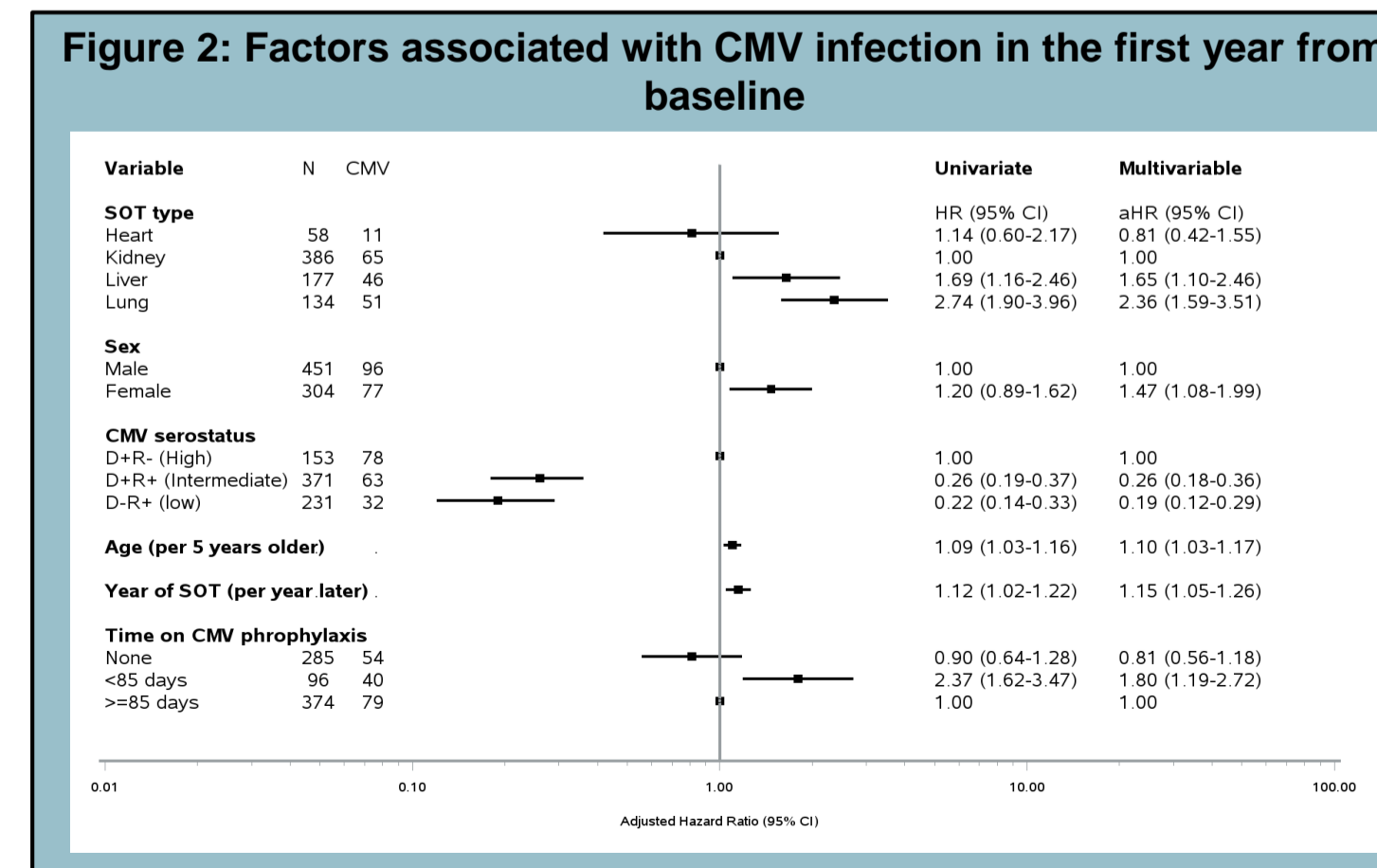
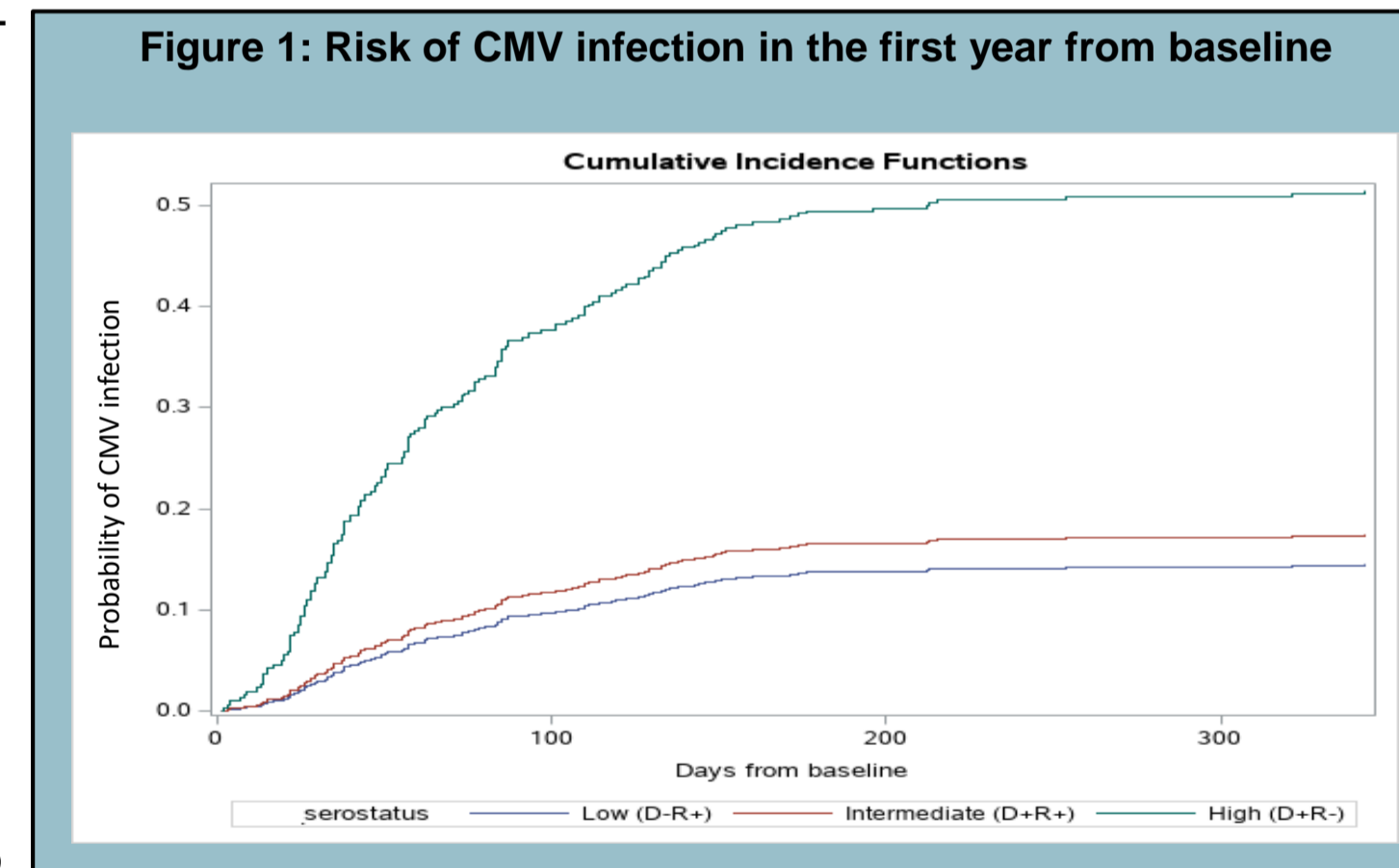
- SOT recipients (aged ≥ 18 years) transplanted between 2011-2016 at Rigshospitalet, Denmark were included.
- Cumulative incidence curves and Cox proportional hazards models were used to investigate factors associated with CMV infection and recurrence.
- Baseline was defined as either SOT date (n=285) or date of stopping CMV prophylaxis for those initiating prophylaxis within 7 days of transplant (n=470).
- Individuals with unknown (n=35), or D-R- (n=117) CVM IgG serostatus at transplant and those who experienced breakthrough CMV while on prophylaxis (n=29) were excluded.
- Individuals who had a first CMV infection but did not have a treatment record (n=44) or follow-up CMV PCR measurements (n=22) were excluded from the recurrent CMV analysis.

Table 1: Demographics at the time of SOT

| | All SOT recipients N=755 | | Assessed for recurrent CMV N=99 | |
|---|-----------------------------|-----------|------------------------------------|-----------|
| | n | % | n | % |
| Transplant type (n, %) | | | | |
| Heart | 58 | 7.7 | 7 | 7.1 |
| Kidney | 386 | 51.1 | 33 | 33.3 |
| Liver | 177 | 23.4 | 23 | 23.3 |
| Lung | 134 | 17.8 | 36 | 36.4 |
| Male (n, %) | 451 | 59.7 | 60 | 60.6 |
| CMV IgG serostatus (n,%) | | | | |
| D+R- (High) | 153 | 20.3 | 49 | 49.5 |
| D+R+ (Intermediate) | 371 | 49.1 | 36 | 36.4 |
| D-R? (low) | 231 | 30.6 | 14 | 14.1 |
| Time on prophylaxis (n,%) | | | | |
| None | 285 | 37.7 | 24 | 24.2 |
| <85 days | 96 | 12.7 | 28 | 28.3 |
| ≥ 85 days | 374 | 49.5 | 47 | 47.5 |
| Age (median, IQR) | 50 | 41-59 | 53 | 45-59 |
| Year of transplant (median, IQR) | 2014 | 2012-2015 | 2014 | 2012-2015 |

Table 2: Characteristics of the first two CMV infection episodes following SOT

| | First CMV infection | | CMV recurrence | |
|---|---------------------|-------------|----------------|----------|
| | N | % | N | % |
| Total assessed for outcome (N, %) | 755 | 100 | 99 | 100 |
| CMV infection (N, % of total) | 173 | 22.9 | 40 | 40.4 |
| CMV viral load at detection, IU/ml (median, IQR) | 637 | 273-2457 | 364 | 273-1228 |
| Days from baseline to CMV infection (median, IQR) | 57 | 33-110 | 28 | 20-45 |
| Cleared infection (N, % with infection) | 165 | 95.4 | 38 | 95.0 |
| Days from detection of CMV infection to clearance (median, IQR) | 29 | 21-39 | 23 | 18-32 |
| Maximum CMV viral load, IU/ml (median, IQR) | 3185 | 1001-20,930 | 1137 | 364-2138 |



RESULTS

First CMV infection

- 755 SOT recipients were included in the analysis (Table 1).
- 173 (23%) developed CMV infection within one year of baseline (Table 2) with CMV disease present at diagnosis in 17% of the cases.
- The risk of CMV infection was lower in patients with low and intermediate risk CMV IgG serostatus compared to high risk (Figure 1).
- Liver and lung transplant, female sex, older age and year of transplant were also associated with an increased risk of CMV infection (Figure 2).
- Among the 470 (62%) patients who received CMV prophylaxis, those who received < 85 days had a higher risk of CMV infection than those receiving ≥ 85 days (aHR 1.80, 95%CI 1.19-2.72).

Recurrent CMV

- 99 recipients were investigated for recurrent CMV (Table 1).
- 40 (40%) experienced relapse within 6 months of stopping treatment for their first infection (Table 2).
- The risk of recurrent CMV was significantly lower in those with low and intermediate risk serostatus (Figure 3).
- Older age (aHR 1.23 per 5 years older, 95%CI 1.06-1.44) was significantly associated with recurrent CMV infection (Figure 4).

CONCLUSIONS

- Recurrent CMV infection remains a significant complication among SOT recipients, especially in those with high risk CMV IgG serostatus.
- These findings highlight the necessity to successfully treat and monitor this subgroup following their first infection.
- Novel medical interventions and strategies to prevent CMV infection are of particular importance to this high-risk group.