Lymphocyte Subsets as Predictors of Cytomegalovirus Infection after Transplantation

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Abstract

Background: Cellular immunity plays a critical role in controlling cytomegalovirus (CMV) infection after solid organ transplantation (SOT). We correlated lymphocyte subsets with the risk and course of CMV after SOT.

Methods: We studied 130 selected kidney, heart, lung, pancreas, liver and composite tissue transplant patients who had blood samples collected for immunologic testing. We abstracted absolute lymphocyte count (ALC) and CD4+ and CD8+ T cell subsets, and correlated them with CMV infection and disease. CMV infection was diagnosed by quantitative PCR in blood and other clinical samples, or histopathology.

Results: Fifty-nine of 130 SOT patients developed CMV infection or disease. The median age was 57.5 years (IQR: 47.8-64). Gender distribution was equal. The median onset to CMV infection or disease was 10.5 months (IQR 5.5-18.7). The median ALC for the whole cohort was 565 (IQR, 310-1083) cells/mm^3. An ALC <630 cells/mm^3 was correlated with CMV infection or disease (sensitivity 85%; specificity 70%). The median CD4+ T cell count for the whole cohort was 160.5 (IQR, 17.5-424.5) cells/mm^3. Patients with CD4+ T cell count <196 cells/mm^3 were at a higher risk of CMV infection or disease (sensitivity 88%; specificity 71%). The 59 SOT recipients with CMV infection or disease had a significantly lower median number of CD4+ T cells compared to those who did not develop CMV (29 vs. 325.5 cells/mm^3, p<.0001). A median CD4+ T cell count <45 cells/mm^3 was associated with CMV syndrome or tissue-invasive disease (sensitivity 66%; specificity 68%). Patients who had CMV relapse had significantly lower median CD4+ T cell count (9 vs. 68 cells/mm^3, p=0.005). There was no association between CD8+ T cell count and CMV infection or disease. However, T cell functional analysis was not considered in this analysis.

Conclusions: Lower ALC and CD4+ counts, but not CD8+ T cell count, are significantly correlated with the risk and course of CMV infection and disease after SOT. These readily available clinical measures have the potential to assist in CMV disease management.

Objectives

We correlated lymphocyte subsets with the risk and course of CMV after SOT.

Results

Fifty-nine of 130 SOT patients developed CMV infection or disease. The median age was 57.5 years (IQR: 47.8-64). Gender distribution was equal. The median onset to CMV infection or disease was 10.5 months (IQR 5.5-18.7).

The median ALC for the whole cohort was 565 (IQR, 310-1083) cells/mm^3. An ALC <630 cells/mm^3 was correlated with CMV infection or disease (sensitivity 85%; specificity 70%).

The median CD4+ T cell count for the whole cohort was 160.5 (IQR, 17.5-424.5) cells/mm^3. Patients with CD4+ T cell count <196 cells/mm^3 were at a higher risk of CMV infection or disease (sensitivity 88%; specificity 71%). The 59 SOT recipients with CMV infection or disease had a significantly lower median number of CD4+ T cells compared to those who did not develop CMV (29 vs. 325.5 cells/mm^3, p<.0001). A median CD4+ T cell count <45 cells/mm^3 was associated with CMV syndrome or tissue-invasive disease (sensitivity 66%; specificity 68%). Patients who had CMV relapse had significantly lower median CD4+ T cell count (9 vs. 68 cells/mm^3, p=0.005).

There was no association between CD8+ T cell count and CMV infection or disease. However, T cell functional analysis was not considered in this analysis.

Discussion

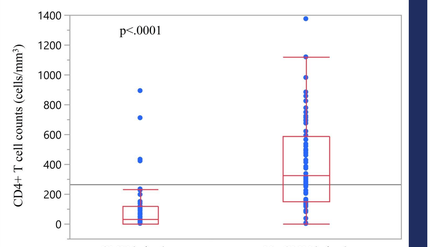
- Our study demonstrates the important role of cellular immunity to prevention CMV end organ disease in SOT recipients.
- CMV infection and disease is higher in subjects with lower absolute lymphocyte counts and lower CD4+ T lymphocyte counts.
- CMV infection and disease is not correlated CD8+ T lymphocyte counts.

Table 1: Baseline characteristics

Age (years)(IQR)	57.5 (47.8-64.0)
Male (%)	67 (51.5)
White ethnicity (%)	119 (91.5)
CMV status (%)	
• **D+R+**	30 (23.1)
• **D+R-**	59 (45.3)
• **D-R+**	17 (13.1)
• **D-/R-**	10 (7.7)
• **R+**	12 (9.2)
• **R-**	1 (0.8)
• **Not known**	1 (0.8)
Type of transplant (%)	
• **Lung**	60 (46.2)
• **Heart/lung**	4 (3.1)
• **Kidney**	25 (19.2)
• **Kidney/pancreas**	11 (8.5)
• **Liver**	7 (5.3)
• **Heart/liver**	2 (1.5)
• **Pancreas**	11 (8.5)
• **Heart**	8 (6.1)
• **Heart/kidney**	1 (0.8)
• **Face**	1 (0.8)
Infected organ (%), n=21	
• **Enterocolitis**	17 (28.8)
• **Pneumonitis**	12 (20.3)
• **CMV syndromes**	10 (17.0)
• **CMV replication**	9 (15.3)
• **Multiple organ infection**	6 (10.2)
• **Glomerulonephritis**	2 (3.4)
• **Retinitis**	2 (3.4)
• **Myocarditis**	1 (1.7)
Rejection	23 (35.9)
Onset to CMV infection (months) (IQR), n=59	10.5 (5.5-18.7)

IQR; interquartile range

Figure 1



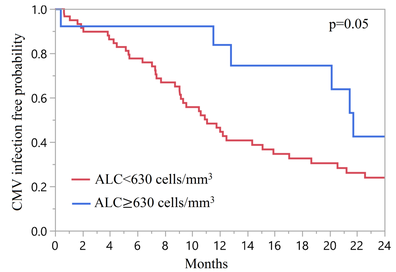
CD4+ T cell in solid organ recipients with and without CMV infection

Table 2: Lymphocyte subsets

	CMV infection/disease N=59	No CMV infection N=71	*P* value
ALC (cells/mm^3) (IQR)	380 (240-540)	940 (551-1210)	<.0001
Total CD8+ T cell (cells/mm^3) (IQR)	153 (65-367)	139 (60-221)	0.38
Total CD4+ T cell (cells/mm^3) (IQR)	29 (1.3-116.0)	412 (151.5-589.8)	<.0001

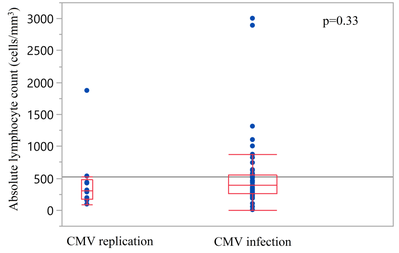
Absolute lymphocyte count, IQR; interquartile range

Figure 2



CMV infection free survival

Figure 3



ALC of solid organ recipients with CMV replication and with CMV infection

Conclusions

- Low absolute lymphocyte and CD4+ T lymphocyte counts are associated with higher risk of CMV infection and disease.
- Measure of absolute lymphocyte and CD4+ T lymphocyte counts following transplantation might be useful potential to assist in its clinical management.
- These readily available clinical measures have the potential to assist in CMV disease management.

References

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Declaration of Interest

- Nothing to disclose