# Absolute Lymphocyte Threshold: A Simple Readily Available Tool to Predict Risk of Cytomegalovirus Infection after Transplantation


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## Abstract

### Background

Cytomegalovirus (CMV) is a common infection after solid organ (SOT) and hematologic stem cell transplantation (HSCT). We correlated peripheral blood absolute lymphocyte count (PBALC) with risk of CMV infection and disease in a cohort of SOT and HSCT patients.

### Methods

Sixty-four consecutive patients (36 SOT and 28 HSCT) with plasma CMV viral load (VL) testing for surveillance of CMV infection were enrolled. Patient's clinical variables, including PBALC, were abstracted for correlation with CMV infection and disease.

### Results

The median age of the population was 54.5 years (IQR: 40 to 63). Forty-three (67.2%) patients developed CMV infection or disease (asymptomatic, 67.4%; CMV syndrome, 14%; gastrointestinal disease, 14%) at median of 4.4 months (IQR 1.4 to 7.7). Median peak VL was significantly higher for symptomatic than asymptomatic infection (10,110 vs. 262 IU/mL, p = 0.006), particularly after SOT but not HSCT (Table 1). PBALC <830 cells/mm$^3$ correlated with CMV infection or disease (sensitivity 95%; specificity 71%). Median PBALC among all 43 patients with CMV infection or disease was lower than those without infection (450 vs. 1,060 cells/mm$^3$, p <0.0001). Among 64 transplant recipients, a PBALC <830 cells/mm$^3$ conferred a higher risk of CMV infection or disease compared to ≥830 cells/mm$^3$ (HR 7.5, 95% CI 2.69-31.03; p<.0001). Among 36 SOT patients, PBALC <610 cells/mm$^3$ correlated with CMV infection or disease (sensitivity 80%; specificity 73%); the median PBALC was significantly lower among those who developed CMV disease and infection (270 and 450 versus 1120 cells/ mm$^3$). Among 28 HSCT recipients, PBALC <830 cells/mm$^3$ correlated with CMV infection or disease (sensitivity 100%; specificity 80%); median PBALC was lower among HSCT patients with CMV infection and disease than those without infection (520 and 510 versus 1,020 cells/mm$^3$).

Among 43 patients with CMV, the median PBALC declined from pre-transplant value of 1,050 cells/mm$^3$ (IQR, 810-1,520) to 450 cells/mm$^3$ (IQR, 330-640; p<.0001) at onset of infection; the median PBALC 2-4 weeks prior to onset of CMV was 490 cells/mm$^3$ (IQR, 170-950) (Figure 3). Ten symptomatic patients had lower median PBALC (315 cells/mm$^3$ [IQR, 155-520]) than 33 asymptomatic patients (450 cells/mm$^3$ [IQR, 365-670]; p=0.03). In contrast, the median PBALC of 21 CMV-negative transplant recipients increased from pre-transplant baseline of 870 cells/mm$^3$ (IQR, 635-1,430) to 1,060 cells/mm$^3$ (IQR, 630-2,215; p=0.07).

### Conclusions

In the current era when sophisticated immunologic measures are being proposed as CMV prognosticator, we highlight the clinical importance of a simple readily-available PBALC. PBALC <830 cells/mm$^3$ can serve as a clue to a transplant patient's heightened risk for CMV infection or disease.


## Objectives

We correlated peripheral blood absolute lymphocyte count (PBALC) with risk of CMV infection and disease in a cohort of SOT and HSCT patients.

## Results

Sixty-four SOT (56%) and HSCT (44%) patients were enrolled. The median age of the whole population was 54.5 years (IQR: 40 to 63) and most were male (Table 1). Forty-three (67.2%) patients developed CMV infection or disease (asymptomatic, 67.4%; CMV syndrome, 14%; gastrointestinal disease, 14%) at median of 4.4 months (IQR 1.4 to 7.7). Median peak VL was significantly higher for symptomatic than asymptomatic infection (10,110 vs. 262 IU/mL, p = 0.006), particularly after SOT but not HSCT (Table 2 and Figure 2).

PBALC <830 cells/mm$^3$ correlated with CMV infection or disease (sensitivity 95%; specificity 71%). Median PBALC among all 43 patients with CMV infection or disease was lower than those without infection (450 vs. 1,060 cells/mm$^3$, p <0.0001) (Figure 1).

Among 64 transplant recipients, a PBALC <830 cells/mm$^3$ conferred a higher risk of CMV infection or disease compared to ≥830 cells/mm$^3$ (HR 7.5, 95% CI 2.69-31.03; p<.0001). Among 36 SOT patients, PBALC <610 cells/mm$^3$ correlated with CMV infection or disease (sensitivity 80%; specificity 73%); the median PBALC was significantly lower among those who developed CMV disease and infection (270 and 450 versus 1120 cells/ mm$^3$). Among 28 HSCT recipients, PBALC <830 cells/mm$^3$ correlated with CMV infection or disease (sensitivity 100%; specificity 80%); median PBALC was lower among HSCT patients with CMV infection and disease than those without infection (520 and 510 versus 1,020 cells/mm$^3$).

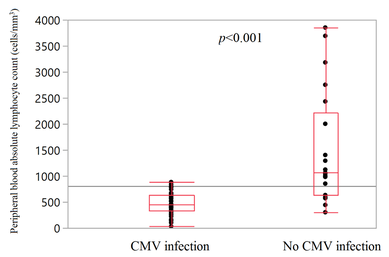
Among 43 patients with CMV, the median PBALC declined from pre-transplant value of 1,050 cells/mm$^3$ (IQR, 810-1,520) to 450 cells/mm$^3$ (IQR, 330-640; p<.0001) at onset of infection; the median PBALC 2-4 weeks prior to onset of CMV was 490 cells/mm$^3$ (IQR, 170-950) (Figure 3). Ten symptomatic patients had lower median PBALC (315 cells/mm$^3$ [IQR, 155-520]) than 33 asymptomatic patients (450 cells/mm$^3$ [IQR, 365-670]; p=0.03). In contrast, the median PBALC of 21 CMV-negative transplant recipients increased from pre-transplant baseline of 870 cells/mm$^3$ (IQR, 635-1,430) to 1,060 cells/mm$^3$ (IQR, 630-2,215; p=0.07).

## Table 1: Baseline characteristics

| | SOT N=36 | HSCT N=28 |
|---|---|---|
| **Age (years)(IQR)** | 52 (40-62) | 60 (37-66) |
| **Male (%)** | 26 (72.2) | 15 (53.4) |
| **White ethnicity (%)** | 33 (91.7) | 28 (100) |
| **CMV status (%)** | | |
| ○ **D+R+** | 11 (30.6) | 10 (35.7) |
| ○ **D+R-** | 21 (58.3) | 2 (7.1) |
| ○ **D-R+** | 4 (11.1) | 12 (42.9) |
| ○ **D-R-** | 0 | 4 (14.3) |
| **Type of transplant (SOT) (%)** | | |
| ○ **Lung** | 2 (5.6) | |
| ○ **Heart/lung** | 3 (8.3) | |
| ○ **Kidney** | 5 (13.9) | |
| ○ **Kidney/pancreas** | 3 (8.3) | |
| ○ **Liver** | 17 (47.2) | |
| ○ **Liver/heart** | 1 (2.8) | |
| ○ **Pancreas** | 2 (5.6) | |
| ○ **Heart** | 1 (2.8) | |
| ○ **Heart/kidney** | 2 (5.6) | |
| **Type of transplant (HSCT) (%)** | | |
| ○ **Matched related** | | 9 (32.1) |
| ○ **Matched unrelated** | | 16 (57.1) |
| ○ **Haploidentical** | | 1 (3.6) |
| ○ **Autologous** | | 2 (7.1) |
| **Onset to CMV infection (months) (IQR)** | 7 (2.4-9.3) | 1.6 (1.4-6.1) |

CMV: cytomegalovirus; HSCT: hematologic stem cell transplantation; IQR: interquartile range; PBALC: Peripheral blood absolute lymphocyte count; SOT: solid organ transplantation

## Figure 1



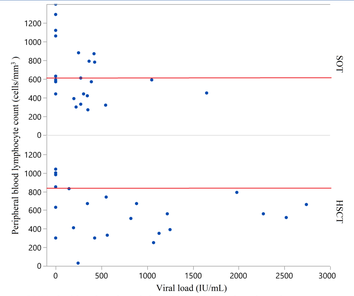

Peripheral blood absolute lymphocyte counts and at the 1st CMV infection

## Table 2: Lymphocyte subsets

| | CMV disease | Asymptomatic CMV viremia | No CMV infection | *P* value |
|---|---|---|---|---|
| **SOT, N = 36** | N = 7 | N = 18 | N = 11 | |
| **Median CMV VL (IQR) (IU/mL)** | 32,500 (352 - 118,000) | 423 (297 - 6,315) | 0 | 0.05* |
| **Median PBALC (IQR) (cells/mm³)** | 270 (140 - 460) | 450 (388 - 675) | 1,120 (590 - 1,400) | 0.001 |
| **HSCT, N = 28** | N = 3 | N = 15 | N = 10 | |
| **Median CMV VL (IQR) (IU/mL)** | 1,220 (426 - 2,520) | 884 (347 - 1,980) | 0 | 0.62* |
| **Median PBALC (IQR) (cells/mm³)** | 520 (300 - 560) | 510 (330 - 670) | 1,020 (795 - 3,308) | 0.03 |

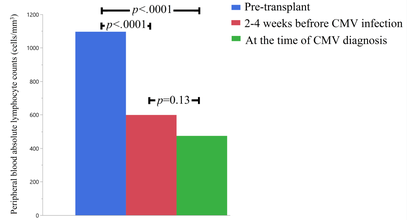
PBALC: Peripheral blood absolute lymphocyte count; CMV: cytomegalovirus; HSCT: hematologic stem cell transplantation; IQR: interquartile range; SOT: solid organ transplantation; VL: viral load
*Comparison between CMV invasive disease and CMV viremia recipients

## Figure 2




CMV viral load and peripheral blood absolute lymphocyte count

## Figure 3




Mean peripheral blood absolute lymphocyte counts among 43 CMV infection and disease patients.

## Discussion

- This study reports the significant association between peripheral blood absolute lymphocyte count and CMV infection and disease in SOT and HSCT cohort
- CMV infection and disease is higher in subjects with lower peripheral blood absolute lymphocyte counts.

## Conclusions

- In the current era when sophisticated immunologic measures are being proposed as CMV risk prognosticator, a simple PBALC remains as a good prognostic marker.
- We highlight the clinical importance of a simple readily-available PBALC. PBALC <830 cells/mm3 can serve as a clue to a transplant patient's heightened risk for CMV infection or disease.

## References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## Declaration of Interest

- Nothing to disclose