CD4/CD8 Cell Ratio in Acute HIV Infection and the Impact of Early Antiretroviral Therapy

To the Editor—We read with interest the manuscript by Caby and colleagues [1] who reported that early initiation of antiretroviral therapy (ART) seems to improve the CD4/CD8 cell ratio. However, the dynamic of CD4/CD8 ratios during early human immunodeficiency virus (HIV) infection remains poorly studied, especially in the context of early ART initiation.

We analyzed CD4/CD8 cell ratios in relation to (1) signs and symptoms of acute HIV infection (AHI) and (2) early versus delayed initiation of ART in 90 individuals with a diagnosis of AHI during 2007–2014 [2, 3]. AHI was defined as Fiebig stage I–II [4]. Detailed methods, including demographics of the study cohort, have been published elsewhere [5].

CD4/CD8 cell ratios were significantly lower (median, 0.71 [interquartile range (IQR), 0.43–1.02] vs 1.11 [0.58–1.47]; $P = .047$) in the 72 individuals reporting signs and symptoms consistent with AHI before or at the time of diagnostic testing than in the 18 who did not. No difference was found for CD4 and CD8 cell counts alone. A significant negative correlation was found between CD4/CD8 ratios and duration of signs and symptoms (median [IQR], 9 [5–13] days), with lower ratios observed in those with longer duration (Spearman $\rho = -0.403$; $P = .001$). Significantly lower CD4/CD8 ratios (median [IQR], 0.44 [0.33–0.72] vs 0.92 [0.59–1.24]; $P = .03$) were also observed in those individuals who sought medical attention because of their signs and symptoms (12 of 42; 29%).

CD4/CD8 ratios over time are displayed in Table 1. A total of 57 of 90 individuals with AHI (63%) started ART with our program; 16 (28%) started ART within 30 days of AHI diagnosis (ie, within 40 days of the estimated date of infection, categorized as *early ART*), and 41 started ART later (*delayed ART*). Among those with early ART, CD4/CD8 ratios did not differ between nucleic acid testing (NAT) and ART initiation ($P = .73$; Wilcoxon signed rank test), whereas lower ratios were observed at ART initiation (compared with NAT) among those with delayed ART ($P = .001$).

At follow-up in week 36 of ART (±12 weeks; week of follow-up did not differ between those with early and delayed ART; 89% overall were virally suppressed), CD4/CD8 ratios were significantly higher than at ART initiation (week 0) in both those with early ART ($P = .006$) and those with delayed ART ($P < .001$). Compared with the time of NAT, CD4/CD8 ratios increased significantly in those with early ART ($P = .02$), but no difference was observed in those with delayed ART ($P = .12$).

Low CD4/CD8 ratios in HIV infection have been linked to higher risk non-AIDS-related morbidity and mortality risks [6–8]. We found that CD4/CD8 ratios were generally lower in individuals with symptomatic AHI and were correlated with duration of AHI symptoms. Importantly, very early ART (initiated within 40 days of the estimated date of infection) was associated with a significant increase in CD4/CD8 ratios. Our data indicate that CD4/CD8 ratios decline rapidly during AHI but may increase significantly once ART is initiated. Very early initiation of ART may lead to a significant increase in CD4/CD8 ratios and reduce the non-AIDS morbidity and mortality risks.

Notes

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Table 1. CD4/CD8 Cell Ratios, CD4 and CD8 Counts, and Viral Loads Over Time in Individuals With Acute Human Immunodeficiency Virus Infection and Early Versus Delayed Antiretroviral Therapy Initiation[a]

Characteristics and Time Points	Diagnostic NAT (Early ART Initiation) (n = 16)	Diagnostic NAT (Delayed ART Initiation) (n = 41)	Early ART Initiation (n = 16)	Delayed ART Initiation (n = 41)	Follow-up at wk 2–4 After Early ART Initiation (n = 15)[b]	Follow-up at wk 2–4 After Delayed ART Initiation (n = 30)[b]	Follow-up at wk 24–48 After Early ART Initiation (n = 13)[b]	Follow-up at wk 24–48 After Delayed ART Initiation (n = 23)[b]
CD4/CD8 cell ratio, median (IQR) [*P* value]	0.61 (0.21–1.18)	0.92 (0.51–1.29)	0.58 (0.17–1.03)	0.61 (0.41–0.78)	0.67 (0.33–0.94) [.34]	0.86 (0.55–1.08) [.001]	1.14 (0.65–1.26) [.006]	1.29 (0.89–1.44) [.001]
CD4 cell count, median (IQR), cells/μL [*P* value]	387 (309–539)	460 (301–581)	426 (349–607)	504 (340–739)	603 (477–904) [.008]	595 (486–723) [.23]	921 (616–1088) [.002]	626 (511–790) [.04]
CD8 cell count, median, (IQR), cells/μL [*P* value]	645 (349–1746)	600 (281–1090)	795 (469–1431)	918 (653–1155)	993 (511–2074) [.96]	734 (578–917) [.001]	850 (538–1089) [.55]	581 (423–757) [.002]
Viral load median (IQR), $\log_{10}$ RNA, copies/mL [*P* value]	6.2 (5.5–6.6)	5.1 (4.0–6.2)	5.4 (5.1–6.7)	4.5 (3.9–4.9)	3.0 (2.3–4.2) [.001]	2.6 (1.7–2.9) [.001]	1.3 (1.3–1.7) [.001]	1.7 (1.4–1.7) [.001]

Abbreviations: ART, antiretroviral therapy; IQR, interquartile range; NAT, nucleic acid testing.

[a] Early ART initiation was defined as initiation ≤40 (median [IQR], 28 [25–32]) days after the estimated date of infection (EDI); delayed ART initiation, initiation ≥40 (106 [70–387]) days after the EDI.

[b] *P* values were determined with Wilcoxon signed rank tests and represent comparison with value at ART initiation.

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