Prediction of liver disease, AIDS and mortality based on discordant absolute and relative peripheral CD4 T lymphocytes in HIV/HCV co-infected individuals

Sandra Hansen[1], Gitte Kronborg[1,2] and Thomas Benfield[1,2]

[1]Department of Infectious Diseases, Hvidovre Hospital, University of Copenhagen, Hvidovre, Denmark; [2] Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

BACKGROUND

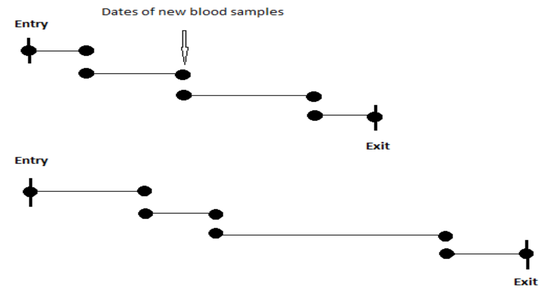
Hepatitis C virus (HCV) induced liver fibrosis and splenomegaly may lead to discordance between absolute numbers and percentages of lymphocytes and subpopulations because of sequestration. Here we investigated **lymphocyte discordance in HIV/HCV co-infected individuals and its relationship to progression to liver disease, AIDS and all-cause mortality.**

METHOD

Observational prospective cohort study. Adjusted hazard ratios with 95% confidence intervals associated with liver disease, AIDS or mortality were computed by time-updated Cox proportional hazards regression. Adjusted for gender, age, race, HIV exposure group, time-updated ART, time-updated HIV-RNA, time-updated platelet count, time-updated ALT, time-updated HbsAg and time-updated HCV status.

METHOD

We used the Stratify macro to split the the follow-up for the time-updated Cox regression analysis.



RESULTS/CONCLUSION

Both absolute CD4 T lymphocyte count and percentage predicted mortality, whereas only absolute CD4 T lymphocyte count predicted the development of AIDS. Total lymphocyte count was associated with risk of AIDS and death. Neither lymphocyte nor subgroups predicted the development of liver disease in this cohort.

DISCORDANCE

Relationship between CD4 T lymphocyte count and percentage discordance in 380 individuals positive for Hepatitis C virus.

	<100 CD4 cells/µL N (%)	100-200 CD4 cells/µL N (%)	200-300 CD4 cells/µL N (%)	300-500 CD4 cells/µL N (%)	>500 CD4 cells/µL N (%)
<7% CD4	**414 (4.55)**	111 (1.22)	59 (0.65)	85 (0.93)	64 (0.70)
7-14% CD4	245 (2.69)	**572 (6.29)**	344 (3.78)	177 (1.95)	24 (0.26)
14-21% CD4	88 (0.97)	369 (4.06)	**614 (6.75)**	789 (8.68)	269 (2.96)
21-35% CD4	17 (0.19)	180 (1.98)	436 (4.80)	**1407 (15.48)**	1460 (16.06)
>35% CD4	3 (0.03)	19 (0.21)	75 (0.82)	266 (2.93)	**1004 (11.04)**
Overall discordance					**5080 (55.55)**
Median (n=360)					***11***

PROGRESSION TO AIDS

Time-updated analysis of progression to AIDS according CD4 T lymphocyte count, percentage or ratio.

	Absolute CD4		CD4%		CD4:CD8-ratio	
	Adjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Time updated value per doubling	0.73 (0.56-0.96)	0.03	0.75 (0.51-1.10)	0.15	0.56 (0.15-2.04)	0.38
Time updated value[a]						
Low	2.58 (1.19-5.58)	0.02	2.067 (0.91-4.67)	0.08	0.63 (0.22-1.86)	0.39
Mid	1		1		0.361 (0.12-1.13)	0.08
High	0.75 (0.28-1.98)	0.56	1.07 (0.43-2.66)	0.89	1	

Adjusted for age, gender, caucasian race, HIV exposure group, HAART-treatment, resolved HCV, HBsAg, HIV viral load, thrombocytes and ALAT. HR: Hazard ratio; CI: confidence interval

[a] Absolute CD4 divided in <200, 200-500, >500. CD4 % divided in <14, 14-28, >28. Ratio divided in <0.4, 0.4-1.0, >1.0.

MORTALITY

Time-updated analysis of progression to death according CD4 T lymphocyte count, percentage or ratio.

	Absolute CD4		CD4%		CD4:CD8-ratio	
	Adjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Baseline value	1.00 (1.00-1.00)	0.09	0.98 (0.96-1.00)	0.05	0.91 (0.69-1.20)	0.48
Time updated value per 1 increase	0.99 (0.99-0.99)	<0.0001	0.97 (0.96-0.99)	0.0008	0.47 (0.28-0.80)	0.005
Time updated value per doubling	0.63 (0.56-0.72)	<0.0001	0.65 (0.54-0.78)	<0.0001	0.40 (0.22-0.72)	0.003
Time updated value[a]						
Low	2.26 (1.56-3.29)	<0.0001	1.52 (1.02-2.26)	0.04	2.00 (1.04-3.85)	0.04
Mid	1		1		1.44 (0.75-2.77)	0.27
High	0.76 (0.50-1.17)	0.21	0.79 (0.53-1.17)	0.23	1	

Adjusted for age, gender, caucasian race, HIV exposure group, HAART-treatment, resolved HCV, HBsAg, HIV viral load, thrombocytes and ALAT. HR: Hazard ratio; CI: confidence interval

[a] Absolute CD4 divided in <200, 200-500, >500. CD4 % divided in <14, 14-28, >28. Ratio divided in <0.4, 0.4-1.0, >1.0.