

Clinical Impact of Altered T-Cell Homeostasis in Treated HIV Patients Enrolled in a Large Observational Cohort

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Objective

This study investigated the probability of transitioning in or out of normal physiologic ranges (NPR) during the course of ART. The clinical impact of impaired T-cell homeostasis (TCH) on AIDS-defining illness (ADI) or death was also assessed.

Main Finding

- Low CD4+ T-cell counts, detectable HIV RNA, HCV coinfection, and older age were associated with altered TCH.
- Both very low and high CD3+ T-cell percentages were associated with increased risk of ADI or death.

Importance of this Study

- TCH is a crucial component of a functional immune system.
- TCH is the maintenance of T-cell (CD3+) percentages within a NPR representing 65-85% of peripheral blood lymphocytes.
- The inability to maintain T-cells within this range denotes an impairment of TCH regulation and is linked to adverse clinical outcomes, including progression to AIDS.
- Few studies have assessed the effect of long-term successful combination antiretroviral therapy (cART) on TCH maintenance.

How this Study was Conducted

- Data were analyzed from the CANOC collaboration, an interprovincial collaborative cohort of HIV-positive individuals on antiretroviral therapy in Canada.
- CANOC compiled HIV clinical, virological, immunologic, and demographic data from 8 cohorts across British Columbia, Ontario, Quebec.
- 4,463 participants from the CANOC collaboration were included in this analysis.

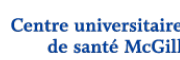
Study Results

- 56% of participants never transitioned from their baseline CD3+ T-cell percentage state.
- Participants with low CD4+ T-cell counts, detectable HIV RNA, HCV coinfection, and of older age were less likely to maintain TCH and more likely to transition to lower NPRs.
- In the survival analysis, participants with very low CD3+ T-cell percentages (<50%) had a 1.91 times greater risk for ADI or death.
- Participants with high CD3+ T-cell percentages (>85%) had a 1.49 times greater risk for ADI or death.
- Older age, HCV seropositivity, time-updated CD4+ T-cell count, and updated detectable viral load were also associated with poor clinical outcomes.

Implications

- The specific immune pathways through which altered TCH may lead to poor clinical outcomes are still unclear, and future research is needed.
- Measuring immune recovery with cART remains challenging because of the limited number of clinically relevant surrogate markers. Monitoring CD3+ T-cell levels as a supplement to CD4+ T-cell counts may provide further insight into immune recovery.

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