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

Patricia Ndumbi, Jennifer Gillis, Janet M. Raboud, Curtis Cooper, Robert S. Hogg, Julio S.G. Montaner, Ann N. Burchell, Mona R. Loutfy, Nima Machouf, Marina B. Klein, Chris M. Tsoukas, the CANOC Collaboration

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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.