

1. Infection duration and inflammatory imbalance are associated with atherosclerotic risk in HIV-infected never-smokers independent of antiretroviral therapy.

Desvarieux M, Boccara F, Meynard JL, Bastard JP, Mallat Z, AIDS. 2013 Oct 23;27(16):2603-14.

OBJECTIVES: To determine whether the reported increased atherosclerotic risk among HIV-infected individuals is related to antiretroviral therapy (ART) or HIV infection, whether this risk persists in never-smokers, and whether inflammatory profiles are associated with higher risk.

DESIGN: Matched cross-sectional study.

METHODS: A total of 100 HIV-infected patients (50 ART-treated >4 years, 50 ART-naive but HIV-infected >2 years) and 50 HIV-negative controls were recruited in age-matched never-smoking male triads (mean age 40.2 years). Carotid intima-media maximal thickness (c-IMT) was measured across 12 sites.

Pro-inflammatory [highly sensitive C-reactive protein (hs-CRP), resistin, interleukin-6, interleukin-18, insulin, serum amyloid A, D-dimer) and anti-inflammatory (total and high molecular weight adiponectin, interleukin-27, interleukin-10) markers were dichotomized into high/low scores (based on median values). c-IMT was compared across HIV/treatment groups or inflammatory profiles using linear regression models adjusted for age, diabetes, hypertension, and, for HIV-infected patients, nadir CD4 cell counts.

RESULTS: Although adjusted c-IMT initially tended to be thicker in ART-exposed patients ($P=0.2$), in post-hoc analyses stratifying by median HIV duration we observed significantly higher adjusted c-IMT in patients with longer (>7.9 years: $0.760\pm 0.008\text{mm}$) versus shorter prevalent duration of known HIV infection (<7.9 years: $0.731\pm 0.008\text{mm}$, $P=0.02$), which remained significant after additionally adjusting for ART ($P=0.04$). Individuals with low anti-inflammatory profile (<median versus >median score) had thicker c-IMT ($0.754\pm 0.006\text{mm}$ versus $0.722\pm 0.006\text{mm}$, $P<0.001$), with anti-inflammatory markers declining as prevalent duration of HIV infection increased (P for linear trend <0.001).

CONCLUSION: Known HIV duration is related to thicker c-IMT, irrespective of ART, in these carefully selected age-matched never-smoking HIV-treated and ART-naïve male individuals. Higher levels of anti-inflammatory markers appeared protective for atherosclerosis.

2. Clinical impact of altered T-cell homeostasis in treated HIV patients enrolled in a large observational cohort

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Abstract

Objective(s): We investigated the probability of transitioning in or out of the CD3+ T-cell homeostatic range during antiretroviral therapy, and we assessed the clinical impact of lost T-cell homeostasis (TCH) on AIDS-defining illnesses (ADIs) or death.

Design: Within the Canadian Observational Cohort (CANOC), we studied 4463 antiretroviral therapy (ART)-naive HIV-positive patients initiating combination ART (cART) between 2000 and 2010.

Methods: CD3+ trajectories were estimated using a four state Markov model. CD3+ T-cell percentage states were classified as follows: very low (<50%), low (50–64%), normal (65–85%), and high (>85%). Covariates associated with transitioning between states were examined. The association between CD3+ T-cell percentage states and time to ADI/death from cART initiation was determined using Cox proportional hazards models.

Results: A total of 4463 patients were followed for a median of 3 years. Two thousand, five hundred and eight (56%) patients never transitioned from their baseline CD3+ T-cell percentage state; 85% of these had normal TCH. In multivariable analysis, individuals with time-updated low CD4+ cell count, time-updated detectable viral load, older age, and hepatitis C virus (HCV) coinfection were less likely to maintain TCH. In the multivariable proportional hazards model, both very low and high CD3+ T-cell percentages were associated with increased risk of ADI/death [adjusted hazard ratio=1.91 (95% confidence interval, CI: 1.27–2.89) and hazard ratio=1.49 (95% CI: 1.13–1.96), respectively].

Conclusion: Patients with very low or high CD3+ T-cell percentages are at risk for ADIs/death. To our knowledge, this is the first study linking altered TCH and morbidity/mortality in cART-treated HIV-positive patients.

3. The effects of age on associations between markers of HIV progression and markers of metabolic function including albumin, haemoglobin and lipid concentrations

M Samuel,¹ S Jose,² A Winston,³ M Nelson,⁴ M Johnson,⁵ D Chadwick, HIV Medicine (2013)

Objectives

We investigated whether age modified associations between markers of HIV progression, CD4 T lymphocyte count and HIV RNA viral load (VL), and the following markers of metabolic function: albumin, haemoglobin, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC).

Methods

A retrospective analysis of data from the United Kingdom Collaborative HIV Cohort was carried out. Analyses were limited to antiretroviral-naïve subjects to focus on the impact of HIV disease itself. A total of 16670 subjects were included in the analysis. Multilevel linear regression models assessed associations between CD4 count/VL and each of the outcomes. Statistical tests for interactions assessed whether associations differed among age groups.

Results

After adjustment for gender and ethnicity, there was evidence that lower CD4 count and higher VL were associated with lower TC, LDL-C, haemoglobin and albumin concentrations but higher triglyceride concentrations. Age modified associations between CD4 count and albumin ($P < 0.001$) and haemoglobin ($P = 0.001$), but not between CD4 count and HDL-C, LDL-C and TC, or VL and any outcome. Among participants aged < 30 , $30-50$ and > 50 years, a 50 cells/ μL lower CD4 count correlated with a 2.4 [95% confidence interval (CI) 1.7–3.0], 3.6 (95% CI 3.2–4.0) and 5.1 (95% CI 4.0–6.1) g/L lower haemoglobin concentration and a 0.09 (95% CI 0.07–0.11), 0.12 (95% CI 0.11–0.13) and 0.16 (95% CI 0.13–0.19) g/L lower albumin concentration, respectively.

Conclusions

We present evidence that age modifies associations between CD4 count and plasma albumin and haemoglobin levels. A given reduction in CD4 count was associated with a greater reduction in haemoglobin and albumin concentrations among older people living with HIV. These findings increase our understanding of how the metabolic impact of HIV is influenced by age.

4. Incomplete adherence to antiretroviral therapy is associated with higher levels of residual HIV-1 viremia

Li, Jonathan Z.a,*; Gallien, Sebastiena,b,*; Ribaud, Heatherc; Heisey, Andreaa; Bangsberg, David R.d; Kuritzkes, Daniel R.a, AIDS: 14 January 2014 - Volume 28 - Issue 2 - p 181-186

Abstract

Objectives: To evaluate the relationship between incomplete antiretroviral therapy (ART) adherence and levels of residual HIV-1 viremia.

Design: Medication adherence and residual viremia less than 50 copies/ml were quantified in participants of a cohort of homeless and marginally housed individuals with HIV/AIDS.

Methods: Participants had at least 6 months of virologic suppression of less than 50 copies/ml and were in the adherence monitoring cohort with monthly unannounced pill counts. Residual viremia was measured by the single-copy assay.

Results: The median average ART adherence over the prior 1 and 2 months were 94% [interquartile range (IQR) 79–100%] and 93% (IQR 82–98%), respectively. Average ART adherence over the past 2 months was significantly associated with levels of residual HIV viremia (Spearman $r = -0.25$, $P=0.04$). One-third of participants with 100% ART adherence over the past 2 months had detectable residual viremia. On multivariate regression analysis, ART adherence over the past 2 months, but not duration of virologic suppression, CD4+ T-cell count or ART regimen, was significantly associated with levels of residual HIV viremia. Detectable residual viremia was associated with virologic failure (>50 copies/ml) on univariate Cox proportional hazard analysis (hazard ratio 2.08, $P=0.02$). However, on multivariate analysis, only ART adherence was associated with risk of virologic failure.

Conclusion: Incomplete ART adherence is associated with higher levels of residual HIV-1 viremia, but detectable residual viremia can be present despite 100% measured ART adherence.