

## **A Lower CD4 Count Predicts Most Causes of Death except Cardiovascular Deaths. The Austrian HIV Cohort Study**

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### **Abstract**

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(1) Objective: To investigate changes in mortality rates and predictors of all-cause mortality as well as specific causes of death over time among HIV-positive individuals in the combination antiretroviral therapy (cART) era. (2) Methods: We analyzed all-cause as well as cause-specific mortality among the Austrian HIV Cohort Study between 1997 and 2014. Observation time was divided into five periods: Period 1: 1997–2000; period 2: 2001–2004; period 3: 2005–2008; period 4: 2009–2011; and period 5: 2012–2014. Mortality rates are presented as deaths per 100 person-years (d/100py). Potential risk factors associated with all-cause mortality and specific causes of death were identified by using multivariable Cox proportional hazard models. Models were adjusted for time-updated CD4, age and cART, HIV transmission category, population size of residence area and country of birth. To assess potential nonlinear associations, we fitted all CD4 counts per patient using restricted cubic splines with truncation at 1000 cells/mm<sup>3</sup>. Vital status of patients was cross-checked with death registry data. (3) Results: Of 6848 patients (59,704 person-years of observation), 1192 died: 380 (31.9%) from AIDS-related diseases. All-cause mortality rates decreased continuously from 3.49 d/100py in period 1 to 1.40 d/100py in period 5. Death due to AIDS-related diseases, liver-related diseases and non-AIDS

infections declined, whereas cardiovascular diseases as cause of death remained stable (0.27 d/100py in period 1, 0.10 d/100py in period 2, 0.16 d/100py in period 3, 0.09 d/100py in period 4 and 0.14 d/100py in period 5) and deaths due to non-AIDS-defining malignancies increased. Compared to latest CD4 counts of 500 cells/mm<sup>3</sup>, lower CD4 counts conferred a higher risk of deaths due to AIDS-related diseases, liver-related diseases, non-AIDS infections and non-AIDS-defining malignancies, whereas no significant association was observed for cardiovascular mortality. Results were similar in sensitivity analyses where observation time was divided into two periods: 1997–2004 and 2005–2014. (4) Conclusions: Since the introduction of cART, risk of death decreased and causes of death changed. We do not find evidence that HIV-positive individuals with a low CD4 count are more likely to die from cardiovascular diseases.

**Keywords:** cohort study, cause-specific mortality, CD4, cART, risk factors