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PART IV CLINICAL IMPLICATIONS

Background

- Biological link between HIV and aging paints a grim picture, however...
- The benefits of ART strongly outweigh the risks associated with ongoing immune activation and inflammation
- Key question:
 - Is the risk of aging-related diseases increased in PLWHIV vs. comparable HIVnegative individuals?



Background

- Answering question comes with challenges
 - Not clear what constitutes a comparable HIVnegative population
 - Not easy to adjust for confounders (hidden variables) between groups
 - Example: PLWHIV are much more likely to be smokers—a major risk factor for disease and death
 - Other confounders may be hard to identify
- Still, results from cohort studies have yielded important data

Italian Study

- Review of medical data between 2002 and 2009 comparing 2,854 ARTexperienced PLWHIV with 8,562 controls
- Matched for:
 - Age, sex, race
- Compared rates of age-related diseases not caused by infections

Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clin Infect Dis. 2011 Dec;53(11):1120–6.



Italian Study

 Greater likelihood of cardiovascular disease, high blood pressure, kidney failure, bone fracture, and diabetes among PLWHIV, particularly at younger ages



Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clin Infect Dis. 2011 Dec;53(11):1120–6.

Italian Study



 Greater likelihood of >1 age-related health complication (polypathology) among PLWHIV, particularly at younger ages



Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clin Infect Dis. 2011 Dec;53(11):1120–6.

Dutch Study

- Cohort study comparing 489 PLWHIV with 452 comparable HIV-negative controls
- Like Italian study, evaluated rates of agerelated diseases not caused by infections
- PLWHIV were somewhat older (53 vs. 52), current smokers, lower body mass index, less likely to be heavy daily drinkers, somewhat higher blood pressure





Dutch Study

 Greater likelihood of >1 age-related disease (60.4% HIV– vs. 74.4% HIV+)



Schouten J, Wit FW, Stolte IG, et al. Comorbidity and ageing in HIV-1 infection: the agehIV Cohort Study (Abstract THAB0205). Paper presented at: 19th International AIDS Conference; 2012 July 22–27; Washington, D.C.

Dutch Study

- Among HIV-positive, higher rates of:
 - High blood pressure
 - Heart attacks
 - Blood vessel problems
 - Reduced blood flow to brain
 - Liver disease
 - Kidney problems
 - Cancer



Schouten J, Wit FW, Stolte IG, et al. Comorbidity and ageing in HIV-1 infection: the agehIV Cohort Study (Abstract THAB0205). Paper presented at: 19th International AIDS Conference; 2012 July 22–27; Washington, D.C.

TAG

VACS Study

- Eight-city U.S.-based Veterans Aging Cohort Study
- Has enrolled more than 7,000 HIV-positive veterans and matching HIV-negative controls since 2002
- More than 150 analyses completed to date
- VACS has documented increased risks of:
 - Cardiovascular diseases
 - Pulmonary diseases
 - Decreased physical functioning
 - Fragility fractures (bone breaks from standing height)
 - Renal disease
 - Cancers



VACS Study

- Heart attacks and kidney disease did not occur at younger ages among HIVpositive veterans
- Non-AIDS cancers occur at younger ages, but only slightly
 - Difference of around 7 months compared with HIV-negative veterans

Althoff K, Wyatt C, Gibert C, et al. HIV+ adults are at greater risk for myocardial infarction, non-AIDS cancer, and endstage renal disease, but events occur at similar ages compared to HIV– adults (Abstract 59). Paper presented at: 20th Conference on Retroviruses and Opportunistic Infections; 2013 March 3–6; Atlanta, GA.

Frailty Phenotype

- Originally pertained to older adults in general population
 - First described in 2001
- Modern-day equivalent of AIDS-related wasting syndrome among PLWHIV
 - Weight loss
 - Weakness
 - Poor endurance and energy
 - Low physical activity
 - Slow walking speed



MACS & Frailty Phenotype

- Frailty among PLWHIV a focus of Multicenter AIDS Cohort Study (MACS)
 – Cohort of HIV+ and HIV– men
- Has demonstrated that risk of frailty increases the further the CD4+ T-cell count falls below 400/mm³
- Frailty can be reversed following start of ART, but symptoms can persist

Desquilbet L, Margolick JB, Fried LP, et al. Relationship between a frailty-related phenotype and progressive deterioration of the immune system in HIV-infected men. J Acquir Immune Defic Syndr. 2009 Mar 1;50(3):299–306.

Ianas V, Berg E, Mohler MJ, Wendel C, Klotz SA. J Int Assoc Provid AIDS Care. 2013 Feb;12(1):62–6.



Impaired Cognition

- HIV can enter brain, resulting in direct and inflammatory damage to central nervous system
 - Asymptomatic neurocognitive impairment
 - Formal tests show impairment, but no change in everyday function
 - Mild neurocognitive impairment
 - Mild-to-moderate impairment in activities
 - HIV-associated dementia
 - Moderate-to-severe impairment in activities

Impaired Cognition

 MACS: Higher incidence of diagnosed neurologic disease among PLWHIV



Mateen FJ, Shinohara RT, Carone M, et al. Neurologic disorders incidence in HIV+ vs HIV- men: Multicenter AIDS Cohort Study, 1996–2011. Neurology. 2012 Oct 30;79(18):1873–80.



Impaired Cognition

- Hawaii Aging with HIV Cohort (HAHAC)
- 127 older (>50) and 110 younger (<40)
 PLWHIV, half with CD4+ T cells <200/mm³
 Compared with matched HIV-negative controls
- Testing results found only marginal differences between the two groups
- Few data exploring duration of HIV infection and ART history on risk of impaired cognition in PLWHIV

Valcour V, Paul R, Neuhaus J, Shikuma C. The effects of age and HIV on neuropsychological performance. J Int Neuropsychol Soc. 2011 Jan;17(1):190–5.



Summary

- Generally speaking, data point to doubling of relative risk of age-related health problems in younger PLWHIV
 - Will greatly increase absolute risk of disease and death as PLWHIV continue to age
- More to learn about age-related health problems in PLWHIV with coinfections (e.g., hepatitis C)
- Better studies to understand risk factors in PLWHIV needed

Summary

- Many studies not included in the Immune System, HIV, & Aging report
- Lack of clarity regarding the extent to which risk may be increased in younger PLWHIV
 - Studies have not yet included detailed measures of immunologic aging, such as senescence and inflammation