HIV & AGING

Jessica L. Castilho, MD MPH
Assistant Professor, Division of Infectious Diseases
Vanderbilt University Medical Center

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I have no conflicts of interest.
“Older adult” (def in HIV research):

Someone over the age of 50 years.
OUTLINE

• Epidemiology

• Clinical challenges: geriatric syndromes
  • Frailty
  • Cognitive decline
  • Polypharmacy

• Complex etiologies: HIV, Aging, & Immunology

• Keys to “successful aging” & resilience in older HIV+ adults
EPIDEMIOLOGY & CLINICAL CHALLENGES
AGING OF HIV+ IN THE US

VCCC DATA

Number of patients with one HIV-1 RNA

Year

2011 2012 2013 2014

<30 yrs 30-39 yrs 40-49 yrs 50-59 yrs 60+ yrs

Unpublished data

Median age of patients with UD VL

30% 37%

Unpublished data
AGE AT HIV DX

Age 18-49 years
Age 50+years

Median CD4 cell count at diagnosis (c/mm3)

% with ADE at diagnosis

Year

Althoff et al. AIDS Res Ther. 2010, 7:45
HIV OUTCOMES IN OLDER ADULTS

Once in care, older adults:

↓  CD4 cell count recovery with ART

↑  Risk of AIDS

↑  Risk of death

Age at Entry Into Care, Timing of Antiretroviral Therapy Initiation, and 10-Year Mortality Among HIV-Seropositive Adults in the United States

HIV-infected adults at ↑risk of:

- CVD
- Cancers
- Metabolic disorders
- Osteoporosis
- Renal disease
- Liver disease

**AGEhIV study:** HIV-infected 45+ yrs (n=540) & matched, HIV-uninfected controls.

And many more....

Figure 2: Projected age distribution of HIV-infected patients
The red box shows the age distribution of patients on antiretroviral therapy in clinical care in the Netherlands in 2010, which matches the data exactly, and the blue box shows model output from 2011-30.

Figure 3: Predicted comorbidities
(A) Predicted burden of NCDs in HIV-infected patients between 2010 and 2030 as simulated by the model. (B) Distribution of the number of NCDs by age group.

How can we begin to synthesize all of this into a comprehensive understanding of HIV & Aging?
An Integrated Model of HIV & Aging

Presenting Conditions
- HIV
- Hepatitis
- EtOH, tob, etc.

Interacting Pathophysiologic Processes
- Immune dysfunction & senescence
- Microbial translocation
- Chronic inflammation
- Medication toxicities
- Oxidative stress
- Multimorbidity

Organ System Reserve (frailty)
- Cognitive & functional decline
- Organ system failure
- Hospitals, nursing home

Advanced Clinical Disease
- Death

Geriatric Syndromes

- Frailty
- Cognitive impairment
- Polypharmacy
- Sarcopenia
- Insulin resistance
- Falls
FRAILTY?

FRAIL

NOT FRAIL
“frailty” (def): a state of increased vulnerability to poor resolution of homeostasis after a stressor event

Figure 1: Vulnerability of frail elderly people to a sudden change in health status after a minor illness

Pathophysiology of Frailty

Genetic factors

Environmental factors

Cumulative molecular & cellular damage

Reduced physiological reserve:
Brain, Endocrine, Immune, Skeletal muscle, Cardiovascular, Respiratory, Renal

Nutrition
Physical Activity

Frailty

STRESSOR EVENT

Disability, Falls, Delirium, Increased care needs

Adapted from Clegg et al. Lancet. 2013;381:752-62
Fried frailty phenotype present at any study visit in MACS cohort

Compared to HIV-/Frail-:
aHR for HIV-/Frail+ 2.63 [1.23-5.66]
aHR for HIV+/Frail- 3.29 [1.85-5.88]
aHR for HIV+/Frail+ 7.06 [3.49-14.3]
• Prevalence of HIV-associated neurocognitive disorder (HAND): 50% of HIV+ adults

HIV-Associated Dementia
(<5%)

Mild Neurocognitive Disorder
(17%)

Asymptomatic Neurocognitive Impairment
(28%)

**HAND**

**HAD**: severe impairment in at least 2 cognitive domains + severe functional impairment

**MND**: mild to mod impairment in at least 2 cognitive domains + mild to mod functional impairment

**ANI**: any impairment in at least 2 cognitive domains + no functional impairment

Cognitive deficits

- Cognitive domains:
  - Not just memory but also...
  - Concentration
  - Attention
  - Working memory
  - Comprehension
  - Motor effects (ex: changes in gait or poor coordination)

- Predicted by:
  - Low CD4+ lymphocyte count
  - High HIV RNA

**Figure 3.** Conversion to symptomatic impairment over time in 347 patients with asymptomatic neurocognitive impairment (ANI) or normal findings on neuropsychologic testing in the CHARTER (Central Nervous System HIV Antiretroviral Therapy Effects Research) cohort. Adapted with permission from Grant et al.12

Aging & Cognition

- Does HIV and/or HAND increase the risk of aging-associated cognitive decline or dementia?

- **Mild cognitive impairment (MCI):** transitional state between typical cognitive aging and dementia (defined for HIV-uninfected populations, prevalence of 5-20%)

- Study of HIV+ and HIV- adults in San Diego. Excluded HIV+ with MND.

- HIV+ were 7.4x more likely to have MCI (95% CI: 1.6-34), particularly older adults.

- MCI was not associated with ANI in older populations

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Aging & cognition

• Does older age increase the risk of HAND (symptomatic or asymptomatic) in aging HIV+ adults?

• Study of HIV+ and HIV- adults in San Diego. Ages <40 and ≥50 yrs

• Underwent battery of neuropsych tests at baseline and 1 year

• HIV seropositivity associated with 5-fold increased incidence in neurocognitive disorders but there was no statistical modification by age

**Polypharmacy**

**Definition:** daily use of 5 or more medications

**Polypharmacy @ VCCC (excludes ART)**

- **<5 medications**
- **5-9 medications**
- **10-14 medications**
- **15-19 medications**
- **20+ medications**

Unpublished data
COMPLICATIONS OF POLYPHARMACY IN ELDERLY

- Medication Complications
  - Adverse drug reactions
  - Drug-drug interactions
  - Non-adherence

- Cognitive Decline

- Falls & Frailty

- Mortality
RISK FACTORS FOR POLYPHARMACY COMPLICATIONS

Aging
- Accumulation of co-morbid conditions related to aging
- Cognitive decline
- Renal & hepatic dysfunction
- Changes in body composition & loss of muscle mass
- Psychological & social risk factors

HIV
- Rates of CVD, cancer, depression, cognitive decline, & other aging-related diseases in addition to HIV
- Rates renal & liver disease
- Lipodystrophy from ART, obesity & metabolic syndrome
- Low SES, poor social support, substance abuse
Epidemiology & Clinical Conclusions

• Increasing number and proportion of older HIV+ adults in care

• High burden for co-morbid conditions

• High rates of geriatric syndromes and need for holistic perspective in approach to care

• Particular attention to frailty, cognition, and polypharmacy is needed for the care of older HIV+
CAUSES OF FRAILTY IN HIV

Aging

Shift naïve $\rightarrow$ memory T cells

$\downarrow$ Thymus volume & function

$\uparrow$ T cell activation

$\downarrow$ T cell co-stimulatory molecule expression

$\uparrow$ T cell terminal differentiation & clonal expansion

$\uparrow$ Systemic inflammation

HIV infection

Shift naïve $\rightarrow$ memory T cells

$\downarrow$ Thymus volume & function

$\uparrow$ T cell activation

$\downarrow$ T cell co-stimulatory molecule expression

$\uparrow$ T cell terminal differentiation & clonal expansion

$\uparrow$ Systemic inflammation
Association of Functional Impairment with Inflammation and Immune Activation in HIV Type 1–Infected Adults Receiving Effective Antiretroviral Therapy

- % CD4 T cells
- % CD8 T cells
- CD4/CD8 ratio
- % CD4+CD38+HLA-DR+
- % CD8+CD38+HLA-DR+
- sCD14 μg/mL
- IL-6 (log10) pg/mL
- TNF-alpha pg/mL
- hs-CRP (log10)pg/mL

Low fxn | High fxn
---|---

P = .004

P = .002

P = .02

P = .02

P = .003

P = .01

P < .001

P = .02

P = .21

RESILIENCE &
“SUCCESSFUL AGING”
IN HIV
Resilience

Generally involves two components:

1. Exposure to significant adversity
2. Positive adaptation despite the adversity

(Inverse of frailty)
Resilience: the ability to become strong, healthy, or successful again after something bad happens.

**Psychological**
- depression
- isolation
- stigma
- poverty
- cognition

**Immunological**
- senescence
- activation
- viral control
- CD4 recovery
- survival bias
- disparities
- age-cohort-period effects

**Physical**
- metabolic function
- multi-morbidity
Older HIV+ adults

Life Stressors:
- General
- HIV-related

Resilience = coping, self-efficacy, hope/optimism, and social support

Physical Well-being
Function & Global Well-being
Emotional Well-being

Higher Self-Reported Successful Aging scores correlated with:

- Improved physical and mental functioning
- Lower depression scores
- Increased happiness
- Resilience
- Optimism
- Personal mastery
- Lower perceived stress

CONCLUSIONS

• Older HIV+ adults are a growing and complex patient population.

• Holistic approach to their medical care and awareness of geriatric syndromes are needed.

• Causes of their health conditions are complex, including immunologic changes that mimic those of aging.

• Building resilience through therapeutic relationships is one way to promote “successful aging” in this population.
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**My patients**
QUESTIONS?