L’*ageing*, le comorbidità e la *polypharmacy*: quanto “pesano” nella scelta terapeutica?

Antonella Castagna
Financial Disclosures

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Modeling aging in HIV infection in nonhuman primates to address an emerging challenge of the post-ART era

Vicious cycle of aging and HIV/SIV infection

He T, Curr Opin Virol 2017
Faces of Frailty in Aging with HIV Infection

Physical, social, emotional, metabolic, sensory and cognitive health

ROBUST

Adults without HIV infection

FRAIL

Adults with HIV infection

DISABLED

Age (years)

From serum lipid phenotype to fatty liver

Guaraldi G, AIDS 2017
CENTRAL ILLUSTRATION  HIV and Ischemic Heart Disease: Etiopathogenesis of HIV-Associated Coronary Artery Disease

HIV

Higher prevalence of traditional risk factors:
Smoking, diabetes, hypertension, hyperlipidemia

Microbial translocation
Coinfection
Immune activation

↑ Interleukin 6
↑ Tumor necrosis factor
↑ C-reactive protein
Activated monocytes
Neutrophil extracellular traps

Inflammation

Coagulation disorders

Harmful side effects of combination antiretroviral therapy

↑ D-dimers
↑ Fibrinogen
↑ Factor VII
↑ Tissue factor
↑ von Willebrand factor
Platelet activation

Insulin resistance
Dyslipidemia
Endothelial dysfunction

Atherosclerosis

- Retrospective cohort of PLWHIV diagnosed in 2011, followed until 2014
- N=1091 PLWHIV were compared to N=2181 controls: mean age in 2011: 46.7 vs 49.7 yrs, respectively

Prevalence of the age-related comorbidities commonly associated with HIV is significantly higher in PLWHIV patients than for matched controls.

Time trend in hypertension prevalence, awareness, treatment, and control in a contemporary cohort of HIV-infected patients: the HIV and Hypertension Study

Giuseppe Vittorio De Socio, Elena Ricci, Paolo Maggi, Giustino Parruti, Benedetto Maurizio Celesia, Giancarlo Orofino, Giordano Madeeddu, Canio Martinelli, Barbara Menzagli, Lucia Taramasso, Paolo Bonfanti, Giacomo Pucci, Giuseppe Schiliaci, for the CiSAI study group

De Socio et al.

**Figure 1** Hypertension awareness, treatment and control rates in HIV-positive hypertensive study participants at baseline (left panel) and at the last follow-up visit (right panel).
Association of IMI and CDU outcomes

IMI prevalence rate was found to be 7.3% (95% confidence interval: 4.7% to 11.1%)

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CDU data available in 202 subjects. 100% of subjects with a positive EST had an abnormal CDU compared to 69% of those with a negative EST (p=0.012).

Spagnuolo et al, ICAR 2017
Changes in Cardiovascular Disease Risk Factors With Immediate Versus Deferred Antiretroviral Therapy Initiation Among HIV-Positive Participants in the START (Strategic Timing of Antiretroviral Treatment) Trial

Cardiovascular Disease Risk Factors in the START Trial  Baker et al

Young low risk population overall
Median age of 36, 10 year CHD risk  1.9
Low number of CV events
Low number of deaths due to CVD
Short FU 3 years
The changing face of diabetes complications

Edward W Gregg, Naveed Sattar, Mohammed K Ali

Figure 4: Proportional contribution of different age groups to five diabetes-related complications in the USA, by time period.
Association Between Lowering LDL-C and Cardiovascular Risk Reduction Among Different Therapeutic Interventions: A Systematic Review and Meta-analysis

Michael G. Silverman, MD; Brian A. Ference, MD, MPhil, MSc; Kyungah Im, PhD; Stephen D. Wiviott, MD; Robert P. Giugliano, MD, SM; Scott M. Grundy, MD, PhD; Eugene Braunwald, MD; Marc S. Sabatine, MD, MPH
Switching from a boosted protease inhibitor (PI/r) based regimen to a Dolutegravir (DTG) regimen in virologically suppressed patients with high cardiovascular risk (Framingham score >10% or age > 50 years) is non-inferior and decreases lipids: The NEAT 022 study

J.M. Gatell\textsuperscript{1}, L. Assoumou\textsuperscript{2}, G. Moyle\textsuperscript{3}, L. Waters\textsuperscript{4}, E. Martínez\textsuperscript{5}, H.-J. Stellbrink\textsuperscript{6}, G. Guaraldi\textsuperscript{7}, S. de Wit\textsuperscript{8}, F. Raffi\textsuperscript{9}, A. Pozniak\textsuperscript{10} on behalf of NEAT022 Study Group

\textsuperscript{1}Hospital Clinic/IDIBAPS. University of Barcelona, Infectious Diseases, Barcelona, Spain, \textsuperscript{2}Sorbonne Universités, INSERM, UPMC Univ Paris 06. IPLESP UMRS 1136, Paris, France, \textsuperscript{3}Chelsea and Westminster Hospital, London, United Kingdom, \textsuperscript{4}Mortimer Market Center, London, United Kingdom, \textsuperscript{5}Hospital Clinic/IDIBAPS. University of Barcelona, Barcelona, Spain, \textsuperscript{6}Infectiologisches Zentrum, Hamburg, Germany, \textsuperscript{7}University of Modena and Reggio Emilia, Modena, Italy, \textsuperscript{8}Saint Pierre University Hospital, Université Libre de Bruxelles, Brussels, Belgium, \textsuperscript{9}CHU Hotel-Dieu Nantes, Nantes, France, \textsuperscript{10}Chelsea & Westminster Hospital, London, United Kingdom
No changes in the utilization of lipid lowering agents. Around 30% in each arm and both at baseline and week 48.

NEAT22/SSAT060 week 48 data
Study 1489: B/F/TAF vs ABC/3TC/DTG in Treatment-Naïve Adults

Grade 3 or 4 Laboratory Abnormalities

<table>
<thead>
<tr>
<th>Grade 3 or 4 (rate ≥ 2% in either arm)</th>
<th>B/F/TAF n=314</th>
<th>DTG/ABC/3TC n=315</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine kinase elevation (&gt; 10x ULN)</td>
<td>3.5%</td>
<td>3.2%</td>
</tr>
<tr>
<td>LDL elevation (&gt;190 mg/dL [fasting]) §</td>
<td>2.3%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Amylase elevation (&gt; 2x ULN)</td>
<td>1.9%</td>
<td>2.2%</td>
</tr>
<tr>
<td>Neutropenia (&lt; 1,500 cells/mm$^3$)</td>
<td>1.6%</td>
<td>3.2%</td>
</tr>
</tbody>
</table>

§ SI units for grade 3 or 4 lab abnormalities: Fasting LDL elevation > 4.92 mmol/L

B/F/TAF vs ABC/3TC/DTG:
Rates of Grade 3 or 4 lab abnormalities were low and similar between arms


LDL, low-density lipoprotein.
LATTE-2: 96-week results

Heart failure in the aging HIV population

- Age
- Hypertension
- Diabetes
- Chronic kidney disease
- Myocardial fibrosis and steatosis
- HEART FAILURE
  - Antiretroviral therapy
  - Mitochondrial toxicity
  - HIV

Boccara F, AIDS 2017
HIV and Nonischemic Heart Disease

Pravin Manga, MBChB, PhD, Keir McCutcheon, MBChB, Nqoba Ts Abedze, MBChB, Ahmed Vachiat, MBChB, Don Zachariah, MBChB

Pathogenesis and Risk Factors Associated With HIV Infection and Heart Disease

A. Pulmonary arterial hypertension
   - Endothelial dysfunction and a procoagulant state (caused by inflammation)
   - Vasoconstriction (caused by invasion of lung endothelium and endothelin 1 release)
   - Endothelial proliferation (caused by negative factor, gp120 proteins, and HIV-trans-activator of transcription protein)

B. Aortopathy
   - Occlusion of vasa vasorum (caused by inflammation)
   - Aortic regurgitation and aneurysm (caused by inflammation-induced vessel wall and autoimmune response)

C. Cardiomyopathy
   - Inflammation
   - Immune dysregulation
   - Opportunistic infections
   - Myocyte invasion
   - Cardiac steatosis (induced by combination anti-retroviral therapy)

D. Pericardial disease
   - Inflammation
   - Low immune status
   - Co-infection: Tuberculosis, Nocardia, Cytomegalovirus
   - Malignancies: Lymphoma, Kaposi sarcoma
   - Hypoalbuminemia
   - Capillary leak syndrome

Features of heart failure in persons living with HIV according to treatment status

<table>
<thead>
<tr>
<th></th>
<th>Untreated PLWHIV</th>
<th>PLWHIV receiving ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>Decreasing with increased ART availability</td>
<td>Increasing with improved survival of PLWHIV</td>
</tr>
<tr>
<td>Type of HF</td>
<td>Mainly systolic</td>
<td>More often HF with preserved EF</td>
</tr>
<tr>
<td>Cause</td>
<td>HIV ± opportunistic infections, inflammatory,</td>
<td>CAD, LVH, or both</td>
</tr>
<tr>
<td></td>
<td>and nutritional deficiencies</td>
<td></td>
</tr>
<tr>
<td>Time course</td>
<td>Acute</td>
<td>Chronic</td>
</tr>
<tr>
<td>Treatment</td>
<td>ART + standard HF care</td>
<td>Standard HF care</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Poor without ART</td>
<td>Similar to HF in persons without HIV</td>
</tr>
</tbody>
</table>
We identified 21,435 human immunodeficiency virus–infected patients in the United States Veterans Health Administration actively using antiretrovirals between 2002 and 2011. We excluded patients with a prior diagnosis of HF.
Atrial fibrillation incidence rate per 1000 person years in population studies

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Veterans Affairs Case Registry HIV Study</th>
<th>Framingham study</th>
<th>Olmsted county study</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>1.1</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>35–44</td>
<td>1.8</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>45–54</td>
<td>3.7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>55–64</td>
<td>8.7</td>
<td>3.1</td>
<td>4.3</td>
</tr>
<tr>
<td>65–74</td>
<td>15.5 (≥65)</td>
<td>9.0</td>
<td>12.9</td>
</tr>
<tr>
<td>75–84</td>
<td>–</td>
<td>18.9</td>
<td>24.5</td>
</tr>
<tr>
<td>≥85</td>
<td>–</td>
<td>38.0</td>
<td>39.7</td>
</tr>
</tbody>
</table>

West T, Curr Opin HIV/AIDS 2017
Use of direct oral anticoagulants in patients with HIV

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Rivaroxaban (CYP3A4 substrate)</th>
<th>Apixiban (CYP3A4 substrate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protease inhibitors (CYP3A4 inhibitors/inducers)</td>
<td>2-h dosing interval</td>
<td>Interaction likely</td>
<td>Interaction likely</td>
</tr>
<tr>
<td>NNRTIs (CYP3A4 inhibitors/inducers)</td>
<td>No interaction expected</td>
<td>Interaction likely</td>
<td>Interaction likely</td>
</tr>
<tr>
<td>Cobicistat (CYP3A4 inhibitor)</td>
<td>No interaction expected</td>
<td>Interaction possible</td>
<td>Interaction possible</td>
</tr>
<tr>
<td>NRTIs renally excreted</td>
<td>No interaction expected</td>
<td>No interaction expected</td>
<td>No interaction expected</td>
</tr>
<tr>
<td>Integrase inhibitors (CYP3A4 substrate)</td>
<td>No interaction expected</td>
<td>No interaction expected</td>
<td>No interaction expected</td>
</tr>
<tr>
<td>CCR5 antagonists (CYP3A4 substrate)</td>
<td>No interaction expected</td>
<td>No interaction expected</td>
<td>No interaction expected</td>
</tr>
</tbody>
</table>

CCR5, CC chemokine receptor type 5; CYP3A4, cytochrome P450 3A4; NNRTIs, nonnucleoside reverse transcriptase inhibitors; NRTIs, nucleoside reverse transcriptase inhibitors.

West T, Curr Opin HIV/AIDS 2017
Geriatric syndromes: new frontiers in HIV and sarcopenia

Kellie L. Hawkins\textsuperscript{a}, Todd T. Brown\textsuperscript{b}, Joseph B. Margolick\textsuperscript{c} and Kristine M. Erlandson\textsuperscript{a}

HIV infection, in many circumstances, can now be managed as a chronic disease due to the marked increase in life expectancy since the introduction of combination antiretroviral therapy (ART). As the patients who first had access to combination ART age into their 50s and 60s, the effects of chronic HIV infection on health have become an important research focus in HIV infection. People living with HIV appear to exhibit an earlier occurrence of some aging-related conditions compared to people without HIV, in part due to higher rates of comorbidities, high-risk behaviors (e.g. smoking, substance use), chronic immune activation, inflammation, and ART-specific factors. Some studies have even suggested an earlier-than-expected appearance of the ‘geriatric syndromes,’ which are complex medical syndromes of older adults that are associated with morbidity and mortality. The geriatric syndromes include a wide variety of disease processes ranging from incontinence and dementia to impairments in physical function. This review will focus on one geriatric syndrome, sarcopenia, in older HIV-infected populations, and its relation to other aging syndromes, including frailty and falls. The contribution of HIV itself, ART exposure, and specific comorbidities, and the importance of early recognition and prevention of these aging syndromes will be highlighted.

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AIDS 2017, 31 (Suppl 2):S137–S146

Keywords: falls, frailty, geriatric syndromes, HIV, sarcopenia
HIV Specific Pillars of Aging

Hawkins CL, AIDS 2017
Pain has always been an important part of human immunodeficiency virus (HIV) disease and its experience for patients. In this guideline, we review the types of chronic pain commonly seen among persons living with HIV (PLWH) and review the limited evidence base for treatment of chronic noncancer pain in this population. We also review the management of chronic pain in special populations of PLWH, including persons with substance use and mental health disorders. Finally, a general review of possible pharmacokinetic interactions is included to assist the HIV clinician in the treatment of chronic pain in this population.

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The Infectious Diseases Society of American considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient’s individual circumstances.
Changes in Fat Mitochondrial DNA and Function in Subjects Randomized to Abacavir-Lamivudine or Tenofovir DF–Emtricitabine With Atazanavir-Ritonavir or Efavirenz: AIDS Clinical Trials Group Study A5224s, Substudy of A5202

There was a significant decrease in fat mtDNA at week 96 compared with baseline in subjects randomized to either ABC/3TC (−341 copies/cell) or TDF/FTC (−400 copies/cell). The decrease did not differ between ABC/3TC and TDF/FTC groups.
Should pts doing well on 3-drug ART with our without booster be switched to 2-drug therapy?

A. Never
B. As often as possible
C. Always

Please respond using your mobile device: pollev.com/CCO2
Never: 32%
As often as...: 67%
Always: 1%