Financial Relationships With Commercial Entities

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Learning Objectives

After attending this presentation, learners will be able to:

- Assess risk for cardiovascular disease in people living with HIV (PLWH)
- Diagnose diabetes mellitus in PLWH
- Assess frailty in older PLWH
People With HIV Are Living Longer!

Additional years of life for a 20 year old

Multimorbidity is More Common in PLWH

- Cardiovascular
- Diabetes mellitus
- Chronic kidney disease
- Neurologic
- Osteoporosis
- Malignancy
- Depression

Aging is...

“Being nibbled to death by goldfish”
- My father in law, Richard Morris
Considerations for Aging with HIV

- Multimorbidity
  - Co-morbidities including ASCVD, DM, frailty
  - Mental health/substance use issues
  - Organ demise: Hearing/vision loss, incontinence
- Polypharmacy
- Social isolation and loneliness
- Stigma
- Financial and housing insecurity; impact of social determinants of health

Cardiovascular Disease in PLWH
Population Attributable Fraction Globally

Risk of MI in PLWH – NA-ACCORD
Cardiovascular Disease More Common in PLWH

- Myocardial infarction, heart failure, stroke: 1.5-2 fold higher than for HIV negative
- Pulmonary hypertension
- Blood clots
- Sudden death

Friedman, Circulation, 2019

AHA SCIENTIFIC STATEMENT

Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV

A Scientific Statement From the American Heart Association

- Recognizes increased risk of ASCVD in persons living with HIV
- Addresses pathophysiology, screening, treatment
- Includes link to patient perspective from PLWH

Friedman, Circulation, 2019
Two approaches
• High risk
• Low-moderate risk

High Risk Approach

- Known clinical ASCVD, or
- LDLc ≥ 190 mg/dL (untx), and/or
- Age 40-75 with diabetes mellitus

OR
- Calculated high ASCVD risk by risk calculator tools
- Presence of 2018 ACC/AHA “risk enhancers”

High Risk Approach

- Consider cardiology referral after risk-benefit discussion with patient
- Lifestyle optimization, particularly smoking cessation
- Lipid lowering therapy
  - Start low – go slow
    - Decrease dose or stop if severe myalgia, unexplained muscle weakness, LFT > 3x ULN, CK > 10x ULN

Friedman, Circulation, 2019
Lipid Lowering Therapy

- Atorvastatin 10-80 mg
- Rosuvastatin 5-40 mg
- Pitavastatin 2-4 mg
  - INTREPID study in HIV+: pitavastatin superior to pravastatin in reduction of LDL-c & non-HDL apolipoprotein B at 12 & 52 weeks; fewer drug-drug interactions; no glucose effect
- Simvastatin & lovastatin contraindicated with PIs or cobicistat
- Statin toxicity or insufficient response
  - Consider adding ezetimibe +/- PCSK9 inhibitor

Low-Moderate Risk Approach: Use Calculators

ASCVD Risk Assessment Tools

- Tools: AHA/ACC calculator; D:A:D; Framingham
- Traditional risk assessment tools may underestimate risk in PLWH by 1.5 - 2 fold, especially if
  - Hx of prolonged viremia: delayed ART initiation, treatment failure, non-adherence
  - Nadir or current CD4 < 350/mm³
  - Metabolic syndrome: lipodystrophy, fatty liver
  - Hepatitis C


Friedman, Circulation, 2019
Low Risk Approach: Risk Enhancers

- Family history of early MI/stroke (men <55, women <65)
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease, pre-eclampsia, premature menopause
- Subclinical atherosclerosis (Arterial plaque; CAC >0; ABI <0.9)
- In selected individuals (if measured): Lp(a) >50 mg/dl (>125 nmol/L); hs-CRP ≥2.0 mg/L; apoB ≥130 mg/dL

But also...

- Control risk factors other than lipids
  - Smoking, smoking, smoking!
  - Diabetes mellitus – 2.4x increased risk of MI
  - Hypertension – 35% prevalence in tx-experience
  - Obesity: encourage exercise and diet: education!
- Aspirin prophylaxis? Not studied in PLWH
- Statin (without hyperlipidemia)?
  - Wait for REPRIEVE trial...

Diabetes Mellitus: ADA Definition (2019)

- Hemoglobin A1C ≥ 6.5%
  - "In conditions associated with an altered relationship between A1C and glycemia, such as...HIV...only plasma blood glucose criteria should be used to diagnose DM." Only applies when on ART
- Fasting plasma glucose ≥ 126 mg/dL, confirmed by repeat
- Plasma glucose ≥ 200 mg/dL 2 hrs after 75 g oral glucose tolerance test
- Random plasma glucose ≥ 200 mg/dL with polyuria and polydipsia
A1C May Under- or Overestimate Depending on ART

Smoking and Cancer in PLWH

- Smoking: up to ¾ of PLWH
- Cancer burden attributable to smoking
  - Lung cancer: 94%
  - Other ‘smoking related’ cancers (esophageal, oral, etc.): 31%
  - Anal cancer: 32%
  - All cancer: 9%

Issues Associated with Polypharmacy

- Drug interactions: DON'T GUESS – LOOK IT UP!
  - Cobicistat, ritonavir: strong CYP3A4 inhibitors
  - PIs: darunavir, atazanavir: check interactions
  - NNRTIs other than doravirine: CYP3A4 inducers; lowered by PPIs
  - INSTIs: polyvalent cations; bictegravir: CYP3A4, UGT1A1: rifampin/rifabutin; metformin (increased 40%); atazanavir contraindicated
- Additive toxicities: nephrotoxic drugs, etc.
- Inappropriate drugs
- Risk for forgetting doses
- Risk for forgetting prescriptions
- Expense: https://www.hiv-druginteractions.org
Tools for Assessing Frailty

- Fried's Frailty Phenotype
  - 5 physical variables
- Short Physical Performance Battery (SPPB)
  - 3 physical tasks
- Frailty Index
  - 40 physical, psychological, social/functional variables

Fried's Frailty Phenotype

<table>
<thead>
<tr>
<th>Frailty indicator</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>Self-reported weight loss of more than 10 pounds or recorded weight loss of ≥ 5% per annum</td>
</tr>
<tr>
<td>Self-reported exhaustion</td>
<td>Self-reported exhaustion on CES-D depression score ≥ 3 days per week or most of the time</td>
</tr>
<tr>
<td>Low energy expenditure</td>
<td>Energy expenditure ≤ 185 kcal/week (males) or ≤ 120 kcal/week (females)</td>
</tr>
<tr>
<td>Slow gait speed</td>
<td>Standardized cut-off times to walk 15 feet, stratified by sex and height</td>
</tr>
<tr>
<td>Weak grip strength</td>
<td>Grip strength, stratified by sex and BMI</td>
</tr>
</tbody>
</table>

Key: CES-D, Center for Epidemiological Studies Depression; BMI, body mass index.

Fried, J of Gerontology, 2001
Frailty Phenotype as a Predictor

Frailty phenotype predicts:
- Death
- Worsening disability
- Incident fall
- 1st hospitalization

Frailty phenotype was more common in women and African-Americans.

Frailty Phenotype as a Predictor (Fried, J of Gerontology, 2001)

<table>
<thead>
<tr>
<th>Hazard Ratio* Estimated Over 5 Years</th>
<th>Frail*** (Versus Not Frail)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsening mobility disability</td>
<td>1.50**</td>
</tr>
<tr>
<td>Worsening ADL disability</td>
<td>1.98**</td>
</tr>
<tr>
<td>Incident fall</td>
<td>1.29**</td>
</tr>
<tr>
<td>First hospitalization</td>
<td>2.24**</td>
</tr>
<tr>
<td>Death</td>
<td></td>
</tr>
</tbody>
</table>

Frailty: Short Physical Performance Battery (SPPB)

3 Physical Tasks:
- Repeated chair stands (sit then stand 5 times)
- Balance tests
- 4-meter (10-foot) walk test

gate.checkin.missouri.edu/SPPB-Score-Test.pdf; Greene, AADL, 2014

Frailty Index

- Relates deficit accumulation to risk of death
- 40 variables
  - Physical: e.g. walk outside < 3d/wk; wt loss > 5 kg/yr
    - Comorbid diseases, without regard to severity
  - Psychological: feel depressed, happy, lonely, etc.
  - Social/Functional: help bathing, dressing, eating, etc.
- Scored between 0-1 = deficits/variables
  - < 0.08 = robust; ≥ 0.25 = frail

Source: BMJ Geriatrics, 2008
Interventions to Prevent Frailty

- Exercise, strength and balance training
- Social interaction
- Healthy diet
- Preventative health care and screening
- Management of medications
- Smoking cessation

Screening for HIV-Associated Neurocognitive Disorders

Screening tools have variable sensitivity/specificity
- Mini-mental state examination (MMSE)
- International HIV dementia scale (IHDS)
- Montreal cognitive assessment (MoCA)
- Simioni symptom questionnaire (SSQ)
- Cognitive assessment tool-rapid version (CAT-rapid)

Screening for HIV dementia
- IHDS + CAT-rapid = most sensitive/specific

Screening for asymptomatic/mild HAND
- No screener had adequate sensitivity/specificity: need full neuropsych testing

Don’t forget reversible causes ... syphilis, thyroid disease, B12 deficiency, depression

Joska, AIDS Behavior, 2016
Screening for Mental Health and Substance Use Issues

- Depression and substance use are common; screening is uncommon
- Easy screening tools available (and reimbursable!)
- Depression - PHQ 2 and 9; Anxiety - GAD-2 and 7
  - PHQ-2: Over the last 2 weeks, how often have you been bothered by the following (score 0-3)
    • Little interest or pleasure in doing things
    • Feeling down, depressed or hopeless
- Alcohol: CAGE and AUDIT
- Drug Use: TICS; opioid risk tool

Tools for Screening

National HIV Curriculum
• https://www.hiv.uw.edu/page/mental-health-screening/phq-2

Social Isolation Is Associated with Increased Mortality
PLWH ≥ 65 yo are 2-7 times more likely to experience social isolation than those who are HIV -

Greysen et al., Journal of American Geriatrics Society, 2013

Does Social Isolation Predict Hospitalization and Mortality Among HIV+ and Uninfected Older Veterans?
S. Ryan Greysen, MD, MPH, MA*; Lynn J. Honickel, MD, MPH;
Kenneth R. Courneya, MD, MPH, PhD†; Rachel Constant, MD; Michael G. Calk, MD, MPH‡
and Amy C. Jeste, MD, PhD

The Social Isolation Score (SIS)
- Visits from close family
- Visits from close friends
- Number of close family/friends
- Use of self-help or support group in last year
- Volunteer work or involvement in community organization
- Frequency of attendance to religious events
- Relationship status
- Living alone

Greysen et al., Journal of American Geriatrics Society, 2013

Patient Centered Care Coordination for Older PLWH

2020 Ryan White HIV/AIDS Program CLINICAL CONFERENCE, August 9-12, 2020
Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America

2020 UPDATE COMING!!

Question-and-Answer Session