Aging and Frailty in People With HIV

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Financial Relationships With Ineligible Companies*

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*The ACCME recently updated the term from commercial interests to ineligible companies.

Learning Objectives

- Describe the clinical relevance of physical function and frailty measures
- Select tools for physical function and frailty in the clinical or research setting
- Review interventions to attenuate or reverse frailty or impairments in physical function
Functional Impairment, Frailty, Disability...

You know it when you see it, but how can you best describe it?

Defining the Conditions

Frailty: A Measure of Vulnerability
Frailty: By Phenotype

- Reflects a vulnerability as result of multiple impairments:
  - Slow gait
  - Weak grip
  - Low activity
  - Fatigue
  - Weight loss
- Requires ~ 5-10 minutes to assess
- 4-m walking course and a dynamometer
- Must be assessed prospectively

Frailty: By Index

- Accumulation of deficits
- Variables that increase with age but are not ubiquitous with age (e.g., presbyopia) and are associated with health status
- Can often be derived from chart review
- # of variables impaired / # variables assessed
- Veterans Aging Cohort Study Index is a similar concept of routinely obtained laboratory-derived variables

Frailty Appears to Occur More Frequently, and Perhaps Early with HIV
Frailty Differs in Prevalence (Sampling of Studies)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Site</th>
<th>Study Population</th>
<th>Prevalence of Frailty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onen</td>
<td>US</td>
<td>Median age 47; 95% on ART</td>
<td>5%</td>
</tr>
<tr>
<td>Erlandson</td>
<td>US</td>
<td>Aged 40+, 95% on ART</td>
<td>6%</td>
</tr>
<tr>
<td>Umbiaja</td>
<td>US</td>
<td>Age 46+, substudy of REPRIEVE</td>
<td>8%</td>
</tr>
<tr>
<td>Onen</td>
<td>US</td>
<td>≥18 years; 75% on ART</td>
<td>9%</td>
</tr>
<tr>
<td>Rees</td>
<td>Amsterdam</td>
<td>Age 49+, 94% on ART</td>
<td>11%</td>
</tr>
<tr>
<td>Allesina</td>
<td>France</td>
<td>SEPTAVIH Study of 510 PWH aged ≥70 yrs</td>
<td>13.3%</td>
</tr>
<tr>
<td>Piggott</td>
<td>US</td>
<td>≥18 years; IVDU; 54% ART</td>
<td>15%</td>
</tr>
<tr>
<td>Pathai</td>
<td>Capetown</td>
<td>≥30 years; ART</td>
<td>18% ART</td>
</tr>
<tr>
<td>Rees</td>
<td>US</td>
<td>CD4&lt;200, weight loss, poor adherence</td>
<td>19%</td>
</tr>
</tbody>
</table>

References:

What Factors Contribute to Physical Function Impairments and Frailty in HIV?

- Biobehavioral Factors
- HIV- or ART-Associated Factors
- Mechanisms of Aging
- Comorbidities in Older PWH
- Structural Inequalities
- Frailty

Adapted from Erlandson & Schmader Hazzard Textbook of Geriatric Medicine (Chapter on HIV).

What Factors Contribute to Frailty in HIV?

CROI 2021 Updates

- Age, socioeconomic factors, and comorbidities are associated with frailty in PWH ≥70 years of age (not HIV factors)

- Cardiovascular disease risk is associated with frailty, to a greater extent in men than women

References:
- Allesina, CROI 2021 Science Spotlight™
What Tools Should We Use?

68 year old woman with generally fair health, treated HIV, obesity. Non-smoker, no diabetes. Since her last visit, she admits to 2 falls and some decreased medication adherence due to “thinking problems”. When you ask about her physical activity, she admits to difficulty in walking several blocks.

ARS Question 1: What is the best way to assess her function at her visit today?

• 1) Veterans Aging Cohort Study Index
• 2) Time to Rise from a chair 5 times
• 3) Fried Frailty Phenotype
• 4) Short Physical Performance Battery
• 5) Potentially any of the above, but it depends on the question, time available, and equipment available

Ideally we can identify early impairments to most effectively intervene

Early interventions are more likely to shift function back to the “normal” trajectory

Frailty is hard to reverse
What Tool(s) Should I Choose (of 100s of options)?

<table>
<thead>
<tr>
<th>Test</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>400-1000 m walk or 6 min walk</td>
<td>Continuous, outcome, identify more subtle</td>
<td>Takes ~ 5-10 min, requires more space,</td>
</tr>
<tr>
<td>Chair rise</td>
<td>impairments</td>
<td>prospective</td>
</tr>
<tr>
<td>Short Physical Performance</td>
<td>Easy/fast, only requires chair, continuous,</td>
<td>Lower extremity focused, prospective</td>
</tr>
<tr>
<td>Battery</td>
<td>less ceiling effect</td>
<td></td>
</tr>
<tr>
<td>VASCI index</td>
<td>Data in HIV; well-validated outcome in</td>
<td>Associated with frailty, but more of a</td>
</tr>
<tr>
<td></td>
<td>older populations, includes strength, gait</td>
<td>mortality risk. Doesn’t identify specific</td>
</tr>
<tr>
<td></td>
<td></td>
<td>areas to intervene</td>
</tr>
<tr>
<td>Clinical Frail Scale</td>
<td>Well-validated, correlates with frailty,</td>
<td>No published data in HIV, prospective</td>
</tr>
<tr>
<td></td>
<td>very quick, no tools</td>
<td></td>
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</table>

Continued...Example Case: 68 y/o female with HIV

- The provider attempted to do a timed up-and-go. Patient was unable to complete due to difficulty standing up from the chair without using her arms.
- Provider estimates Clinical Fraility Scale ~ 4.
- She was identified as high-risk for frailty:
  - Referred to the geriatric clinic, PT for balance and strength training, and home occupational therapy assessment for falls safety
  - Pharmacist provided pill box, reminders on phone, discussed med escalation

From CROI to the Clinic: A Special 2-day Virtual Course, Day 2: Improving the Management of HIV: Current Key Issues in HIV Management
What Tests are Feasible to Implement in the Clinical Setting?

- Study evaluating the feasibility of administering the Short Physical Performance Battery across 3 HIV clinics
  - 2 clinics before/after a routine clinic visit
  - 3rd site administered at separate visit
- Training for staff was ~ 1 hour, assessment time was ~ 7 min
- Feasible to implement without ‘serious disruptions’ or injuries

ARS Question 2: How can these findings inform her ongoing care?

She returns to the clinic 3 months later. She continues to have difficulties in walking several blocks although is improved, and her ability to manage her finances and medications has worsened somewhat. Do her functional impairments change your recommendations for her screening mammogram and colonoscopy?

1. No, refer for mammogram and colonoscopy
2. Yes, she should not be referred for mammogram or colonoscopy
3. Yes, the risk may be greater than benefit for either mammogram or colonoscopy, but this should be discussed with the patient and inform a mutual decision
How can these findings inform her ongoing care?

Without Impairments

With Impairments

Can guide individualized discussions on risk vs benefit to...
- Continue cancer screening?
- Continue aspirin or statins?

Can We Use Physical Function to Guide Decisions in Adults with HIV?

- In the clinic:
  - Ensure advance care planning
  - Refer for geriatric care
  - Determine frequency of clinic visits
  - Inform need for home/community resources

- In clinical trials:
  - Do newer ART regimens or adjuvant therapies impact subjective and objective physical function of older participants with HIV? Example: REPRIEVE

How Can We Treat Frailty?

From CROI to the Clinic: A Special 2-day Virtual Course,
Day 2: Improving the Management of HIV: Current Key Issues in HIV Management
Exercise or Physical Activity Improves Functional Measures in HIV (Few in Older)

- Exercise training (aerobic +/- resistance) improved 400-m walk, strength, 6-minute walk time, endurance
- Physical activity counseling and home-based walking or rehabilitation programs improved 6-minute walk distance and/or chair rise time
- Multi-component Tai chi intervention improved SPPB scores
- Multidimensional physiotherapy improved 6-minute walk time, strength, flexibility, and quality of life


Exercise and Frailty in People with HIV

- Compared 2 intensities of exercise (aerobic + resistance) for 24 weeks in sedentary people aged 50 or older with and without HIV
  - 10-45% improvement in most measures (chair rise, strength) in both groups with greater in high-intensity

- More non-frail and fewer pre-frail people with HIV after the intervention

Erlandson, et al. AIDS 2018

#1 Treatment for Frailty = Exercise

Just Get Started!

- Endurance
  - "Zumba Gold for Older Adults"
  - "Low impact, high intensity cardio workout"
  - "Seated exercises for older adults"
- Strength
  - "15-minute Sample Workout for Older Adults from Go4Life"
  - "15-minute senior strength workout"
- Balance
  - "Tai Chi for Beginners"
  - "3 Balance Exercises for Older Adults from Go4Life"
- Flexibility
  - "7-minute Yoga Workout for Older Adults from Silver Sneakers"
  - "4 Flexibility and Cool Down Exercises for Older Adults from Go4Life"

All FREE on YouTube
Interventions to Prevent/Improve Frailty:

<table>
<thead>
<tr>
<th>Non-Pharmacologic Interventions</th>
<th>Pharmacologic Interventions*</th>
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<tbody>
<tr>
<td>Physical activity and exercise</td>
<td>mTOR pathway (rapamycin)</td>
</tr>
<tr>
<td>Nutritional (supplements, protein, obesity</td>
<td>Sirtuin/NAD pathway (nicotinamide,</td>
</tr>
<tr>
<td>management)</td>
<td>resveratrol)</td>
</tr>
<tr>
<td>Multimodal approaches</td>
<td>mTOR signaling/metabolic regulators</td>
</tr>
<tr>
<td>Genetic consultative clinics</td>
<td>Metformin, etc.</td>
</tr>
<tr>
<td>Reduce fall risk</td>
<td></td>
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<tr>
<td>Evaluate/final mood disorders and cognitive</td>
<td>Testosterone</td>
</tr>
<tr>
<td>impairment</td>
<td></td>
</tr>
<tr>
<td>Polypharmacy (De-escalation)</td>
<td>Other therapies (ART, alfacalcidol,</td>
</tr>
<tr>
<td>Address social determinants of health that</td>
<td>capromorelin, teriparatide, tesamorelin,</td>
</tr>
<tr>
<td>underline risk of frailty and access to</td>
<td></td>
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<tr>
<td>treatment and care for frailty-associated aging</td>
<td></td>
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<tr>
<td>related conditions</td>
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*Very limited data, especially in HIV

Summary

- Functional limitations and frailty can provide a window into patient vulnerability
  - May guide clinical decision making, protect from harm, avoid strategies not likely to benefit
- Interventions should ideally focus on early impairments that occur in midlife, before an individual becomes frail or experiences disability
- Physical activity is safe and effective in improving physical function
- Some promising pharmaceutical options in the general population, but more research needed
- Physical activity counseling should be a routine component of our HIV visits, to increase both the lifespan and healthspan

Question-and-Answer Session