Frailty

Sara E. Espinoza, M.D., M.Sc.

Professor
Department of Medicine - Division of Geriatrics, Gerontology & Palliative Medicine
The Sam and Ann Barshop Institute for Longevity and Aging Studies

Director
San Antonio Geriatric Research, Education & Clinical Center
South Texas Veterans Health Care System
Frailty, a geriatric syndrome
Aging Mechanisms

- Pillars of Aging
  - Age-related disease/conditions
  - Environment & Genetics

Animal Models

Biomarker Discovery

- Inflammation
- Insulin resistance
- Sarcopenia
- Coagulopathy
- Neuroendocrine dysregulation
- Reduced stress response
- Immune system dysfunction

Measurement

Frailty
&
Loss of resilience

Adapted from review of Fried et al, SAGE KE, 2005; Bisset Howlett Aging Med 2019; Walston JAGS 2006
Frailty Assessment Instruments: Review

<table>
<thead>
<tr>
<th>Category</th>
<th>Calculations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk assessment (31%)</td>
<td>- Physical Frailty Phenotype (132 uses)</td>
</tr>
<tr>
<td></td>
<td>- Deficit Accumulation Index (37 uses)</td>
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<tr>
<td></td>
<td>- Gill Frailty Measure (12 uses)</td>
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<tr>
<td></td>
<td>- Clinical Frailty Scale &amp; Vulnerable Elders Survey (11 uses each)</td>
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<tr>
<td></td>
<td>- Winograd Screening Instrument (10 uses)</td>
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<tr>
<td></td>
<td>- Brief Frailty Instrument (6 uses)</td>
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<tr>
<td>Etiology of frailty (22%)</td>
<td>- Physical Frailty Phenotype (121 uses)</td>
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<tr>
<td></td>
<td>- Deficit Accumulation Index (37 uses)</td>
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<tr>
<td>Methodology (14%)</td>
<td>- Physical Frailty Phenotype (33 uses)</td>
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<tr>
<td></td>
<td>- Deficit Accumulation Index (32 uses)</td>
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<tr>
<td></td>
<td>- Brief Frailty Instrument (11 uses each)</td>
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<tr>
<td></td>
<td>- Vulnerable Elders Survey (11 uses each)</td>
</tr>
<tr>
<td></td>
<td>- FRAIL Scale (10 uses)</td>
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<tr>
<td>Biomarkers of frailty (12%)</td>
<td>- Physical Frailty Phenotype (77 uses)</td>
</tr>
<tr>
<td></td>
<td>- Deficit Accumulation Index &amp; FRAIL Scale (5 uses each)</td>
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<tr>
<td>Inclusion / exclusion criteria (10%)</td>
<td>- Physical Frailty Phenotype (22 uses)</td>
</tr>
<tr>
<td></td>
<td>- Vulnerable Elders Survey &amp; Brief Frailty Instrument (11 uses each)</td>
</tr>
<tr>
<td></td>
<td>- Winograd Screening Instrument (10 uses)</td>
</tr>
<tr>
<td></td>
<td>- Deficit Accumulation Index, Frailty / Vigor Assessment, &amp; Clinical Frailty Scale (5 uses each)</td>
</tr>
<tr>
<td>Estimating prevalence as primary goal (5%)</td>
<td>- Physical Frailty Phenotype (33 uses)</td>
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<tr>
<td></td>
<td>- Vulnerable Elders Survey (5 uses)</td>
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<tr>
<td>Guide for clinical decision-making (2%)</td>
<td>- Physical Frailty Phenotype (11 uses)</td>
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<td></td>
<td>- Vulnerable Elders Survey (5 uses)</td>
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<tr>
<td>Frailty as a target for intervention (2%)</td>
<td>- Physical Frailty Phenotype (11 uses)</td>
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<tr>
<td></td>
<td>- Clinical Frailty Scale (5 uses)</td>
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What is Frailty?

• Clinical, geriatric syndrome
• At risk population for poor outcomes
• Vulnerable to decline
• Poor tolerance to stressors
### Fried Criteria

- **Non-frail:** 0-1, **Pre-frail:** 2, **Frail:** 3+

<table>
<thead>
<tr>
<th>Grip Strength</th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>BMI ≤ 24:</td>
<td>≤ 29 kg</td>
<td>BMI ≤ 23:</td>
</tr>
<tr>
<td>BMI 24.1-28:</td>
<td>≤ 30 kg</td>
<td>BMI 23.1-26:</td>
</tr>
<tr>
<td>BMI &gt;28:</td>
<td>≤ 32 kg</td>
<td>BMI 26.1-29:</td>
</tr>
<tr>
<td>BMI &gt;29:</td>
<td></td>
<td>BMI &gt;29:</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Walking Speed</th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>15-foot walk</td>
<td>Height ≤ 173 cm: ≥ 7 sec</td>
<td>Height ≤ 159 cm: ≥ 7 sec</td>
</tr>
<tr>
<td></td>
<td>Height &gt; 173 cm: ≥ 6 sec</td>
<td>Height &gt; 159 cm: ≥ 6 sec</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical activity</th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td></td>
<td>&lt; 383 kcal/week</td>
<td>&lt; 270 kcal/week</td>
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<thead>
<tr>
<th>Exhaustion</th>
<th></th>
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<tr>
<td></td>
<td>“I felt everything I did was an effort.”</td>
<td></td>
</tr>
<tr>
<td></td>
<td>“I could not get going.”</td>
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<table>
<thead>
<tr>
<th>Weight loss</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Unintentional loss of ≥ 10 lbs in last year</td>
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</table>
Frailty Predicts Surgical Outcomes

**Elective procedures**
- Postoperative complications
  - OR=2.5, 95% CI: 1.1-5.8
- Length of stay
  - OR=1.7, 95% CI: 1.3-2.2
- Discharge to SNF
  - OR=20.5, 95% CI: 5.5-75.7

**Kidney transplantation**
HR for death by frailty
2.17 (95% CI: 1.01-4.65, p =0.047)

Makary et al., J Am Coll Surg, 2010
McAdams-DeMarco, Am J Transplantation, 2015
Frailty Prevalence Across Cohorts

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Frail</th>
<th>Pre-frail</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHS</td>
<td>7%</td>
<td>47%</td>
</tr>
<tr>
<td>WHI</td>
<td>16%</td>
<td>28%</td>
</tr>
<tr>
<td>SALSA</td>
<td>9%</td>
<td>28%</td>
</tr>
<tr>
<td>H-EPESE</td>
<td>20%</td>
<td>36%</td>
</tr>
</tbody>
</table>
Frailty, Disability & Comorbidity

Fried LP, Tangen CM, Walston J. Geron 56:M146-M157 (2001)
Frailty index

• Accumulation of deficits with age

• Deficits:
  › Impairments
  › Disabilities
  › Diseases

• Derived from CGA
• Continuous value
• Adaptable to
  • Existing data sets
  • Electronic health record data

Searle et al., BMC Geriatrics, 2008
Rockwood et al., Sci Rep, 2016 (NHANES data)
Self-Report & Laboratory Frailty Index Predicts Mortality

Self-Report
• Diseases, impairments, symptoms
• ADL/IADLs

Laboratory
• Vital signs
• Chemistries
• CBC
• Iron studies
• Vit D, B12

Blodgett et al., Geroscience, 2017
Clinical Frailty Scale – Predicts Hospital LOS & Readmission

Juma et al., Canadian Geriatrics J, 2016

Clinical Frailty Scale*

1. **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2. **Well** – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3. **Managing Well** – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4. **Vulnerable** – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5. **Mildly Frail** – These people often have more evident slowing, and need help in higher order IADLs (finances, transportation, heavy housework, medications). Typically mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6. **Moderately Frail** – People need help with all outside activities, and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (sitting, standby) with dressing.

7. **Severely Frail** – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8. **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. **Terminally Ill** – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia:

The degree of frailty corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In moderate dementia, recent memory is very impaired, even though they seemingly can remember past life events well. They can do personal care with prompting.

In severe dementia, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging: Revised 2000
   2. K Fried et al.: A global clinical measure of frailty in elderly people, CMAJ 2001;165(9):1115-1120

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### FRAIL Scale

- Approximates Fried frailty phenotype

| **Fatigue:** Are you fatigued? |
| **Resistance:** Cannot walk up 1 flight of stairs? |
| **Aerobic:** Cannot walk 1 block? |
| **Illnesses:** Do you have more than 5 illnesses? |
| **Loss of weight:** Have you lost more than 5% of your weight in the past 6 months? |

**Scoring:**
- Robust (score=0), Prefrail (score=1-2), and Frail (score=3-5)

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Morley et al., *J Nutr Health Aging*, 2013; Gleason et al., *JAMDA*, 2017
The Geroscience Approach to Improve Healthspan

Translational Geroscience Network
https://www.gerosciencenetwork.org/


Kennedy, Brian K., et al. "Geroscience: linking aging to chronic disease." Cell 159.4 (2014): 709-713.

Espinoza, Justice, Kuchel, Newman, Pignolo; Chapter 2 Clinical Geroscience, Hazzard’s Geriatric Medicine and Gerontology, 8th edition
Frailty as an outcome in clinical trials

- Few clinical trials including frailty as a primary outcome
- Differing frailty measures used, components of frailty or physical function
  - Components of frailty phenotype
    - gait, strength, physical activity, exhaustion
  - Physical function: strength, balance, flexibility
  - Disability
  - Falls, fear of falling
  - Cardiometabolic: BMI, CV indices
  - Cognition, depressive symptoms
  - Quality of life
- Trials including frailty have focused on differing stages of frailty or specific populations
  - Primary prevention
  - Secondary prevention (i.e., progression of frailty)

Summary

• Frailty is a geriatric syndrome
• Increased risk for poor health outcomes
• Several instruments available
• Selection of instrument influenced by the research/clinical goal
• Frailty assessment is becoming more common in research & clinical practice

Resources
Frailty Science – https://frailtyscience.org
Global Frailty Network – Frailty Seminar Series
Acknowledgements

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Pepper Center Clinical Core
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UT Health
San Antonio
Barshop Institute

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Geroscience
Education & Training Network

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Geriatric Research Education & Clinical Center