Frailty in Older Adults

Farshad Sharifi, MD, MPH
Elderly Health Research Center
Outlines

• Definition of frailty
• Significance of frailty
• Conceptual Frailty Models
• Pathogenesis of frailty
• Management of frailty
• Prevention of Frailty
Definition of frailty
Definition of Frailty

- Frailty is conceptually defined as a clinically recognizable state of older adults with increased vulnerability, resulting from age-associated declines in physiologic reserve and function across multiple organ systems, such that the ability to cope with everyday or acute stressors is compromised.
Significance of Frailty
Frailty Cornerstone of Geriatric Medicine

- Frailty is **cornerstone of geriatric medicine**
- Main concern of geriatric medicine is **identification, evaluation, treatment and prevention of frailty** and its outcomes.
Frailty and Aging

• Aging is associated with increased likelihood of frailty, and that older persons have reduced physiological reserve than younger persons and these changes are likely independent of disease.
Frailty is Compelling

- Frail individuals are at highest risk for a number of adverse health outcomes.
- Frail older adults have high need of health care and community and informal support services, as well as long-term care.
Frail Elderly at risk for multiple adverse health outcomes

a. Medical instability
b. Disability, dependency
c. Institutionalization
d. Injuries
e. Falls
f. Acute illness
g. Hospitalization
h. Health care resources utilization
i. Slow or incomplete recovery from illness and/or hospitalization
j. High risk of iatrogenesis and side effects from medical interventions
k. Mortality
l. Cognitive impairment
m. Osteoporosis
n. Osteoarthritis
o. Depression
Frailty is at the Core of Geriatric Medicine

1- The prevalence of frailty increases dramatically with age.

2- Frailty is manifested as an impaired ability to cope with challenges in health and reduced ability to regain a stable health status, possibly related to reduced functional reserve. Severity of frailty spans from subclinical to a clinical stage to impending death.

3- In aging individuals, the variability in health and functional status is explained less and less by the effect of clinically evident or even subclinical diseases. Older age is associated with increased vulnerability to multiple diseases with no evident pathogenetic connections. Such global vulnerability is not explained by changes in recognizable risk factors.

4- Frail older persons require intensive and multidimensional continuous care and have high need of community and informal support services. These care needs necessitate a shift in the deployment of heath care resources.

5- Geriatrics is a medical specialty particularly skilled in care of frail older adults.
Frailty as a Core Clinical Concept

• Frail older adults are a subset of older population who are at high risk from stressors such as extreme of heat and cold, acute infection or injury, or the stress of hospitalization or surgery.
Frailty and Associated Vulnerability

• All geriatrically oriented definitions of frailty have in common that frailty involves heightened vulnerability to adverse outcomes, and that this vulnerability may most likely manifest in the face of stressors.
Conceptual Frailty Models
Conceptual Frailty models

- Two major conceptual definitions with proposed assessment tools:
  1. The frailty phenotype (FP)
  2. The frailty index (FI)
Frailty Phenotype

• The phenotypic definition of frailty as a geriatric syndrome was proposed by Fried et al and tested in the CHS.

• Frailty is operationalized as a syndrome meeting three or more of five phenotypic criteria:
  • Weakness as measured by low grip strength
  • Slowness by slowed walking speed
  • Low level of physical activity
  • Low energy or self-reported exhaustion
  • Unintentional weight loss.
Prefrail Definition

• A prefrail stage, in which one or two criteria not adequately treated, and/or more diseases are accumulated, these patients may develop frailty.
# Frailty Phenotype

<table>
<thead>
<tr>
<th>FP criteria</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>Grip strength: lowest 20% (by sex, body mass index)</td>
</tr>
<tr>
<td>Slowness</td>
<td>Walking time/15 feet: slowest 20% (by sex, height)</td>
</tr>
<tr>
<td>Low level of physical activity</td>
<td>Kcal/week: lowest 20%</td>
</tr>
<tr>
<td></td>
<td>Males: 383 Kcal/week</td>
</tr>
<tr>
<td></td>
<td>Females: 270 Kcal/week</td>
</tr>
<tr>
<td>Exhaustion; poor endurance</td>
<td>“Exhaustion” (self-report)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>&gt;10 lb lost unintentionally in prior year</td>
</tr>
</tbody>
</table>

Clinical Concepts of Frailty Phenotype

• Frailty is a distinct physiologic process resulting from dysregulation of multiple physiologic system,; many of these systems interact with each other and resulting impairments contribute to clinical manifestations.

• The aggregate impact of dysregulated systems is a decreased ability to maintain homeostasis in face of stressors.
Prevalence of Frailty Phenotype

• Based on the FP and its various modified versions, the overall prevalence of frailty in community-dwelling older adults aged 65 years and over in the US ranges from 7% to 25%.

• It increases with age from 3.9% in the age-group 65–74 years to 25% - 45% in the age group older than 85 years.
Frailty Index

• The Frailty Index was developed by Rockwood et al based on a comprehensive geriatric assessment by counting the number of deficits accumulated, including diseases, physical and cognitive impairments, psychosocial risk factors, and common geriatric syndromes other than frailty.

• The total number of deficits that can be used in the FI is considered to be 80, with 30–70 items being typically counted.
<table>
<thead>
<tr>
<th></th>
<th>Deficits</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Eyesight</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Hearing</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>Help to eat</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Help to dress</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Ability to take care of appearance</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>Help to walk</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>Help to get in and out of bed</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>Help to go to the bathroom</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>Help to take a bath or shower</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>Help to use the telephone</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>Help to travel beyond walking distance</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>Help with shopping</td>
<td>3</td>
</tr>
<tr>
<td>13</td>
<td>Help to prepare own meals</td>
<td>3</td>
</tr>
<tr>
<td>14</td>
<td>Help to do housework</td>
<td>3</td>
</tr>
<tr>
<td>15</td>
<td>Ability to take medications</td>
<td>3</td>
</tr>
<tr>
<td>16</td>
<td>Ability to handle own money</td>
<td>3</td>
</tr>
<tr>
<td>17</td>
<td>Self-rated health</td>
<td>5</td>
</tr>
<tr>
<td>18</td>
<td>Troubles prevent normal activities</td>
<td>3</td>
</tr>
<tr>
<td>19</td>
<td>Lives alone</td>
<td>2</td>
</tr>
<tr>
<td>20</td>
<td>Having a cough</td>
<td>2</td>
</tr>
<tr>
<td>21</td>
<td>Feeling tired</td>
<td>2</td>
</tr>
<tr>
<td>22</td>
<td>Nose stuffed up or sneezing</td>
<td>2</td>
</tr>
<tr>
<td>23</td>
<td>High blood pressure</td>
<td>2</td>
</tr>
<tr>
<td>24</td>
<td>Heart and circulation problems</td>
<td>2</td>
</tr>
<tr>
<td>25</td>
<td>Stroke or effects of stroke</td>
<td>2</td>
</tr>
<tr>
<td>26</td>
<td>Arthritis or rheumatism</td>
<td>2</td>
</tr>
<tr>
<td>27</td>
<td>Parkinson's disease</td>
<td>2</td>
</tr>
<tr>
<td>28</td>
<td>Eye trouble</td>
<td>2</td>
</tr>
<tr>
<td>29</td>
<td>Ear trouble</td>
<td>2</td>
</tr>
<tr>
<td>30</td>
<td>Dental problems</td>
<td>2</td>
</tr>
<tr>
<td>31</td>
<td>Chest problems</td>
<td>2</td>
</tr>
<tr>
<td>32</td>
<td>Trouble with stomach</td>
<td>2</td>
</tr>
<tr>
<td>33</td>
<td>Kidney trouble</td>
<td>2</td>
</tr>
<tr>
<td>34</td>
<td>Losing control of bladder</td>
<td>2</td>
</tr>
<tr>
<td>35</td>
<td>Losing control of bowels</td>
<td>2</td>
</tr>
<tr>
<td>36</td>
<td>Diabetes</td>
<td>2</td>
</tr>
<tr>
<td>37</td>
<td>Trouble with feet or ankles</td>
<td>2</td>
</tr>
<tr>
<td>38</td>
<td>Skin problems</td>
<td>2</td>
</tr>
<tr>
<td>39</td>
<td>Fractures</td>
<td>2</td>
</tr>
<tr>
<td>40</td>
<td>Trouble with nerves</td>
<td>2</td>
</tr>
</tbody>
</table>
Measuring frailty as an index of (40) deficits

- Range = 0 to 0.66, mean 0.16
- The higher the Frailty Index, the more frail the individual
Comparing of FP & FI

• The FI appears to be a more sensitive predictor of adverse health outcomes,
• The FI does not attempt to distinguish frailty from disability or comorbidity.
• Counting the number of accumulated deficits does not constitute a clinical geriatric syndrome per se.
Type of frailty

- Primary frailty: it results of intrinsic aging processes.
- Secondary frailty: it is associated with the end stages of several chronic diseases associated with inflammation and wasting such as cancer, heart failure, COPD, and HIV.
Domains of Clinical Manifestation of Frailty

- Strength
- Balance
- Motor processing
- Nutrition
- Endurance
- Physical activity
- Cognition
Pathogenesis of Frailty
Pathogenesis of Frailty Syndrome

- Chronic inflammation and immune activation
- Musculoskeletal system
- Complex multifactorial etiology
Chronic inflammation and immune activation

• Direct association between frailty and elevated circulating levels of interleukin (IL)-6, a proinflammatory cytokine, was reported.
• C-reactive protein and tumor necrosis factor, have also been shown to have elevated levels in frail older adults.
• Elevated levels of neopterin, a well-known molecular marker for immune activation mediated by monocytes and macrophages, are associated with frailty.
Cellular/Immune System and Pathway Activation in Frailty

- Direct associations between frailty and increased total WBC count were seen in some studies.
- Frailty is associated with increased counts of cluster of differentiation (CD)8+/CD28− T cells and CCR5+ T cells, the latter of which has a type 1 pro-inflammatory phenotype.
- Up-regulation in ex vivo expression of several stress-responsive inflammatory pathway genes in frailty has shown in a study.
Cellular/Immune System and Pathway Activation in Frailty (Cont.)

- Frailty-associated up-regulated monocytic expression of CXCL10, a potent pro-inflammatory chemokine, and elevated circulating IL-6 levels.
- Cytomegalovirus (CMV) infection, as positive anti-CMV immunoglobulin G titers have been shown to be associated with frailty.
contribution of chronic inflammation to frailty

- Elevated cellular and molecular inflammatory mediators have inverse associations with
- Hemoglobin concentrations,
- Insulin-like growth factor (IGF)-1 levels,
- Levels of albumin,
- Micronutrients
- Vitamins
Musculoskeletal system

• Weakness and slowed motor performance are cardinal features of the frailty syndrome,
• sarcopenia is likely a key pathophysiologic contributor to frailty.
• Sarcopenia is defined as the loss of muscle mass and strength, which can occur rapidly after the age of 50 years.
Musculoskeletal system (Cont.)

• Age-related changes in a-motor neurons, type I muscle fibers, muscular atrophy, poor nutrition, growth hormone (GH) production, sex-steroid levels, and physical activity.

• Chronic inflammation is also an important contributor to sarcopenia.

• Skeletal muscle provides support for bone health.

• Direct relationships of frailty with osteopenia and osteoporosis.
Endocrine system

- Sex steroids and IGF-1 are essential to skeletal muscle metabolic dysregulation.
- Age-related rapid decrease of estrogen in postmenopausal women and gradual decrease of testosterone in older men lead to decline in muscle mass and muscle strength. Circulating levels of the sex hormone dehydro-epiandrosterone sulfate and IGF-1, a signaling target of GH, are significantly lower in frail than non-frail older adults.

•
Endocrine system

- Cortisol and vitamin D, have also been associated with the frailty syndrome in the elderly.
- Higher levels of evening, 24-hour mean cortisol, and blunted diurnal variation of cortisol with frailty burden and clinical presentation has been observed in frail older women.
- Vitamin D insufficiency is associated with both prevalent and incident frailty, particularly in older men.
Complex Multifactorial Etiology

• There is a significant association between obesity and frailty (defined by FP) in women and men.

• Acute episodes of illness or exacerbation of chronic conditions may accelerate the development of frailty or worsen its clinical presentation and adverse outcomes.
Pathogenesis of the frailty syndrome

Etiology/risk factors
- Aging
- Genetics
- Lifestyle
- Diseases
- Environment

Potential mechanisms
- Chronic inflammation
- Intermediary systems
- Musculoskeletal
- Endocrine
- Cardiovascular
- Hematologic
- Immune cells
- Immune/inflammatory pathway activation
- Chronic CMV infection

Frailty phenotype
- Weakness
- Weight loss
- Exhaustion
- Low activity
- Slowed performance

Healthy outcomes
- Falls
- Disability
- Dependency
- Death
Clinical applications

• Frailty is a useful risk assessment tool for preoperative evaluation for postoperative complications.

• It is useful for risk assessment in older patients with cardiovascular conditions, patients undergoing cardiac surgery, for overall immune functional decline in older adults, and to heighten vulnerability and risk stratification of older patients with cancer and about dementia.

• Frailty is used as a determine of treatment protocol for HTN and Diabetes mellitus
Primary Frailty

• Sarcopenia or loss of lean body mass, is a central component of frailty and key predictor of the other clinical manifestation.

• The vulnerability and clinical presentation of frailty syndrome results from an aging-associated dysregulation of the complex biology of mutual regulating and compensation systems that maintain a robust organism.

• With compromising of to many systems vital reserve and resilience are lost and decrease ability to maintain homeostasis in face of stressors.
Primary Frailty
Decrease Anabolic Indicators and Factors

- Decrease IGF 1 levels
- Decrease testosterone levels
- Reduce nutritional intake (protein, energy, Vitamin D and other micronutrients)
- Diminish physical activity because of aging
- Increase IL-6 and C-reactive protein
- Decrease immune function
- Anemia
- Increase insulin resistance
- Decrease of DHEA-S
- Decrease heart rate variability
- Decrease serum carotinoid
Clinical Manifestation of Frailty

• The clinical syndrome has a chronic and progressive course but not inexorable.

• Early stages of frailty are likely most amenable to intervention.

• The first manifestation of frailty tend to be weakness, slow walking speed, and/or decrease physical activity.
**Secondary Frailty**

- Inflammatory and wasting disease independently predict frailty.
- Secondary frailty theoretically develop as a result of the core wasting process of these illness, perhaps precipitating an independent, finally common process that lead to frailty phenotype.
Secondary Frailty
Most important causes

• Cardiopulmonary diseases (COPD, Heart Failure)
• Immune disease (HIV, Chronic cytomegalovirus infection)
Assessment of Frailty

Screening for frailty is appropriate to:

• Identify those at risk of adverse outcome
• To gauge severity of risk factors
• To find those who may benefit from risk amelioration
• To determine eligibility for palliative care for those at end stage.
Screening Measure of Frailty

• For frailty as clinical syndrome with distinct phenotypic presentation.
• For frailty as clinical composite, an instrument providing a clinical global impression of change in frailty has been validated.
• Walking speed is a predictor of mortality and morbidity.
• The cumulative number of symptoms, signs, illness and disability present is useful to understand morbidity burden such as multiple comorbidity.
# Criteria of Frailty Syndrome

≥ 3 characteristics identified indicates frailty

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Criteria for Frailty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wright loss</td>
<td>Lost &gt; 10 pounds unintentionally last year</td>
</tr>
<tr>
<td>Exhaustion</td>
<td>Felt last week that “everything I did was a effort” or “I could not get going”</td>
</tr>
<tr>
<td>Slowness</td>
<td>Time to walk 15 feet (cutoff depends on sex and height)</td>
</tr>
<tr>
<td>Low activity level</td>
<td>Expends &lt; 270 kcal/week (calculated from activity scale incorporating episodes of walking, household chores, yard work, etc.)</td>
</tr>
<tr>
<td>Weakness</td>
<td>Grip strength measured using hand dynamometer (cutoff depends on sex and body mass index)</td>
</tr>
</tbody>
</table>
# Clinical Course of Frailty in Older Adults

<table>
<thead>
<tr>
<th>Resilient; recovers readily from stressors</th>
<th>Appears resilient, but recovers slowly or incompletely from stressors &amp; may manifest adverse consequences</th>
<th>Clinical appearance of being frail</th>
<th>Clinical appearance of being frail</th>
<th>Clinical appearance of severe frailty; low LDL, cholesterol, strength; weight loss</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Poor tolerance of stressors; no disability</td>
<td>Poor tolerance of stressors very slow recovery</td>
<td>Outcomes: disability due to decreased energy, strength</td>
<td>Outcomes: dependent; high risk of death within 12 months</td>
</tr>
<tr>
<td><strong>Clinical Frailty Scale</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1 Very Fit</strong> – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2 Well</strong> – 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.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3 Managing Well</strong> – People whose medical problems are well controlled, but are not regularly active beyond routine walking.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>4 Vulnerable</strong> – 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.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5 Mildly Frail</strong> – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>6 Moderately Frail</strong> – 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 (cuing, standby) with dressing.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>7 Severely Frail</strong> – 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).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>8 Very Severely Frail</strong> – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>9 Terminally Ill</strong> – Approaching the end of life. This category applies to people with a life expectancy &lt;6 months, who are not otherwise evidentelly frail.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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 their past life events well. They can do personal care with prompting.

In severe dementia, they cannot do personal care without help.
Management of Frailty
Common Approach Model

• Comprehensive geriatric assessment (CGA) and management is a clinical care model design to optimize outcomes among frail older adults, particularly prevent loss of independence.

• This approach has positive effects on polypharmacy, falls, functional decline, nursing home admission and mortality.
Goals of Management of Frailty

• To exclude any modifiable precipitating causes of frailty such as treatable or environmental stressors
• To improve the core manifestations of frailty such as physical activity, strength of muscles, nutrition, and so on
• To minimize the consequences of vulnerability such as social support, change of environment, falls prevention
Managements of Frailty

1. Resistance or strengthening exercise
2. Aerobic exercise
3. Nutritional support particularly protein supplements
4. Behavioral therapy for age-related psychosocial losses adaptation
5. Adaptation to environment to decrease stressors
Prevention of Frailty
Decrease precipitating Factors

• Decrease exposure to any of a variety of stressors
• Decrease immobility regardless of cause of immobility such as pain, illness or in context of hospitalization
• Treatment of depression decrease energy and activity and nutritional intake.
• Treatment of chronic disease
Potential Pharmacological Treatments

• Hormone replacement therapy is not effective for frailty.
• Decrease of polypharmacy may be effective in progressing of frailty.
Behavioral Prevention

• Increase physical activity
• Exercises including resistance, strengthening, aerobic, and stretching exercises cause maintain muscles mass, prevent sarcopenia, decrease inflammatory factors, stop functional decline.
• Nutritional supplements are effective if add to resistance exercises.
• Early treatment of depression is effective in prevention of frailty.
Preventing frailty

- optimise management of chronic diseases
- control vascular risk factors
- review medications for side-effects/interactions
- screen for physical impairments
- exercise
- adequate diet.