Frailty: what, who and why do we care?

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I have no conflicts of interest with respect to any product or commercial interest.
Objectives

• Understand what frailty is and why it is important to patient outcomes
• Learn how to identify frail patients in practice
• Be able to apply evidence based interventions to improve outcomes in frail patients.
Frailty

• Understand what frailty is and why it is important to patient outcomes
  – What is it?
  – What causes it?
  – Why is it important?
Overview

Walston,

“The biological basis of frailty has been difficult to establish owing to the lack of a standard definition, its complexity, and its frequent coexistence with illness.”
Overview

van den Beld and Lamberts,

“frailty is characterized by generalized weakness, impaired mobility and balance and poor endurance. Loss of muscle strength is an important factor in the process of frailty, and is the limiting factor for an individual’s chances of living an independent life until death.”
Frailty: What is it?

Definition:
• vulnerability which precedes disability
• physiologic decline in multiple body systems marked by loss of function
• loss of physiologic reserve
• increased vulnerability to disease and death.
Frailty: What causes it?

• Dimensions- physical, social, cognitive, psychological, co-morbidities
• Physiologic correlates: weakness, fatigue
• Sarcopenia is likely a key component
- Total body protein declines with age
- Skeletal—disuse from chronic underactivity
- Visceral—may also be important in frailty
- NHANES prevalence of sarcopenia >60 yrs 10% women, 7% men
What might cause weakness and fatigue?

- Endocrine changes
- Effects of inflammation
- Interaction of systemic changes
Endocrine changes

DECREASES in:

- Estrogen and testosterone
- Growth hormone
- Dehydroepiandosterone, DHEA
- Insulin-like growth factor 1, IGF-1
- Cortisol (loss of diurnal variation)
- Vitamin-D
Women’s Health and Aging Studies

• IGF-1, DHEAS, and free testosterone
• If one deficiency not more likely to be frail
• If 2 or 3 deficiencies likelihood of being frail
  (OR 2.79, CI 1.06 – 7.32),
Duke EPESE

• Both high IL-6 and D-dimer increase mortality; those with both have highest mortality and greater functional decline
Women’s Health and Aging Studies

Vitamin D

- Odds of frailty if:
  - deficient (< 15) = 2.5
  - insufficient (15-30) = 3.6

- replacement might be a modifiable risk factor for frailty
What Might Cause Weakness and Fatigue?

Inflammation in frail people:

• IL-6 $\uparrow$
• CRP $\uparrow$

May cause
• Catabolism
• Anorexia, ↓ GH and IGF-1
Effects of Inflammation

IL-6 (↑) strongly associated with:

• Weight loss,
• Sarcopenia
• Susceptibility to infection
Effects of Inflammation

• Contributes to anemia by
  • directly inhibiting production of erythropoietin
  • or by interfering with normal iron metabolism
Effects of Inflammation

Chronic inflammation may:

• Trigger coagulation cascade
• Frail elderly have higher levels of:
  • Factor VIII,
  • Fibrinogen
  • D-dimer
What might cause weakness and fatigue?

- Endocrine changes
- Inflammation
- Interaction of systemic changes
INTERACTING FACTORS IN FRAILTY

- Sarcopenia
- Anemia
- Inflammatory markers
- Clotting
- Endocrine changes
- Frailty
Frailty: Why is it important?

High Prevalence
- 20–30% over 75 years
- 30% after 80 years
- Twice as common in women
- 28% of moderately-severely disabled women ≥65
Frailty: Why is it important?

Predicts outcomes

- Falls, fractures
- Hospitalization
- Mortality
- Institutionalization
Frailty: Why is it important?

One characteristic of frailty that distinguishes it from aging is the potential reversibility of many of its features.
Objective 2

LEARN HOW TO IDENTIFY FRAIL PATIENTS IN PRACTICE

Many Definitions & Tools Have Been Proposed
Chin 1999

• Frailty = inactivity combined with:
  – low energy intake
  or
  – weight loss
  or
  – low body mass index
Inactivity/weight loss was associated with lower subjective health and performance and more diseases and disabilities at baseline; Three-year relative risks of mortality (odds ratio [OR]: 4.1, 1.8–9.4) and functional decline (OR: 5.2, 1.04–25.8 for disabilities, OR: 3.7, 0.8–16.2 for performance) were higher as well.
Medicare HMO & VA, 2003

- Gait speed alone and with chair stands, & tandem balance test
- Predicts 12-mo rates of hospitalization, ↓ health, and ↓ function
- Proposed: “vital signs” to screen older adults
Canadian Study Of Health and Aging

- Frailty based on impairments in: cognition, mood, motivation, communication, mobility, balance, bowel & bladder function, ADL, IADL, nutrition, social resources, and comorbidities
- Highly predictive of death or institutionalization
The French Three-City Study

- The frail scored lower on MMSE and IST than the prefrail and nonfrail.
- Frail with cognitive impairment were more likely to develop disability in ADLs and IADLs over 4 years.
- Cognitive impairment improves the predictive validity of frailty, because it ↑risk of adverse outcomes in the frail elderly.
Cardiovascular Health Study, 2001

• Tested its definition of frailty prospectively in men and women ≥65 yrs
• Frailty is a syndrome with a critical mass of signs and symptoms.

Three out of five:
• Slow walking speed
• Poor hand grip
• exhaustion
• Weight loss
• Low energy expenditure
## Comparison Of Frailty Indexes

<table>
<thead>
<tr>
<th></th>
<th>SOF</th>
<th>CHS</th>
<th>Fried</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shrinking</strong></td>
<td>Wt loss ≥ 5% over 3 yrs</td>
<td>Unintentional wt loss 5% over 3 yrs</td>
<td>Wt loss ≥ 10% since age 60 or 10 lb in 1 yr or BMI&lt;18.5</td>
</tr>
<tr>
<td><strong>Weakness</strong></td>
<td>Unable to do 5 chair stands</td>
<td>Grip strength in lowest quartile</td>
<td>Grip strength adjusted for sex and BMI</td>
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<tr>
<td><strong>Poor energy</strong></td>
<td>“Do you feel full of energy” = no</td>
<td>“Do you feel full of energy” = no</td>
<td>Scores on 3 questions of CES-D</td>
</tr>
<tr>
<td><strong>Slowness</strong></td>
<td></td>
<td>Walking speed in lowest quartile</td>
<td>Walking speed adjusted for height and sex</td>
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<tr>
<td><strong>Low physical activity</strong></td>
<td></td>
<td>Physical Activity Scale for the Elderly</td>
<td>Short Minnesota Leisure Time Activity questionnaire, by sex</td>
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Objective 3

BE ABLE TO APPLY EVIDENCE BASED INTERVENTIONS TO IMPROVE OUTCOMES IN FRAIL PATIENTS. PHARMACOLOGIC AND NON-PHARMACOLOGIC INTERVENTIONS
Symptom relief
Set patient centered goals
Family & caregiver support

Exercise Interventions
CGA, GEM, PACE, ACE

Hospice, comfort & dignity

INCREASINGLY FRAIL

From Espinoza & Walston
INTERACTING FACTORS IN FRAILTY

- Sarcopenia
- Anemia
- Clotting
- Inflammatory markers
- Endocrine changes
- Frailty
Sarcopenia

• Total body protein = muscle + visceral
  – Declines with age, faster after 65 yrs
• Major contributor is disuse atrophy
Sarcopenia

Protein

• Inadequate protein & calories
• ↑ body fat masks sarcopenia
• Sarcopenia in NHANES > 60 yrs
  – 10 % women
  – 7 % men
Aging of skeletal muscle

![Graph showing aging of skeletal muscle]

- Total Thigh
- All MM
- Extensors
- Flexors

- 1985
- 1997
### Nutritional components of frailty in selected studies

<table>
<thead>
<tr>
<th>Study/cohort</th>
<th>Nutrition criteria</th>
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</thead>
<tbody>
<tr>
<td>Women’s Health &amp; Aging Study</td>
<td>BMI &lt;18.5; 10% wt loss since age 60; overweight associated with prefrailty</td>
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<tr>
<td>Cardiovascular Health Study</td>
<td>wt loss &gt;10 pounds in past yr</td>
</tr>
<tr>
<td>Women’s Health Initiative</td>
<td>wt loss &gt;5% or self reported loss of &gt;5 lb</td>
</tr>
<tr>
<td>inChIANTI Study</td>
<td>wt loss: 4.5 kg in past yr</td>
</tr>
<tr>
<td>Canadian Study of Health and Aging</td>
<td>cooking, GI problems ADL</td>
</tr>
<tr>
<td>Zutphen &amp; SENECA Studies</td>
<td>wt loss 6% or more in 4–5 yrs, low BMI</td>
</tr>
<tr>
<td>EPIDOS</td>
<td>shopping, cooking</td>
</tr>
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</table>
Exercise Interventions

Why

• Muscle mass and strength ↓ with age, more so in frail
• Benefits even the frailest
• Improves mobility, ADL, gait, fewer falls, ↑BMD, improves well being
Nursing Home (NH) Residents

Randomized, placebo-controlled trial of progressive resistance exercise training, multinutrient supplement, both, and neither in 100 frail NH residents over 10-wks
Exercise Results

NH Residents

• Age ≈ 87 yrs
• Resistance training
• ↑ muscle strength >100%
• ↑ LE muscle size 3%
• ↑ gait velocity 12%
• ↑ mobility
• ↑ spontaneous activity
Home Based Frail

• **Frail:**
  – Fails chair rise
  – Long 3 min walk

• **Intervention:** 6 mo home-based PT to improve function, balance, muscle strength, transfers and mobility vs control education program.

• **Outcome:** change in composite function score at 3, 7 & 12 months. Intervention significantly slowed functional decline
Sarcopenia and Hip Fracture Study:

- 5-year prospective cohort study
- Persons admitted to 3 Sydney hospitals for hip fracture.
- 193 participants enrolled
- 71% of participants were sarcopenic, 58% undernourished, and 55% vitamin D deficient.
- Poorer nutrition & walking endurance, greater pre-fracture disability and inactivity predicted ↑ length of hospital stay
Interventions: CGA, VA

- Inpatient CGA improves functional outcomes
- Outpatient CGA improves mental health
- Neither affect survival
- No increase in cost
CGA: Medicare Population

- ≥ 70 yrs at risk for hospital admission
- Experimental less likely than controls to:
  - Lose functional ability
  - Have restrictions in ADLs
  - Have depression
  - Use HHC services
- Mortality, and total Medicare payments did not differ. The intervention cost $1,350 per person.

CONCLUSION:

- Targeted outpatient GEM slows functional decline.
Complex Interventions: meta-analysis

- Trials of 97,984 people.
- Interventions reduced risk of not living at home, NH admission hospital admissions and falls but not death, and physical function was better.
- Benefit for any specific type or intensity of intervention was not noted. In populations with increased death rates, interventions were associated with reduced nursing-home admission.
- Interpretation Complex interventions help elderly people live safely and independently, and could be tailored to meet individuals’ needs and preferences.
- Lancet 2008
Pharmacotherapy: DHEA

- 280 healthy ambulatory and independent people 60-80 yrs.
- Results: The results give evidence that DHEA administration restores DHEA to the normal range for adults 20-50 years. However, no positive effect inherent to DHEA was observed on muscle strength cross-sectional areas.
- Conclusions: Correcting the deficit of DHEA does not induce beneficial effects on muscle. The conditions in which DHEA could contribute to muscle strength and morphology still need to be determined.
Pharmacotherapy: Ace-Inhibitors

- Hypothesis: (ACE) inhibitors reduce morbidity, mortality, number of admissions, and decline in physical function and exercise capacity in patients with congestive HF
- Population: WHA Study
- 3-year rates of decline in knee extensor strength & walking speed continuous ACE inhibitor users was less than in intermittent users (p=0.015), and never users of antihypertensive drugs (p=0.001).
- **Interpretation** ACE inhibitor Rx may halt or slow decline in muscle strength in elderly women with hypertension and without CHF.
Hormones?

• Testosterone ↑ muscle mass & strength in hypo and eugonadal men, especially with exercise

• But affects lipids, and ± prostate size.

• Hormones not recommended for frail unless clearly deficient