Update on Frailty

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Agenda

• What is frailty? Overlap with sarcopenia, slow walking and multimorbidity
• Frailty markers as clinical prognostic indicators
• Causes
• Treatment
• Gaps and next steps
Clinical Case

You provide care for an 84 year old previously independent woman who is recovering from pneumonia. During her illness, she lost weight and is very weak. With efforts at nutritional supplementation and rehabilitation, she is now able to perform basic ADL including walking around her room, but is limited in IADL and tires easily.

Does she have frailty?
What might you do about it?
What is frailty?

Overlap with sarcopenia, slow walking and multimorbidity.
What is frailty?

- Loss of physiological reserve
- Intolerance to stress
- Multiple system declines
- Prevalence increases with age
- Associated with increased risk of disability, hospitalization and mortality
Frailty and Function

• There is a high concordance between disability and frailty although exceptions exist.
• It is reasonable to assume that most people with ADL disability are intolerant to physiological stress and have multiple organ system deficits. Most persons who have ADL disability should be treated as if they are likely to be intolerant to stress.
• Therefore, it is probably most helpful clinically to identify nondisabled persons who may be frail and might otherwise be missed.
The two main approaches to frailty

**Fried et al**
- Shared underlying biology
- Overlap with sarcopenia and decreased gait speed

**Rockwood et al**
- Cumulative burden independent of cause
- Overlap with multimorbidity

Cognition?
Frailty markers as clinical prognostic indicators
Sequence of screening procedures

- **Self report of function**: if disabled, they are probably frail and don’t need further testing for the presence of frailty
- **Performance screening**: to identify preclinical frailty
- **Physiological screening**: to detect covert early changes?

Future evaluations of frailty screens might consider using such a sequence instead of the same measure in everyone.
Measures of frailty

- Currently over 20 different scales have been published
- Most common are Fried, Rockwood and VES-13. Newer include brief self-reports and physical performance screens
- Most shown to predict adverse outcomes such as disability, utilization and death
- Most are developed for screening and detection not for measuring change over time
Frequency of use of domains and outcomes  

The Identification of Frailty: A Systematic Literature Review  
Shelley A. Sternberg, MD, MSCE,† Andrea Wershof Schwartz, MD, MPH,§ Sathya Karunanathan, MSc,§ Howard Bergman, MD,§ and A. Mark Clarfield, MD§

Figure 3. A. Prevalence of identifying factors for frailty in definitions and screening tools. B. Prevalence of outcomes of frailty predicted by definitions and screening tools. BMI = body mass index.
VES-13
derived from US survey
all self report

1. Age

   SCORE: 1 POINT FOR AGE 75-84
   3 POINTS FOR AGE ≥ 85

2. In general, compared to other people your age, would you say that your health is:
   □ Poor, *(1 POINT)
   □ Fair, *(1 POINT)
   □ Good,
   □ Very good, or
   □ Excellent

   SCORE: 1 POINT FOR FAIR or POOR

3. How difficulty, on average, do you have with the following physical activities:

   No Difficulty  A little Difficulty  Some Difficulty  A Lot of Difficulty  Unable to do

   a. stooping, crouching or kneeling? ..........  □  □  □  □  □
   b. lifting, or carrying objects as heavy as
      10 pounds? ...........................................  □  □  □  □  □
   c. reaching or extending arms above
      shoulder level? ........................................  □  □  □  □  □
   d. writing, or handling and grasping small
      objects? ...............................................  □  □  □  □  □
   e. walking a quarter of a mile? ...............  □  □  □  □  □
   f. heavy housework such as scrubbing floors
      or washing windows? .................................  □  □  □  □  □

   SCORE: 1 POINT FOR EACH * RESPONSE
   IN Q3a THROUGH f:  MAXIMUM OF 2 POINTS

4. Because of your health or a physical condition, do you have any difficulty:

   a. shopping for personal items (like toilet items or medicines)?
      □ YES → Do you get help with shopping?  □ YES * □ NO
      □ NO
      □ DON'T DO → Is that because of your health?  □ YES * □ NO
   b. managing money (like keeping track of expenses or paying bills)?
      □ YES → Do you get help with managing money?  □ YES * □ NO

   e. walking across the room? USE OF CANE OR WALKER IS OK.
      □ YES → Do you get help with walking?  □ YES * □ NO
      □ NO
      □ DON'T DO → Is that because of your health?  □ YES * □ NO

   d. doing light housework (like washing dishes, straightening up, or light cleaning)?
      □ YES → Do you get help with light housework?
      □ NO
      □ DON'T DO → Is that because of your health?  □ YES * □ NO

   e. bathing or showering?
      □ YES → Do you get help with bathing or showering?
      □ NO
      □ DON'T DO → Is that because of your health?  □ YES * □ NO

   SCORE: 4 POINTS FOR ONE OR MORE *
   RESPONSES IN Q4a THROUGH Q4e

- Self reported ADL, IADL and limitations
- Diseases and conditions don’t add
Sample with low prevalence of sarcopenia
SARC-F is specific but not sensitive
Clinical Global Impressions of Change in Frailty (CGIC-F)

• While frailty is considered an easily recognized geriatric syndrome, it is difficult to characterize and has been defined in many ways.
• As interventions to prevent or treat frailty are devised, outcome measures that capture meaningful change in its manifestations over time must be developed.
• Meaningful change should be based on clinical anchors. One form of anchor is a clinician’s global impression of change (CGIC). The concept of structured clinical judgment as a foundation for meaningful measurement, pioneered by Alvan Feinstein, emphasizes the need to integrate clinical meaning with traditional measurement properties.
• An advantage of a CGIC is its face validity as an indicator of how treatment decisions are made in the real world. The clinician integrates the patient’s opinion, the medical findings, the course of events, and clinical experience into a decision about whether treatment is helpful, should be continued or should be offered to other similar cases.
Clinical Global Impressions of Change in Physical Frailty

Based on focus groups with patients, families and providers

**intrinsic** (impairments and limitations n=6)
- strength
- balance
- stamina
- mobility
- nutrition
- psychomotor speed

**all** (intrinsic + consequences n=13)
- general appearance
- global self-reported health
- functional status
- disease activity
- health care utilization
- social roles
- mental health

Studenski et al JAGS 2004
Methods

The provider interviews and examines the patient and takes notes in recommended domains. On follow up, the provider again interviews and examines the patient, takes notes and then provides assessment of the magnitude and direction of change. Provider can identify the domains that most influenced his or her assessment of change.

Global impression scale (SCORE 1-7)

1 = marked improvement
4 = no change
7 = marked worsening

Definitions are based on a concept of provider decision making. The provider is asked how the observed change would affect his or her assessment of the effectiveness of a hypothetical care plan.

eg 1= the provider care plan has shown substantial benefit
   3 = the care plan has detectable benefit but may need to increase intensity or add other interventions
   5 = the care plan has detectable worsening, would consider modifying plan
   7= the care plan has clearly failed and the patient is much worse
Results: Participants

- Consented: geriatricians N=20 patients N = 237
- Censored by 6 months: 22
  - 8 died
  - 10 changed provider
  - 4 withdrew
- age: mean 80 years (range 65-98)
- gender: 76% female
- ethnicity: 13% African American
Factors that Influenced Geriatrician’s Rating at 6 Months

20 geriatricians following 237 of their primary care patients

<table>
<thead>
<tr>
<th></th>
<th>CGIC-PF Intrinsic</th>
<th>CGIC-PF All</th>
</tr>
</thead>
<tbody>
<tr>
<td>domain</td>
<td>frequency</td>
<td></td>
</tr>
<tr>
<td>mobility</td>
<td>75%</td>
<td>65%</td>
</tr>
<tr>
<td>stamina</td>
<td>57%</td>
<td>42%</td>
</tr>
<tr>
<td>strength</td>
<td>36%</td>
<td>36%</td>
</tr>
<tr>
<td>balance</td>
<td>26%</td>
<td>35%</td>
</tr>
<tr>
<td>nutrition</td>
<td>17%</td>
<td>34%</td>
</tr>
<tr>
<td>neuromotor</td>
<td>17%</td>
<td>30%</td>
</tr>
</tbody>
</table>
Baseline factors predicting change vs no change in frailty

• **Improvement** (score 1-2) (n=12)
  - Shorter Stroop time
  - Less apathy
  - More resilience

• **Worsening** (score 6-7 n=22)
  - SF36 (worse baseline PFI, physical role, emotion, pain)
  - More disability
  - Slower peg time
  - Longer Stroop time
Change in gait speed showed strongest relationship with physician impression of change in frailty
Frailty and gait speed
Gait Speed and Survival: Forest Plot and Pooled Survival Nomograms

Median survival for age and gender at about 0.8 m/sec

Consortium analysis of over 34,000 older adults followed for up to 21 years

<table>
<thead>
<tr>
<th>Men</th>
<th>% alive at 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Women</th>
<th>% alive at 10 years</th>
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</table>

Speeds of 1.0 m/sec or higher suggest healthy aging

CHS (22 [1991])
EPESE (23 [2005])
Health ABC (11 [2009], 12 [2006])
HEPSE (13 [1995])
InChianti (20 [2000])
MoCO (27 [2005])
NHANES III (21 [2004])
PEP (26 [2003])
SOF (26 [1995])
Pooled (Random Effects)
Pooled (Frailty)
Gait Speed in Hospitalized Older People

Inability to walk or slow walking on hospital admission predicts increased LOS and decreased probability of discharge to home. These effects are independent of functional status.
Gait Speed and risk of cardiac surgery

Gait speed alone did as well as 30+ factor risk score
Both together were better than either alone

5 meter walking speed dichotomized at 6 sec= about 0.83 m/sec

PostOP Morbidity= stroke, renal failure, prolonged ventilation, deep infections or need for reoperation

Surgical risk score with > 30 factors

Table 3. Risk List of Candidate Variables and Coding for STS Risk Model

<table>
<thead>
<tr>
<th>Candidate Variables</th>
<th>Coding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous variables</td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>Linear spline with knots at 50 and 65.</td>
</tr>
<tr>
<td>Ejection fraction*</td>
<td>Linear values &gt; 0.5 are mapped to 0.5. Only 6.9% of patients have ejection fraction &lt; 0.5, and that is presumed to be a data entry error; these values are considered censored and are treated like missing data. The decision to truncate values &gt; 0.5 was based on initial exploratory analysis in which data were used to suggest the functional form of continuous variables. Qualitative polynomial modeled separately for males and females. Note: body surface area &lt; 1.4 and &gt; 2.6 were mapped to these values, respectively.</td>
</tr>
<tr>
<td>Body surface area*</td>
<td>Linear spline with knots at 1.4 and 2.6. Only 5% of patients on data list have body surface area &lt; 1.4. Qualitative polynomial was used to map these values, respectively.</td>
</tr>
<tr>
<td>Calcium*</td>
<td>Linear spline with knots at 9.0 and 10.0. Only 0.1% of patients on data list have calcium &lt; 9.0. Qualitative polynomial was used to map these values, respectively.</td>
</tr>
<tr>
<td>Time trend*</td>
<td>Ordinal categorical variable with quartile category for each 4-month harvest interval.</td>
</tr>
<tr>
<td>Binary variables</td>
<td></td>
</tr>
<tr>
<td>Diabetes*</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Preoperative atherosclerosis*</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Shock</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Female*</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Intravenous diuresis treatment*</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Percutaneous coronary intervention ≥ 4 branches</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Preoperative intra-aortic balloon pump or intrapericardial balloon</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Pulmonary vascular disease</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Unstable angina (no myocardial infarction &lt; 7 days)</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Left main disease</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td>Defined at ≥ 2+ moderate (moderate)</td>
</tr>
<tr>
<td>Mitral insufficiency</td>
<td>Defined at ≥ 2+ moderate (moderate)</td>
</tr>
<tr>
<td>Tricuspid insufficiency</td>
<td>Defined at ≥ 2+ moderate (moderate)</td>
</tr>
<tr>
<td>Categorical variables</td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>4 groups: (1) none, (2) mild, (3) moderate, (4) severe</td>
</tr>
<tr>
<td>CVD/CVA</td>
<td>3 groups: (1) no CVD, (2) CVD or CVA, (3) CVD + CVA</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3 groups: (1) insulin-dependent, (2) insulin-resistant, (3) other or undetermined</td>
</tr>
<tr>
<td>Number diseased coronary vessels</td>
<td>5 groups: (1) none, (2) 1 diseased vessel, (3) 2 diseased vessels, (4) 3 diseased vessels, (5) none, in patients who did not have any previous CABG surgery, CABG surgery, or PTCA</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>4 groups: (1) 0 days, (2) 4 days, (3) 7 days, (4) &gt; 21 days</td>
</tr>
<tr>
<td>Renal</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Status</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Previous coronary artery operations</td>
<td>4 groups: (1) no prior CABG, (2) prior CABG, (3) prior PCI, (4) other operation</td>
</tr>
<tr>
<td>CHF and NYHA class</td>
<td></td>
</tr>
<tr>
<td>Interactions</td>
<td></td>
</tr>
<tr>
<td>Age by sex interaction*</td>
<td></td>
</tr>
<tr>
<td>Age by angina status*</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Incremental Value of Gait Speed Above the STS Risk Score to Predict Mortality or Major Morbidity

<table>
<thead>
<tr>
<th>Variables Entered in Model</th>
<th>Model Without Gait Speed</th>
<th>Model With Gait Speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS risk score</td>
<td>1.06 (1.02-1.11)</td>
<td>1.05 (1.004-1.10)</td>
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<td>Model performance</td>
<td>3.05 (1.23-7.54)</td>
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<td>STS risk score</td>
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<td>1.05 (1.004-1.10)</td>
</tr>
<tr>
<td>Gait speed</td>
<td>0.70 (0.60-0.80)</td>
<td>0.74 (0.64-0.84)</td>
</tr>
<tr>
<td>Model performance</td>
<td>3.05 (1.23-7.54)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 4. Mortality or Major Morbidity According to Gait Speed and the STS Risk Score

The data was restricted to one gait speed (1 s to make 5 m) and high Society of Thoracic Surgeons (STS) score (14+). The predicted mortality or major morbidity identified patients at the highest risk, among those with the slowest mobility. 43.2% experienced a major morbidity or mortality compared with only 5.5% of those with either risk factor.
New Utility for an Old Tool
Can a Simple Gait Speed Test Predict Ambulatory Surgical Discharge Outcomes?

ABSTRACT

TABLE 2 Predicting the likelihood of early home discharge readiness (≤90 mins)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.007 (0.99–1.02)</td>
<td>1.01 (0.99–1.03)</td>
</tr>
<tr>
<td>Preoperative heart rate</td>
<td>1.007 (0.99–1.02)</td>
<td>1.02 (1.008–1.04)</td>
</tr>
<tr>
<td>Preoperative gait speed</td>
<td>1.92 (0.80–4.72)</td>
<td>3.70 (1.21–11.26)</td>
</tr>
<tr>
<td>Postoperative pain</td>
<td>1.02 (0.97–1.07)</td>
<td>1.01 (0.96–1.08)</td>
</tr>
</tbody>
</table>

Area under the curve for the model = 0.78 (95% CI, 0.74–0.82).
For a 0.1 unit change in gait speed, the OR of early discharge was 1.14 (1.02–1.27).
Surgical risk was categorized as major intervention vs. minor intervention. Minor intervention was defined as all of the following: surgery duration of less than 1 hr, expected blood loss of less than 500 ml, and no opening of visceral cavity (except in case of diagnostic laparoscopic procedures). Major intervention was defined as any of the following: duration of procedure of 1 hr or longer, expected blood loss of 500 ml or more, opening of visceral cavity, and potential massive respiratory or hemodynamic effects as a result of surgery.

Model was adjusted for sex (P = 0.07), anesthesia technique (P = 0.14), surgical risk (P = 0.8), preoperative mean arterial pressure (P = 0.001), and comorbidity status (P = 0.02).
OR indicates odds ratio.

TABLE 4 Likelihood of unplanned admissions based on gait speed cut-off of 1 m/sec.

<table>
<thead>
<tr>
<th>Gait Speed, m/sec</th>
<th>n (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>422 (70)</td>
<td>Reference</td>
</tr>
</tbody>
</table>
| ≥1                | 180 (30) | 0.35 (0.16–0.76)

*Results of 2 analyses.

bP = 0.008; positive predictive value = 85.9 (95% CI, 74.2–93.7); negative predictive value = 31.6 (95% CI, 27.7–35.7).

602 patients undergoing elective ambulatory surgery
Outcomes: ready for home discharge within 90 minutes after surgery and admission

After ambulatory surgery, pre-op gait speed predicted rapid discharge and need for hospitalization
Gait Speed and Hemodialysis

> 750 hemodialysis patients from the US Renal Data System.

Table 4. One-Year Outcomes by Baseline Gait Speed Category

<table>
<thead>
<tr>
<th>Outcome</th>
<th>0.6–0.8 m/s (n = 169)</th>
<th>0.8–1.0 m/s (n = 181)</th>
<th>≥1.0 m/s (n = 169)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>New hospitalization No. (%)</td>
<td>62 (36.5)</td>
<td>95 (52.5)</td>
<td>63 (37.3)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>2.04 (1.19 to 3.49)</td>
<td>2.05 (1.30 to 3.25)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>ADL difficulty reported No. (%)</td>
<td>21 (18.3)</td>
<td>18 (10.1)</td>
<td>8 (4.8)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>3.88 (1.46 to 10.33)</td>
<td>2.11 (0.82 to 5.42)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>SF-36 PF score Mean ± SD</td>
<td>44.8 ± 29.4</td>
<td>59.7 ± 26.5</td>
<td>73.3 ± 24.6</td>
</tr>
<tr>
<td>Estimates (95% CI)</td>
<td>-8.21 (-13.57 to -2.82)</td>
<td>-4.01 (-8.45 to 0.43)</td>
<td>1.00 (reference)</td>
</tr>
</tbody>
</table>

Am J Kidney Disease 2015

One and two year mortality lowest in faster walkers

Hospitalization and disability lowest in faster walkers
Gait Speed and Formal Caregiving Demand

Among older adults receiving home and community based services (n=42), gait speed predicted hours of caregiving. Recommends physical performance measures in community programs for frail seniors to help anticipate resource demands.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unstandardized beta</th>
<th>t value</th>
<th>p value</th>
<th>R</th>
<th>R^2</th>
<th>Change in R^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td></td>
<td></td>
<td></td>
<td>.402</td>
<td>.161</td>
<td>.161</td>
</tr>
<tr>
<td>Age</td>
<td>.08</td>
<td>.63</td>
<td>.52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>4.18</td>
<td>2.13</td>
<td>.04*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-4.80</td>
<td>-1.78</td>
<td>.08</td>
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<tr>
<td>Step 2</td>
<td></td>
<td></td>
<td></td>
<td>.445</td>
<td>.198</td>
<td>.036</td>
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<tr>
<td>Age</td>
<td>-.13</td>
<td>-.96</td>
<td>.35</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>3.04</td>
<td>1.61</td>
<td>.12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-.280</td>
<td>-1.05</td>
<td>.30</td>
<td></td>
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<tr>
<td>Grip strength</td>
<td>-.22</td>
<td>-1.30</td>
<td>.20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td></td>
<td></td>
<td></td>
<td>.600</td>
<td>.360</td>
<td>.162*</td>
</tr>
<tr>
<td>Age</td>
<td>-.19</td>
<td>-1.35</td>
<td>.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>3.04</td>
<td>1.63</td>
<td>.11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-1.14</td>
<td>-.40</td>
<td>.69</td>
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<tr>
<td>Grip strength</td>
<td>-.22</td>
<td>-1.40</td>
<td>.17</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Gait speed</td>
<td>-8.62</td>
<td>-2.57</td>
<td>.02*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TUG</td>
<td>.04</td>
<td>.86</td>
<td>.40</td>
<td></td>
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</tr>
</tbody>
</table>

TUG: Timed Up and Go.

*p < .05.
Frailty as Tested by Gait Speed is an Independent Risk Factor for Cirrhosis Complications that Require Hospitalization

*Am J Gastroenterol* 2016;

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**OBJECTIVES:** Frailty is a known risk factor for major liver transplant complications, deaths, and waitlist attrition. Whether frailty indicates risk for adverse outcomes in cirrhosis short of lethality is not well defined. We hypothesized that clinical measurements of frailty using gait speed and grip strength would indicate the risk of subsequent hospitalization for the complications of cirrhosis.

**METHODS:** We assessed frailty as gait speed and grip strength in a 1-year prospective study of 373 cirrhotic patients evaluated for or awaiting liver transplantation. We determined its association with the outcome of subsequent hospital days/100 days at risk for 7 major complications of cirrhosis. We tested potential covariate influences of Model for Endstage Liver Disease (MELD) and Child-Turcotte-Pugh (CTP) scores, age, sex, height, depression, narcotic use, vitamin D deficiency, and hepatocellular carcinoma using multivariable modeling.

**RESULTS:** Patients experienced 2.14 hospital days/100 days at risk, or 7.81 days/year. Frailty measured by gait speed was a strong risk factor for hospitalization for all cirrhosis complications. Each 0.1 m/s gait speed decrease was associated with 22% greater hospital days (P<0.001). Grip strength showed a similar but nonsignificant association. Gait speed remained independently significant when adjusted for MELD, CTP, and other covariates. At hospital costs of $4,000/day, patients with normal 1 m/s gait speed spent 6.2 days and $24,800/year; patients with 0.5 m/s speed spent 21.2 days and $84,800/year; and patients with 0.25 m/s speed spent 40.2 days and $160,800/year.

**CONCLUSIONS:** Frailty as measured by gait speed is an independent and potentially modifiable risk factor for cirrhosis complications requiring hospitalization. The potential clinical value of frailty measurements to help define such risk merits broader evaluation.
Diagnosis of dismobility for gait speed < 0.6

Increase clinical awareness

Begin to allow for coding in inpatient and outpatient records

Allow for evaluation of utility in care planning

Evaluate intervention effects
Sarcopenia and Frailty
What is sarcopenia?

Originally defined as low muscle mass associated with aging with the assumption that the low mass caused functional problems due to weakness

(Baumgartner, Rosenberg, Janssen)
What should the term “Sarcopenia” refer to?

- NOT to weakness without low mass
- Should there be a general term for weakness and low mass? (“muscle wasting disease”, “myopenia”, “skeletal muscle function deficit”)
- Among the causes of weakness and low mass (cachexia, inactivity, denervation, aging), which are included in “sarcopenia”?
- **ICD-10 proposal** defines primary age-related sarcopenia and sarcopenia secondary to another condition

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**Classification by aetiology**
- due to Cancer
- due to Chronic heart failure (CHF)
- due to Chronic kidney disease (CKD)
- due to Chronic obstructive pulmonary disease (COPD)
- due to Neuromuscular diseases *
- due to Chronic infection
- due to Ageing / Senescence (Sarcopenia)
- due to Multi-morbid disease processes **
- due to Metabolic disease associated disease processes **
  * including neuropathies, disorders of the neuromuscular junction, myopathies and muscular dystrophies
  ** these forms of MWD may also be considered sarcopenia or sarcopenia-like disease

**Classification by disease severity & progression**
- Mild MWD ± frailty
- Moderate MWD ± frailty (pre-cachexia)
- Severe MWD (with cachexia) ***

*** Advanced MWD associated with weight loss and with loss of fat tissue resulting in frank cachexia and is typically associated with frailty

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Fig. 1 Framework for the suggested classification of muscle wasting disease by disease etiology and disease progression

Anker et al J Cachexia Sarcopenia Muscle 2014
Sarcopenia Screening and Diagnosis: Proposed Criteria

**EWGSOP Cruz-Jentoft Age and Aging 2010**

- Three stages: **presarcopenia** (low mass), **sarcopenia** (low mass plus low strength OR performance), **severe sarcopenia** (all three low)

**Mass**: DXA ASM/ht\(^2\) 7.2xkg/m\(^2\) men
5.6kg/m\(^2\) women (alternatives with residuals for fat, BIA, total mass)

**Strength**: grip strength <30kg men, <20kg women (several alternatives)

**Performance**: gait speed < .8m/sec (alternatives several gait speed and SPPB thresholds)

**IWG Morley JAMDA 2011**

- Consider **Sarcopenia** dx in: observed decline in physical function, strength or overall health, especially in bed ridden, can’t rise independently from chair or gait speed < 1.0 m/sec (perhaps also recurrent falls, reports mobility difficulty, weight loss, post hospitalization, certain chronic conditions)

- **Dx**: performance: gait speed < 1.0 m/sec and mass: DXA ASM/ht\(^2\) men< 7.23 kg/m\(^2\), women 5.61 kg/m\(^2\)

- Recommends search for better reference values, evaluate role of fat, considers other DXA and BIA indicators

- **Does not recommend strength measures**
FNIH sarcopenia project >27,000 older adults
Studenski et al JGMS 2014

Grip Strength Cut-points

Figure 2
BMI adjusted Lean Body Mass

**Men**

- $N=7582$
  - Prevalence of weakness (grip strength <26 kg): 4.3%

  - $ALM_{\text{standardizedBMI}} < 0.789$
    - $N=1531$
      - Prevalence of weakness (grip strength <26 kg): 11.8%
    - LOW LEAN MASS

  - $ALM_{\text{standardizedBMI}} \geq 0.789$
    - $N=6051$
      - Prevalence of weakness (grip strength <26 kg): 2.4%

**Women**

- $N=3688$
  - Prevalence of weakness (grip strength <16 kg): 19.2%

  - $ALM_{\text{standardizedBMI}} < 0.512$
    - $N=617$
      - Prevalence of weakness (grip strength <16 kg): 31.0%
    - LOW LEAN MASS

  - $ALM_{\text{standardizedBMI}} \geq 0.512$
    - $N=3071$
      - Prevalence of weakness (grip strength <16 kg): 16.8%

  - $BMI < 23.7$
    - $N=2048$
      - Prevalence of weakness (grip strength <16 kg): 12.0%

  - $BMI \geq 23.7$
    - $N=1023$
      - Prevalence of weakness (grip strength <16 kg): 24.2%
There is a negative association between lean mass and walking speed in women: Is this an effect of adipose tissue that is sex-specific?
ALM/BMI shows strong cross-sectional relationships with function

Table 2. Risk Factor-Adjusted Logistic Regression Displaying the Association of Low Lean Mass According to the Criteria Low ALM/Height\textsuperscript{2} and Low ALM\textsubscript{tot} With Self-Reported Physical Limitations

<table>
<thead>
<tr>
<th>Moderate/Severe Self-Reported Limitations in...</th>
<th>Low ALM/Height\textsuperscript{2}</th>
<th>Low ALM\textsubscript{tot}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exhauting activities</td>
<td>1.086 (0.807-1.462)</td>
<td>2.035 (1.830-4.371)</td>
</tr>
<tr>
<td>Lifting or carrying</td>
<td>1.116 (0.825-1.499)</td>
<td>1.588 (1.041-2.332)</td>
</tr>
<tr>
<td>Climbing several flights of stairs</td>
<td>0.973 (0.709-1.357)</td>
<td>2.068 (1.449-2.951)</td>
</tr>
<tr>
<td>Kneeling and bending</td>
<td>0.728 (0.537-0.987)</td>
<td>1.525 (1.080-2.134)</td>
</tr>
<tr>
<td>Walking (&gt;1 km)</td>
<td>0.659 (0.406-1.071)</td>
<td>2.002 (1.243-3.148)</td>
</tr>
<tr>
<td>Bathing and dressing</td>
<td>0.537 (0.254-1.11)</td>
<td>2.937 (1.598-5.360)</td>
</tr>
</tbody>
</table>

Notes: Logistic regression adjusted for age, sex, and comorbidities (presence of COPD, CKD, CAD, CHF, hypertension, diabetes, and depressive symptoms). ALM = appendicular lean mass, BMI = body mass index, CAD = coronary artery disease, CHF = congestive heart failure, CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease; OR = odds ratio.

Table 3. Risk Factor-Adjusted Logistic Regression Displaying the Association of Low Lean Mass According to the Criteria Low ALM/Height\textsuperscript{2} and Low ALM\textsubscript{tot} With Frailty Status

<table>
<thead>
<tr>
<th>Frailty Criteria</th>
<th>Low ALM/Height\textsuperscript{2}</th>
<th>Low ALM\textsubscript{tot}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>1.245 (0.472-3.269)</td>
<td>0.443 (0.094-1.970)</td>
</tr>
<tr>
<td>Exhaution</td>
<td>0.881 (0.533-1.452)</td>
<td>1.451 (0.819-2.572)</td>
</tr>
<tr>
<td>Wrenching</td>
<td>1.185 (0.587-2.343)</td>
<td>4.836 (2.584-9.256)</td>
</tr>
<tr>
<td>Slow walking speed</td>
<td>1.239 (0.775-1.980)</td>
<td>1.661 (1.000-2.738)</td>
</tr>
<tr>
<td>Low physical activity</td>
<td>0.800 (0.477-1.344)</td>
<td>2.094 (1.283-3.414)</td>
</tr>
<tr>
<td>Prefrail frail</td>
<td>0.997 (0.722-1.376)</td>
<td>2.401 (1.670-3.453)</td>
</tr>
</tbody>
</table>

Notes: Logistic regression adjusted for age, sex, and comorbidities (presence of COPD, CKD, CAD, CHF, hypertension, diabetes, and depressive symptoms). ALM = appendicular lean mass, BMI = body mass index, CAD = coronary artery disease, CHF = congestive heart failure, CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease; OR = odds ratio.
Sarcopenia and Disease
wasting/adiposity

Wasting
• COPD-emphysema
• Dialysis
• Cancer-late
• Systolic heart failure
• Ischemic peripheral vascular disease

Adiposity
• COPD- airway disease
• Diastolic heart failure
• Diabetes
• Metabolic syndrome
Physiological Aging: Links Among Adipose Tissue Dysfunction, Diabetes, and Frailty

Michael B. Stout,1,2*, Jamie N. Justice,3*, Barbara J. Nicklas,2 and James L. Kirkland*  
1Department of Nutritional Sciences, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma; 2Raymond

SubQ and visceral fat, muscle and frailty

Physiology 2017

Review
Muscle function and fat content in relation to sarcopenia, obesity and frailty of old age — An overview
Assaf Buch a,b, Eli Carmeli a,c, Lilal Keinan Boker c, Yonit Marcus a,b, Gabi Shefer a,b, Ofer Kis a, Yitshal Berner b,d, Naftali Stern a,b

Adipose Tissue Dysfunction

Muscle Pathology

Motor Impairments

Physical Function Decline & Frailty

Senescent Cells & SASP

Insulin Resistance & Diabetes

Pro-inflammatory Cytokines

Young age = 20 years
Middle age = 50 years
Old age > 70 years

Fig. 3. Fat distribution in human body — demonstration (adapted from Cartwright MJ et al. (Cartwright et al. 2007)). This figure shows schematically the changes in muscle and fat mass morphology over time and the changes in the subtypes of fat. Yellow cells represent subcutaneous fat, red cells represent visceral fat, and yellow cells within muscle represent ectopic fat deposits. As can be seen, muscle mass is decreasing through 70 years, whereas fat mass (visceral and subcutaneous) increases in size until midlife. Older age is associated with decrease in subcutaneous fat (paralleled to the loss of lean body mass) and the emergence of ectopic fat in muscle (but also in other organs).
Challenges

• Sex differences in how body composition relates to physical function: generally sarcopenia is more clear in men
• Noncontractile proteins in lean mass estimates: old meat is tougher!!
  ❖ The role of nerve in muscle function
  ❖ The effect of somatotype/body habitus on risk and presentation of sarcopenia: should we evaluate the effect of change in lean mass rather than absolute mass on strength and function?
Frailty and multimorbidity
Organ system impairments and frailty

Systems: CV, **neuro**, endocrine, **kidney**, lung

<table>
<thead>
<tr>
<th>Physiological Index or Component</th>
<th>Mean ± Standard Deviation</th>
<th>Crude β</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiologic index (point)</td>
<td>4.5 ± 2.1</td>
<td>0.60; &lt; .001</td>
<td>0.23; &lt; .001</td>
</tr>
<tr>
<td>Separate model for each component</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carotid artery thickness (mm)</td>
<td>1.42 ± 0.56</td>
<td>0.23; &lt; .001</td>
<td>0.06; .14</td>
</tr>
<tr>
<td>White matter grade (unit)</td>
<td>2.19 ± 1.33</td>
<td>0.36; &lt; .001</td>
<td>0.15; &lt; .001</td>
</tr>
<tr>
<td>Serum fasting glucose (mg/dL)</td>
<td>106 ± 30</td>
<td>0.19; &lt; .001</td>
<td>-0.00; .99</td>
</tr>
<tr>
<td>Serum cystatin-C (mg/L)</td>
<td>1.10 ± 0.23</td>
<td>0.44; &lt; .001</td>
<td>0.21; &lt; .001</td>
</tr>
<tr>
<td>Forced vital capacity (L)</td>
<td>2.95 ± 0.88</td>
<td>-0.41; &lt; .001</td>
<td>-0.26; &lt; .001</td>
</tr>
<tr>
<td>All components in the same model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carotid artery thickness (mm)</td>
<td></td>
<td>0.14; .001</td>
<td>0.02; .001</td>
</tr>
<tr>
<td>White matter grade (unit)</td>
<td></td>
<td>0.25; &lt; .001</td>
<td>0.14; &lt; .001</td>
</tr>
<tr>
<td>Serum fasting glucose (mg/dL)</td>
<td></td>
<td>0.18; &lt; .001</td>
<td>0.01; .37</td>
</tr>
<tr>
<td>Serum cystatin-C (mg/L)</td>
<td></td>
<td>0.38; &lt; .001</td>
<td>0.19; &lt; .001</td>
</tr>
<tr>
<td>Forced vital capacity (L)</td>
<td></td>
<td>-0.38; &lt; .001</td>
<td>-0.25; &lt; .001</td>
</tr>
</tbody>
</table>

PI is associated with mortality, disability, slow gait speed and more rapidly declining gait speed

Sanders et al JGMS 2012
Rosso et al JGMS 2015

10 point frailty scale= 2 points for each element of the Fried frailty index
Treatment
Interventions for frailty

Medical:
- Stabilize subtle physiologic disruptions
- Geriatric Evaluation and Management
- Pharmacologic agents for appetite and muscle?

Nonmedical:
- Nutrition
- Exercise including “prehab” prior to aggressive interventions
Interventions for multimorbidity have modest impact

Interventions aimed at improving outcomes for people with multimorbidity compared with usual care

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Impacts</th>
<th>Number of studies</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical outcomes</td>
<td>There is no clear effect on clinical outcomes with a range of standardised effect sizes from 0.00 to 2.24 with 4 of 7 studies having moderate to large effect sizes (≥0.5). Standardised mean difference of −0.41 (95% CI, −0.63 to −0.20) was calculated from combining data from 8 studies.</td>
<td>11</td>
<td>Moderate</td>
</tr>
<tr>
<td>Mental health outcomes</td>
<td>There are improved depression-related outcomes in studies targeting comorbid conditions that include depression with a range of standardised effect sizes from 0.00 to 2.24 with 4 of 7 studies having moderate to large effect sizes (≥0.5). Standardised mean difference of −0.41 (95% CI, −0.63 to −0.20) was calculated from combining data from 8 studies.</td>
<td>9</td>
<td>High</td>
</tr>
<tr>
<td>Patient-reported outcome measures (PROMs)</td>
<td>There are mixed effects on 12 PROMs with only half of studies that reported those outcomes showing any benefit with a range of standardised effect sizes from 0.03 to 1.7. Only 1 of 5 studies with available data on self-efficacy had a moderate effect size, 4 of 7 had a moderate effect size for HRQoL (≥0.5) and effect sizes for other psychosocial outcomes were generally low.</td>
<td>12</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Health Service Utilisation

- There were no effects on health service utilisation and changes in visits were difficult to interpret as some interventions could lead to higher numbers of visits if previous unmet need was being addressed. There was no difference in admission-related outcomes, though numbers of admissions in most of these studies were very small.
  - GRADE Working Group grades of evidence: High quality; Further research is very unlikely to change our confidence in the estimate of effect.

Medication use and adherence

- There are mixed effects on medication use and adherence with half the studies reporting this outcome showing benefit. Proportions adherent to medication were higher in intervention participants with ranges in absolute difference of 10% to 40% but all studies with available data had small effect sizes.
  - GRADE Working Group grades of evidence: Moderate; Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Health-related behaviours

- Studies measuring this outcome reported a range of effects varying from an additional 18 minutes spent walking per week to an absolute difference in kcal expenditure per week of 2516 (no studies presented data that could be used to calculate effect sizes).
  - GRADE Working Group grades of evidence: Moderate; Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Provider behaviour

- The majority of studies reporting provider behaviour indicated improved provider behaviour relating to care delivery; three studies reported a range of 15% to 40% in proportions of intervention providers improving behaviours such as appropriate referral.
  - GRADE Working Group grades of evidence: Moderate; Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.
# Interventions for Sarcopenia

more than increasing mass

<table>
<thead>
<tr>
<th></th>
<th>Muscle Quantity</th>
<th>Muscle Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Build new muscle</td>
<td>Reduce muscle breakdown</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vitamin D</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Orexigenics</strong></td>
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<tr>
<td><strong>Androgens</strong></td>
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<td></td>
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<tr>
<td><strong>SARMS</strong></td>
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<td><strong>GH/IGF-1 axis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anticytokines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Myostatin blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ACE inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neurotrophics</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Exercise</strong></td>
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</tbody>
</table>
Is there a critical role for movement?

- Exercise is the most effective way to increase strength, mobility, endurance and function
- Exercise may be the most effective way to build “quality” muscle
- Exercise helps minimize muscle mass loss with weight loss in obesity
- Resistance exercise is the best way to increase lean mass
- Exercise activates neural controls, may promote neuromuscular junction formation and possibly promote good cognition?
Gaps and next steps
The effect of somatotype/body habitus on risk and presentation of sarcopenia

• Should sarcopenia be about loss of lean mass rather than absolute lean mass?
• Does it matter where you start from?
• Does it matter where and how you add fat?
Summary

- Frailty has substantial overlap with slow gait, sarcopenia and multimorbidity.
- There are many ways to assess frailty: most work well to identify populations at increased risk of adverse outcomes.
- The most useful approach may vary by setting and population.
- Exercise, including aggressive “prehab” might be the most useful current approach and needs formal trials.
Clinical Case Resolution

• You provide care for an 84 year old previously independent woman who is recovering from pneumonia. During her illness, she lost weight and is very weak. With efforts at nutritional supplementation and rehabilitation, she is now able to perform basic ADL but is limited in IADL and tires easily.

• Does she have frailty or sarcopenia?
  ➢ Already has weight loss, fatigue and IADL deficits
  ➢ Evaluate walking speed, grip strength plus cognition and mood

• What might you do about it?
  ➢ Look for subtle ongoing correctable physiologic disruptions, sources of persistent inflammation
  ➢ Add resistance exercise?
  ➢ Vitamin D?
  ➢ Antidepressant?
"We may not have enough ice floes for the boomers."