Ups and Downs of Physical Function in Late Life

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WHI Investigators Meeting - May 4, 2017
Usual walking speed at different ages in Men (n = 711) and Women (n = 766) participants of the Baltimore Longitudinal Study of Aging.

Gait Speed Summary

0.139 m/s ↓ = 50 m shorter 6 min. walk
0.1 m/s difference = 12% mortality diff.
0.1 m/s Δ = lg. clinically significant diff.
0.05 m/s Δ = sm. clinically significant diff.

0.31 mph ↓ = 50 m shorter 6 min. walk
0.22 mph difference = 12% mortality diff.
0.22 mph Δ = lg. clinically significant diff.
0.11 mph Δ = sm. clinically significant diff.

1 m/s = 2.237 mph
1 mph = 0.447 m/s

Kritchevsky, 2014
Clinical Applications for Functional Assessment

– Indicator of Reserve
– Measure of Stress Resistance
– Prediction Therapeutic Response / The degree of recovery
– Measure of Biologic Age / Life or Health Expectancy
– An Explicit Goal of Care
Resilience Framework

Stressor

Initial (I)  →  Post-Recovery (P)

Nadir (N)

Point of No Return (D)
Geriatric assessment predicts survival for older adults receiving induction chemotherapy for acute myelogenous leukemia

Heidi D. Klepin,1 Ann M. Geiger,2 Janet A. Tooze,2 Stephen B. Kritchevsky,3 Jeff D. Williamson,3 Timothy S. Pardee,1 Leslie R. Ellis,1 and Bayard L. Powell1

BLOOD, 23 MAY 2013 · VOLUME 121, NUMBER 21

<table>
<thead>
<tr>
<th>GA scores</th>
<th>Median (25th, 75th)</th>
<th>% Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3MS (range 0-100, impairment &lt; 77)</td>
<td>85.0 (75.0, 91.0)</td>
<td>28.8</td>
</tr>
<tr>
<td><strong>Psychological function</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D (range 0-60, impairment &gt; 16)</td>
<td>11.0 (4.0, 21.0)</td>
<td>39.7</td>
</tr>
<tr>
<td>DT (range 0-10, impairment ≥ 4)</td>
<td>5.0 (2.0, 8.0)</td>
<td>58.9</td>
</tr>
<tr>
<td><strong>PF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAT-D* (range 1-5, impairment &gt; 1) at the time of treatment</td>
<td>1.4 (1.0, 1.8)</td>
<td>72.4</td>
</tr>
<tr>
<td>ADL subscale</td>
<td>1.0 (1.0, 1.4)</td>
<td>50.0</td>
</tr>
<tr>
<td>IADL subscale</td>
<td>1.0 (1.0, 1.7)</td>
<td>40.5</td>
</tr>
<tr>
<td>Mobility subscale</td>
<td>2.0 (1.0, 3.0)</td>
<td>68.9</td>
</tr>
<tr>
<td>PAT-D* 6-mo recall</td>
<td>1.1 (1.0, 1.3)</td>
<td></td>
</tr>
<tr>
<td>ADL subscale</td>
<td>1.0 (1.0, 1.0)</td>
<td>23.3</td>
</tr>
<tr>
<td>IADL subscale</td>
<td>1.0 (1.0, 1.0)</td>
<td>20.6</td>
</tr>
<tr>
<td>Mobility subscale</td>
<td>1.0 (1.0, 1.7)</td>
<td>41.1</td>
</tr>
<tr>
<td>SPPB (range 0-12, impairment &lt; 9)</td>
<td>8.5 (3.0, 10.0)</td>
<td>50.0</td>
</tr>
<tr>
<td><strong>Grip strength (kg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38.0 (32.0, 44.0)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>24.0 (22.0, 28.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCT-CI (impairment &gt; 1)</td>
<td>1.0 (0.0, 3.0)</td>
<td>41.9</td>
</tr>
</tbody>
</table>

For 3MS, SPPB, and grip strength, a higher score reflects better function. For CES-D, DT, PAT-D, and HCT-CI, a higher score reflects worse function.

ADL, Activities of Daily Living; DT, Distress Thermometer; HCT-CI, Hematopoietic Stem Cell Transplantation Comorbidity Index; IADL, Instrumental Activities of Daily Living; PAT-D, Pepper Assessment Tool for Disability.

*Results based on subjects with calculable survey scores (reported in Results section).

†Scores are based on 67 subjects who performed grip strength.
Table 3. Association between clinical characteristics, baseline GA measures, and OS among older adults with AML (N = 73)

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Hazard ratio for mortality (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical and demographic characteristics</strong></td>
<td>Unadjusted</td>
</tr>
<tr>
<td>Age (per 10-y change)</td>
<td>1.1 (0.7-1.7)</td>
</tr>
<tr>
<td>Education (reference &lt; high school)</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>0.8 (0.4-1.5)</td>
</tr>
<tr>
<td>High school</td>
<td>0.9 (0.4-2.0)</td>
</tr>
<tr>
<td>ECOG score (continuous)</td>
<td>1.5 (0.9-2.4)</td>
</tr>
<tr>
<td>Hemoglobin (continuous)</td>
<td>0.8 (0.7-1.0)</td>
</tr>
<tr>
<td>LDH (≥600)</td>
<td>0.5 (0.2-1.4)</td>
</tr>
<tr>
<td>White blood cell count (≥25 000)</td>
<td>0.8 (0.4-1.6)</td>
</tr>
<tr>
<td>Cytogenetic risk group (favorable/intermediate)</td>
<td>0.5 (0.3-0.8)</td>
</tr>
<tr>
<td>Prior MDS (not present)</td>
<td>0.5 (0.3-0.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GA measures</th>
<th>Hazard ratio for mortality (95% CI)</th>
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<tr>
<td>Cognitive impairment (3MS &lt; 77)</td>
<td>2.4 (1.3-4.4)</td>
</tr>
<tr>
<td>Depressive symptoms (CES-D score ≥16)</td>
<td>1.4 (0.8-2.5)</td>
</tr>
<tr>
<td>Distress (score &lt; 4)</td>
<td>1.2 (0.6-2.1)</td>
</tr>
<tr>
<td>IADL impairment (any at the time of treatment)</td>
<td>1.3 (0.7-2.2)</td>
</tr>
<tr>
<td>ADL impairment (any at the time of treatment)</td>
<td>1.3 (0.7-2.1)</td>
</tr>
<tr>
<td>Mobility impairment (any at the time of treatment)</td>
<td>1.4 (0.7-2.6)</td>
</tr>
<tr>
<td>Impaired physical performance (SPPB &lt; 9)</td>
<td>1.9 (1.1-3.4)</td>
</tr>
<tr>
<td>Comorbidity burden (HCT-CI &gt; 1)</td>
<td>1.5 (0.9-2.7)</td>
</tr>
</tbody>
</table>

One subject with missing cytogenetic risk group data was excluded.

ADL, activities of daily living; IADL, instrumental activities of daily living; LDH, lactate dehydrogenase.

*Adjusted model includes age, gender, ECOG performance status, cytogenetic risk group, prior MDS, and hemoglobin.
Gait Speed as an Stress Resistance Indicator

Figure 3 Predicted Probability of Mortality or Major Morbidity According to Gait Speed and the STS Risk Score Slow gait speed (solid circles) conferred a 2- to 3-fold increase in risk of Society of Thoracic Surgeons (STS) predicted outcomes

Outcome: post-op death, stroke, renal failure, prolonged ventilation, sternal wound infection, need for reoperation.

Jonathan Afilalo, Mark J. Eisenberg, Jean-François Morin, Howard Bergman, Johanne Monette, Nicolas Noiseux, ...

Gait Speed as an Incremental Predictor of Mortality and Major Morbidity in Elderly Patients Undergoing Cardiac Surgery
http://dx.doi.org/10.1016/j.jacc.2010.06.039
## Risk Factors can also be Health Status Indicators

<table>
<thead>
<tr>
<th>Factor</th>
<th>Risk factor (Cause)</th>
<th>Health Status (Sign)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>Hypertension</td>
<td>Hypertension &amp; Hypotension</td>
</tr>
<tr>
<td>LDL-C</td>
<td>Hypercholesterolemia</td>
<td>Hypocholesterolemia</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>Obesity</td>
<td>Weight Loss</td>
</tr>
<tr>
<td>Glucose</td>
<td>Hyperglycemia</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Inflammation</td>
<td>inflammation</td>
<td>inflammation</td>
</tr>
</tbody>
</table>

In older populations the conflation of cause and sign relationships makes risk factor interpretation difficult.
Functional Status and the Interpretation of the Risks Associated with Hypertension

**Functional Health and Presence or Absence of Disease**

Scale of Aging Vigor in Epidemiology (0-10):
Rescaling of the CHS/Fried frailty scale to include good performance

- **Expected agers** (n=3,528)
- **Prematurely Frail** (n=855)
- **Adapters** (n=882)
- **Comorbidities** (n=14)

Clinical disease & demographics explained 30% of SAVE variability

Figure 1. Kaplan-Meier cumulative death plot according to aging group over 20 years of follow-up.

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Figure 1. Kaplan-Meier cumulative death plot according to aging group over 20 years of follow-up.
The Patient’s Lived Experience

Focus of Geriatrics
- Systems of Organs
- Organs
- Cells

Focus of Subspecialty Medicine

What is slow gait a sign of?
- Restricted Life Space
- Fatigue
- Depression
- Self-Rated Health
- Pain
- IL-6
- Circulating Mito Resp. Capacity
- Cognitive Speed / Function
- VO2 Max
- White Matter Burden
- Low EGFR / High Cystatin C
- FEV1
- Anemia
- Cardiac Output
- Muscle perfusion
- Muscle strength
- Motor Units
- Capillary Density
- Type I : Type II Fiber Ratio
- Neuromuscular Junction
- Troponin Splice Variants
- Pain
- Cognition Speed / Function
- Restricted Life Space
- Fatigue
- Depression
- Self-Rated Health
- Anemia
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- Type I : Type II Fiber Ratio
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Functional Gains Don’t seem to be Following Gains in Life Expectancy

![Chart showing percentage of Medicare beneficiaries age 65 and over who have limitations in performing activities of daily living (ADLs) or instrumental activities of daily living (IADLs), or who are in a long-term care facility, selected years 1992-2013.]

NOTE: A residence is considered a long-term care facility if it is certified by Medicare or Medicaid; has three or more beds, is licensed as a nursing home or other long-term care facility, and provides at least one personal care service; or provides 24-hour, 7-day-a-week supervision by a caregiver. Limitations in performing activities of daily living (ADL) refer to difficulty performing (or inability to perform for a health reason) one or more of the following tasks: bathing, dressing, eating, getting in/out of chairs, walking, or using the toilet. Limitations in performing instrumental activities of daily living (IADL) refer to difficulty performing (or inability to perform for a health reason) one or more of the following tasks: using the telephone, light housework, heavy housework, meal preparation, shopping, or managing money. Percentages are age adjusted using the 2000 standard population. Estimates may not sum to the totals because of rounding.

Reference population: These data refer to Medicare beneficiaries.

SOURCE: Centers for Medicare & Medicaid Services, Medicare Current Beneficiary Survey, Access to Care.
Potential interventions to maintain function

- ACE inhibitors
- Albuterol
- ARBs
- Aspirin*
- Carnitine
- CoQ10
- Creatine
- Cytokine inhibitors
- DHEA
- Diet – high protein
- Diet – low calorie
- Diet - Mediterranean
- Erythropoietin
- Estrogens
- Growth hormone
- GH secretagogue
- Health education
- Metformin
- Myostatin inhibitors
- NSAIDs
- Pentoxiphylline
- Physical activity*
- Resveratrol
- SARMs
- Statins
- Testosterone
- Thalidomide
- Vitamin D / Vitamin E
Events

Physical Activity: 30.1% (n=246/818)
Health Education: 35.5% (n=290/817)

HR=0.82, 95%CI=0.69-0.98
P=0.03

Pahor et al JAMA 2014
Documented benefits of weight loss in older adults

- Even a small amount of weight loss (~7%) improves:

1) Aerobic endurance/stamina
2) Stair climbing and chair rise ability
3) Strength and Balance
4) Ability to perform daily activities
5) Arthritis and back pain
6) CVD Risk factors (BP, lipids)
7) Inflammation
8) Diabetes symptoms and risk
9) Quality of Life
10) Lifespan?
Meta-analysis of All-Cause Mortality in Trials of Intentional Weight Loss

<table>
<thead>
<tr>
<th>Study</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stamler (1987)</td>
<td>1.42 (0.238, 8.52)</td>
</tr>
<tr>
<td>Davis (1993)</td>
<td>2.03 (0.372, 11.11)</td>
</tr>
<tr>
<td>TOHP I (1992)</td>
<td>1.91 (0.120, 30.59)</td>
</tr>
<tr>
<td>TOHP II (1997)</td>
<td>1.40 (0.443, 4.40)</td>
</tr>
<tr>
<td>Knowler (2002)</td>
<td>0.60 (0.144, 2.52)</td>
</tr>
<tr>
<td>Shea (2010)</td>
<td>0.50 (0.269, 0.93)</td>
</tr>
<tr>
<td>Shea (2011)</td>
<td>0.93 (0.631, 1.38)</td>
</tr>
<tr>
<td>Gabriel (2011)</td>
<td>0.50 (0.046, 5.56)</td>
</tr>
<tr>
<td>Rejeski (2011)</td>
<td>0.97 (0.088, 10.70)</td>
</tr>
<tr>
<td>van Wier (2011)</td>
<td>0.99 (0.090, 10.96)</td>
</tr>
<tr>
<td>Wing (2013)</td>
<td>0.86 (0.705, 1.06)</td>
</tr>
<tr>
<td>Daumit (2013)</td>
<td>0.66 (0.114, 4.07)</td>
</tr>
<tr>
<td>Overall</td>
<td>0.85 (0.723, 1.00)</td>
</tr>
</tbody>
</table>

Kritchevsky et al., PLoS One; 2015 Mar 20: 10(3). Doi:10.1371/journal.pone.0121993
Closing Thoughts

• Interventions to test methods for preserving function need to be large.
• Interventions that train to the task work best.
• How do you scale exercise and diet interventions to allow their evaluation?