Understanding the link between Sarcopenia and Frailty

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Disclosure

☐ None
Learning objectives

- To understand
  - the physiological changes associated with aging leading to sarcopenia
  - the relationship between muscle mass, strength and physical function
  - measures of effective counteracting sarcopenia
Weight changes

○,△: American
●,▲: Canadian

Men

Women

Body Composition (women)

60 kg, 161 cm, BMI 23 kg/m²

Young:
- Muscle: 30%
- ECF: 20%
- Fat: 27%
- Bone: 15%
- Organs: 8%

Elderly:
- Muscle: 19%
- ECF: 20%
- Fat: 43%
- Bone: 11%
- Organs: 7%
Muscle mass maintenance in man

- Relative loss of MM ~ 50%
- Relative gain in FM ~ 84%
Body Composition Changes with Aging

MRI - mid thigh
Body Composition Changes with Aging

MRI - mid abdomen
Inter-relationship between muscle and fat tissues

- Aging
  - Muscle
  - BMR
- Exercise
  - Diet
  - Cytokines
  - Adiponectin
  - Leptin
  - TNF-α
  - IL-6
  - MCP-1

Nair KS 2005; Cesari M 2005; Schrager MA 2007
Sarcopenia: Origins and Clinical Relevance

Irwin H. Rosenberg
Jean Mayer Human Nutrition Research Center on Aging at Tufts University, Boston, MA

“... The Greek roots of the word are sarx for flesh and penia for loss. The term actually describes important changes in body composition and related functions. ...” (term originally proposed in 1988)

“... In fact, there may be no single feature of age-related decline more striking than the age-decline in lean body mass in affecting ambulation, mobility, energy intake, overall nutrient intake and status, independence and breathing. ...”

Sarcopenia

Nutrition & Dietary intake

Inactivity

CNS & PNS (loss of motoneurones)

Hormones GH, E₂, T

Cytokines IL-6, TNF-α

Weaknesses

↓ Metabolic Reserves

Disability, Morbidity, Mortality

Vandervoort AA 2002; Solomon AM 2006; Dreyer HC 2005; Szulc P 2004; Visser M 2002
Both the amount and the proportion of muscle mass decline with age.
Muscle mass versus muscle strength

Verdijk et al., unpublished
Importance of maintaining muscle mass

[Graph showing the changes in muscle mass and strength across different life stages: Early life (Growth and development to maximise peak), Adult life (Maintaining peak), and Older life (Minimising loss)]

Disability threshold

Environmental changes can lower the disability threshold

Rehabilitation and ensuring quality of life

Modified WHO/HPS, Geneva 2000
Muscle Tissues Age-related Changes

**Skeletal muscle fiber loss**
- 1/4 between 30 and 70 years
- type II > I

**Muscle fiber atrophy (type IIa et IIx)**

Subject
27 yrs old

Subject
77 yrs old

Effects of Aging on Skeletal Muscle

Muscle Mass

20-30     40-50     60-70     80-90

Age (years)

25 yrs

50 yrs

-10% per decade
External Causes and Skeletal Muscle Loss with Aging

- Hip Replacement
- Pneumonia
- Injury/Fall
Age-related decline in muscle strength

Maximal strength decline

- 1 to 1.5% / year between 50 & 60 yrs
- 2 to 3% / year after 60 yrs
- ++ isokinetic
- ++ concentric
- ++ lower limbs
- asymmetrical decline agonist / antagonist

Muscle loss versus strength loss

Ferrucci et al., J. Gerontology, 2012
Age-related decline in muscle power

**Muscle power** (strength $\times$ speed) **loss**
- 2 to 3 X more important than strength loss  
  Skelton DA 2002
- / \ contraction speed +++  
  De vito G. 1998, Macaluso A. 2004
- Functional impact +++  
  Rantanen T. 1997, Foldvari M. 2000
- Mobility - Risk of fall - Stair climbing - Sit-to-Stand

**Reduced muscle quality** (Muscle Strength / Muscle mass)
- Knee extension torque/leg lean mass: decreased with age and body fat  
- Strong relationship with muscle fat infiltration (Goodpaster BH 2006)

**Function is more than strength**
- It involves coordination, antagonizing muscles, balance...higher brain function (decision making, risk assessment, emotional state)
Relationship between CNS and muscle: the motor units (MU)

McNeil et al 2005
Sarcopenia - Definition

« Progressive and inevitable age-related skeletal muscle mass loss »
Evans W.J. 1995; Rosenberg I.H. 1997


MM Index = Appendicular skeletal MM (kg) / Height (m²)

Threshold: - 2SD < MMI in a reference young population

Prevalence: 10 to 24 % between 65 and 70 yrs
30 to 60 % > 80 yrs old

Sarcopenia associated with self-reported IADL disability (♂&♀) and balance abnormality and use of cane in ♂
Sarcopenia - Definition

Using Bioimpedance Analysis (BIA)

\[ SMI = \frac{SMM}{\text{Body mass}} \times 100 \]

Class I: 1 SD bellow young

Class II: 2 SD bellow young

Janssen I et al. JAGS 2002;50:889-96

Sarcopenia: associated with 2-4 greater functional impairment and disability vs. non-sarcopenic individuals

- In the absence of a reference young population by either DXA or BIA
  - Sarcopenia: lowest 2 quintiles of MMI or lowest 20% of MMI

Newman A et al. JAGS 2003;51:1602-9; Norman K et al. Clín Nutr 2009;28:78-82
Obesity and disability

Vincent HK Obesity reviews 2010
Sarcopenic-Obesity

- Def. combines those of sarcopenia and obesity
- Obesity: 2 SD > young reference groups %BF
  - $\delta$: 27%; $\gamma$: 38% $\sim$ BMI of 27 kg/m$^2$
  - SO: 2% 60-60 y; 10% > 80 y
  - SO was associated with 2-3 higher IADL disability over 7 y, while either obesity or sarcopenia alone were not
- WHO def. of obesity BMI > 30 kg/m$^2$
- If no ref group
  - Davinson KK JAGS 2002;50:1802-9
  - upper 2 quantiles of FM and lower 3 of MM
  - SO in pop > 70 y: $\delta$: 9.6%; $\gamma$: 7.4%
Relation between sarcopenia, strength, fat mass and function

Variables not retained: muscle mass, muscle quality

Physical function: gait speed & balance (measured) + 5 questions (walking ¼ mile, stair climbing, kneeling, lifting 10 lbs, standing for 2 h)

Bouchard DR. J Aging Health 2010

<table>
<thead>
<tr>
<th></th>
<th>% of variance in physical function explained by the pattern</th>
<th>Model effect loadings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Fat mass</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>6.3 (5.8, 7.1)</td>
<td>-0.54 (-0.65, -0.42)</td>
</tr>
<tr>
<td>55-64 years</td>
<td>4.0 (3.2, 6.3)</td>
<td>-0.36 (-0.59, -0.21)</td>
</tr>
<tr>
<td>65-74 years</td>
<td>7.6 (6.9, 8.1)</td>
<td>-0.65 (-0.86, -0.30)</td>
</tr>
<tr>
<td>≥75 years</td>
<td>4.2 (2.9, 5.5)</td>
<td>-0.32 (-0.54, -0.22)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>7.4 (6.5, 8.9)</td>
<td>-0.49 (-0.30, -0.69)</td>
</tr>
<tr>
<td>55-64 years</td>
<td>6.6 (4.9, 7.4)</td>
<td>-0.51 (-0.60, -0.22)</td>
</tr>
<tr>
<td>65-74 years</td>
<td>8.6 (7.7, 9.3)</td>
<td>-0.87 (-0.98, -0.70)</td>
</tr>
<tr>
<td>≥75 years</td>
<td>6.9 (4.9, 7.5)</td>
<td>-0.52 (-0.63, -0.39)</td>
</tr>
</tbody>
</table>
Dynapenic-Obesity

- *Decrease in strength* = **Dynapenia** (*D*)
- In principle, worse case scenario would be dynapenic-obesity (DO)
- From NHANES: sex, age and height adjusted residuals of leg strength and fat mass were classified in *tertiles* and groups defined for DO, O, D and N
- DO had slower gait speed vs O and normal groups but not vs D!

Sarcopenia - Definition

Evolution of the sarcopenia definition:
Now, it takes into account loss of muscle performance *(muscle strength)* or function

**EWGSOP:** Cruz-Jentoft AJ et al. Age & Ageing 2010;39:412-23


Function: SPPB or gait speed (Guralnik JM J Gerontol 1994;49:M85-94)
Phenotype of Frailty

☐ Frailty: ≥ 3 of the following; pre-frailty ≤ 2
☐ Loss of body mass √
☐ Unintentional weight loss: > 10 lbs prior year
  ■ Sarcopenia
☐ Weakness √
  ■ Low hand grip strength: < 20th perc for BMI and sex
☐ Slowness √
  ■ TUG, gait speed (<0.8 m/s)
☐ Fatigue: reported exhaustion
☐ Low physical activity

Frailty Cycle

- Age
- Anorexia
- Chr. Diseases
- Environment

Chronic Malnutrition

- Dysregulations
  - Hormones
  - Inflammation
  - Coagulation

- Energy Expenditure
- Basal Metabolic Rate

Frailty

- (Central adiposity)
- Sarcopenia
- Osteopenia

- Insulin Resistance
- $\downarrow$ VO$_2$ max

- Physical Activity
- $\downarrow$ Gait Speed
- $\downarrow$ Strength/Capacity
The vicious circle of sarcopenia

Nair KS AJCN 2005
The NuAge Study

Random sample of Quebec Medicare Database from areas of Sherbrooke and Montreal. ♀ & ♂: 68-72y, 73-77y, 78-82y


Disease free & healthy: walk without help (cane accepted) 300 m or climb 10 stairs, cognitively intact (3MS > 79), independent for ADL

Body composition DXA & BIA; Performance: TUG, gait speed, Ms strength (handgrip, knee extension and elbow flexors), sit-to-stand x 5 and balance (one leg stand); blood tests; dietary intake; questionnaires, etc. Annual assessments for 4 y.

For sarcopenia data: Exclusion if diabetes based on reported DM or taking ADM or fasting glu > 7 mmol/L

Available body composition measurements
Sarcopenia and physical function

- Total MM was estimated by DXA (Kim et al 2005) and by BIA (Janssen I et al 2002) and MMI (kg/m²) was calculated as well as %body fat (%BF)

- Quintiles of MMI and %BF were calculated
  - Sarcopenia (S): lowest 2 quintiles for MMI
  - Obesity (O): highest 2 quintiles for %BF
  - Four groups were defined: SO, S, O, Normal

- Groups were compared by GLM with age, sex, smoking, # chr diseases and physical activity (PASE), as co-factors
Body composition and performance

<table>
<thead>
<tr>
<th></th>
<th>SO</th>
<th>S</th>
<th>O</th>
<th>N</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>169 (16)</td>
<td>255 (24)</td>
<td>258 (24)</td>
<td>380 (36)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>75.2±4.1</td>
<td>74.8±4.2</td>
<td>73.8±3.9</td>
<td>73.0±4.0</td>
<td>&lt;0.0001 b,c,d,e,f</td>
</tr>
<tr>
<td>MMI (kg/m²)</td>
<td>7.6±1.3</td>
<td>7.6±1.4</td>
<td>9.2±1.4</td>
<td>9.2±1.4</td>
<td>&lt;0.0001 b,c,d,f</td>
</tr>
<tr>
<td>%BF</td>
<td>40.3±6.7</td>
<td>29.7±7.8</td>
<td>40.4±6.8</td>
<td>29.6±8.0</td>
<td>&lt;0.0001 a,c,d,e</td>
</tr>
<tr>
<td>BMI</td>
<td>28.3±2.7</td>
<td>23.4±2.3</td>
<td>31.9±3.7</td>
<td>26.4±2.8</td>
<td>&lt;0.0001 a,b,c,d,e,f</td>
</tr>
<tr>
<td>TUG (s)</td>
<td>10.6±2.0</td>
<td>10.4±2.2</td>
<td>10.5±2.0</td>
<td>10.0±2.0</td>
<td>0.045 e</td>
</tr>
<tr>
<td>Gait speed (m/s)</td>
<td>1.13±0.21</td>
<td>1.16±0.23</td>
<td>1.10±0.18</td>
<td>1.16±0.19</td>
<td>0.001 d,e</td>
</tr>
</tbody>
</table>

a: SO vs S; b: SO vs O; c: SO vs N; d: S vs O; e: O vs N; f: S vs N
## Body composition and performance

<table>
<thead>
<tr>
<th></th>
<th>SO</th>
<th>S</th>
<th>O</th>
<th>N</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Handgrip R</td>
<td>62.6±17.6</td>
<td>66.6±17.6</td>
<td>66.2±19.3</td>
<td>67.4±19.1</td>
<td>NS</td>
</tr>
<tr>
<td>Elbow flexion R</td>
<td>38.1±13.7</td>
<td>38.2±15.3</td>
<td>42.7±17.3</td>
<td>42.7±16.8</td>
<td>&lt;0.0001 b,c,d,f</td>
</tr>
<tr>
<td>Knee extension R</td>
<td>51.1±20.2</td>
<td>51.9±20.2</td>
<td>58.5±24.1</td>
<td>58.9±22.1</td>
<td>&lt;0.0001 b,c,d,f</td>
</tr>
<tr>
<td>Knee flexion R</td>
<td>35.6±13.1</td>
<td>36.0±14.7</td>
<td>40.2±17.0</td>
<td>40.4±16.1</td>
<td>&lt;0.0001 b,c,d,f</td>
</tr>
<tr>
<td>One leg stand</td>
<td>11.6±14.8</td>
<td>20.4±21.1</td>
<td>11.4±15.0</td>
<td>20.8±20.8</td>
<td>&lt;0.0001 a,c,d,e</td>
</tr>
</tbody>
</table>

* Similar significance in the left/non-dominant side

a: SO vs S; b: SO vs O; c: SO vs N; d: S vs O; e: O vs N; f: S vs N
Conclusions

- Sarcopenia despite contributing to lower strength in several muscle groups had no impact on function (TUG and gait speed).
- Obesity on the other hand affected function and this aspect seems to be mediated by a worse balance.
- These results need to include longitudinal data to capture better the impact of sarcopenia and obesity on function and disability.
Measures to counteract Muscle loss and strength

Olga Kotelko, 93 y.o
Exercise patterns in the U.S. adult population over age 50

- Completely sedentary: 50%
- Some physical activity: 35%
- Muscle strengthening: 10%
- Regular vigorous exercise: 5%

AARP, May 2002
Exercise and Physical Capacity

- Exercise is the best anti-aging strategy (ACSM & AHA, Circulation 2007)
- Any type of physical activity is better than no activity for protection against functional limitations, but exercise confers greater benefit for physical capacity (Brach JS JAGS 2004;52:502-9)
- Aerobic exercise has effects on the progression of MCI (Baker LD Arch Neurol. 2010;67:71-9)
  - ♂: improved executive function
  - ♀: favorable effect only on Trails B test
- Aerobic exercise prevents weight gain (adiposity) and insulin resistance (Solomon TSJ J Appl Physiol 2008;104:1313-19)
## Masters Athletes
McGill University Health Center Collaboration - T Taivassalo, R Hepple, J.A. Morais et al

<table>
<thead>
<tr>
<th></th>
<th>N = 31</th>
<th>Males (17)</th>
<th>Females (14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controls (10)</td>
<td>Athletes (7)</td>
<td>Controls (6)</td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td>82.9 ± 4.8</td>
<td>78.7 ± 3.7</td>
<td>79.3 ± 3.8</td>
</tr>
<tr>
<td><strong>Height (m)</strong></td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>77.6 ± 10.7</td>
<td>71.2 ± 10.8</td>
<td>63.9 ± 10.9</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>26.6 ± 2.6</td>
<td>23.4 ± 2.7*</td>
<td>27.4 ± 4.9</td>
</tr>
<tr>
<td><strong>Fat Mass (%)</strong></td>
<td>32.5 ± 3.3</td>
<td>20.8 ± 4.3*</td>
<td>41.7 ± 7.6</td>
</tr>
<tr>
<td><strong>Athlete Event (Power:Endur)</strong></td>
<td>-</td>
<td>4:3</td>
<td>-</td>
</tr>
<tr>
<td><strong>Dorsiflexion MVC (Nm)</strong></td>
<td>22.7 ± 6.8</td>
<td>31.6 ± 11.1*</td>
<td>12.8 ± 2.7</td>
</tr>
<tr>
<td></td>
<td>+39%</td>
<td></td>
<td>+26%</td>
</tr>
</tbody>
</table>
McGill Masters Athletes

Greater number of MUs in Tibialis Anterior
Effects of exercise training

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>66</td>
<td>49</td>
</tr>
<tr>
<td>Age (y)</td>
<td>83</td>
<td>83</td>
</tr>
<tr>
<td>% Females</td>
<td>52</td>
<td>53</td>
</tr>
<tr>
<td># meds</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>PPT score (out of 36)</td>
<td>28.4</td>
<td>28.3</td>
</tr>
<tr>
<td>$\text{VO}_2 \text{ max} \ (\text{ml/kg/min})$</td>
<td>15.6</td>
<td>15.4</td>
</tr>
<tr>
<td>FS-36</td>
<td>26.6</td>
<td>26.6</td>
</tr>
</tbody>
</table>

9 months of progressive flexibility/balance, resistance and endurance exercise vs. flexibility exercise at home

Binder EF JAGS 2002;50:1921
Proven efficacy of strength training

Meta-analysis on 47 studies including 1079 participants aged 50-92 yrs (mean age 67.4±6.3 yrs)

- **Duration**: 6-52 wks (mean duration 17.6 wks)
- **Frequency**: 1-3 times/wk
- **Intensity**: 40%-85% of 1 RM (mean = 70% 1RM)
- **Sets**: 1-6 sets per muscle
- **Repetitions**: 2-20 (mean 10±2.6 repetitions)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>PRT Mean</th>
<th>PRT SD</th>
<th>Control Mean</th>
<th>Control SD</th>
<th>Control Total</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI</th>
<th>Std. Mean Difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seymour 2004</td>
<td>-0.52</td>
<td>0.59</td>
<td>-1</td>
<td>0.93</td>
<td>8</td>
<td>0.7%</td>
<td>0.58 [0.42, 1.50]</td>
<td></td>
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<tr>
<td>Hitte 1994</td>
<td>45</td>
<td>22</td>
<td>9</td>
<td>53</td>
<td>13</td>
<td>8</td>
<td>-0.41 [-1.36, 0.55]</td>
<td></td>
</tr>
<tr>
<td>Beam 2004</td>
<td>10.4</td>
<td>1.3</td>
<td>11</td>
<td>9.5</td>
<td>15</td>
<td>9</td>
<td>0.62 [-0.29, 1.55]</td>
<td></td>
</tr>
<tr>
<td>Schilke 1996</td>
<td>-7.8</td>
<td>3.5</td>
<td>10</td>
<td>-9.5</td>
<td>4</td>
<td>10</td>
<td>0.48 [-0.41, 1.30]</td>
<td></td>
</tr>
<tr>
<td>Westhoff 2000</td>
<td>-26.4</td>
<td>7.5</td>
<td>10</td>
<td>-23.1</td>
<td>6.6</td>
<td>11</td>
<td>-0.72 [-1.61, 0.17]</td>
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</tr>
<tr>
<td>Tracy 2004</td>
<td>-27.6</td>
<td>5.51</td>
<td>11</td>
<td>-27.4</td>
<td>5.04</td>
<td>9</td>
<td>-0.04 [-0.02, 0.84]</td>
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</tr>
<tr>
<td>Mangione 2005</td>
<td>57.7</td>
<td>21.1</td>
<td>11</td>
<td>48</td>
<td>18.9</td>
<td>10</td>
<td>0.46 [-0.41, 1.33]</td>
<td></td>
</tr>
<tr>
<td>Tsulsumi 1997</td>
<td>91.9</td>
<td>7.5</td>
<td>13</td>
<td>75.7</td>
<td>26.4</td>
<td>14</td>
<td>1.2%</td>
<td>0.80 [0.01, 1.59]</td>
</tr>
<tr>
<td>Miszko 2003</td>
<td>57.7</td>
<td>10</td>
<td>13</td>
<td>57</td>
<td>18</td>
<td>15</td>
<td>1.3%</td>
<td>0.65 [0.01, 1.28]</td>
</tr>
<tr>
<td>Kebrnelson 2006</td>
<td>85</td>
<td>12</td>
<td>15</td>
<td>75</td>
<td>21</td>
<td>16</td>
<td>1.4%</td>
<td>0.11 [-0.60, 0.83]</td>
</tr>
<tr>
<td>Sim 2006</td>
<td>12.45</td>
<td>2</td>
<td>14</td>
<td>12.25</td>
<td>1.4</td>
<td>16</td>
<td>1.4%</td>
<td>0.62 [0.09, 1.22]</td>
</tr>
<tr>
<td>Singh 1997</td>
<td>62.6</td>
<td>18.4</td>
<td>17</td>
<td>70.3</td>
<td>27.8</td>
<td>15</td>
<td>1.4%</td>
<td>-0.55 [-1.26, 0.15]</td>
</tr>
<tr>
<td>Brochu 2002</td>
<td>65</td>
<td>21</td>
<td>19</td>
<td>76</td>
<td>17</td>
<td>14</td>
<td>1.4%</td>
<td>0.08 [0.61, 0.76]</td>
</tr>
<tr>
<td>Boshulhan 2005</td>
<td>-27.5</td>
<td>9.8</td>
<td>16</td>
<td>-28.2</td>
<td>7.9</td>
<td>17</td>
<td>1.5%</td>
<td>0.03 [-0.71, 0.78]</td>
</tr>
<tr>
<td>Singh 2006</td>
<td>71</td>
<td>24</td>
<td>18</td>
<td>72.8</td>
<td>22.6</td>
<td>19</td>
<td>1.7%</td>
<td>0.03 [-0.72, 0.79]</td>
</tr>
<tr>
<td>Beker 2001</td>
<td>63.4</td>
<td>29</td>
<td>19</td>
<td>60.8</td>
<td>30</td>
<td>19</td>
<td>1.8%</td>
<td>0.09 [-0.66, 0.72]</td>
</tr>
<tr>
<td>Quattlette 2004</td>
<td>47.8</td>
<td>9.39</td>
<td>20</td>
<td>47.8</td>
<td>9.62</td>
<td>21</td>
<td>1.9%</td>
<td>0.00 [-0.61, 0.61]</td>
</tr>
<tr>
<td>Donnell 2000</td>
<td>12.7</td>
<td>4.7</td>
<td>26</td>
<td>11.4</td>
<td>4.9</td>
<td>20</td>
<td>2.1%</td>
<td>0.27 [0.32, 0.65]</td>
</tr>
<tr>
<td>Buchner 1997</td>
<td>89</td>
<td>39</td>
<td>22</td>
<td>74</td>
<td>28</td>
<td>29</td>
<td>2.3%</td>
<td>-0.15 [-0.70, 0.41]</td>
</tr>
<tr>
<td>Miller 2006</td>
<td>35.3</td>
<td>11.1</td>
<td>25</td>
<td>32.1</td>
<td>9.8</td>
<td>26</td>
<td>2.4%</td>
<td>0.30 [0.25, 0.85]</td>
</tr>
<tr>
<td>de Vreede 2007</td>
<td>50.1</td>
<td>9.2</td>
<td>28</td>
<td>49.6</td>
<td>9</td>
<td>26</td>
<td>2.5%</td>
<td>0.05 [0.48, 0.59]</td>
</tr>
<tr>
<td>Fosco 2003</td>
<td>61.17</td>
<td>14.11</td>
<td>26</td>
<td>53.49</td>
<td>22.37</td>
<td>32</td>
<td>2.6%</td>
<td>0.40 [-0.13, 0.92]</td>
</tr>
<tr>
<td>Damush 1999</td>
<td>61.8</td>
<td>18.8</td>
<td>33</td>
<td>60.7</td>
<td>24.2</td>
<td>29</td>
<td>2.9%</td>
<td>0.05 [-0.45, 0.55]</td>
</tr>
<tr>
<td>Liu-Antrose 2005</td>
<td>-14.9</td>
<td>13.3</td>
<td>32</td>
<td>-18.8</td>
<td>14.4</td>
<td>32</td>
<td>2.9%</td>
<td>0.35 [-0.14, 0.84]</td>
</tr>
<tr>
<td>Topp 2002</td>
<td>-35.4</td>
<td>10.92</td>
<td>35</td>
<td>-38.7</td>
<td>10.82</td>
<td>35</td>
<td>3.2%</td>
<td>-0.15 [-0.62, 0.31]</td>
</tr>
<tr>
<td>Chin A Paw 2006</td>
<td>39.5</td>
<td>8</td>
<td>40</td>
<td>40.8</td>
<td>9.1</td>
<td>32</td>
<td>3.3%</td>
<td>0.40 [0.07, 0.76]</td>
</tr>
<tr>
<td>Chandler 1998</td>
<td>44.2</td>
<td>20.4</td>
<td>44</td>
<td>42.5</td>
<td>25.8</td>
<td>43</td>
<td>4.1%</td>
<td>0.07 [0.35, 0.49]</td>
</tr>
<tr>
<td>Mikesky 2006</td>
<td>-30.09</td>
<td>13.11</td>
<td>57</td>
<td>-30.03</td>
<td>11.14</td>
<td>75</td>
<td>6.1%</td>
<td>-0.00 [-0.35, 0.34]</td>
</tr>
<tr>
<td>Moreland 2003</td>
<td>63.9</td>
<td>16.9</td>
<td>88</td>
<td>65.5</td>
<td>17.3</td>
<td>85</td>
<td>6.2%</td>
<td>-0.03 [-0.43, 0.25]</td>
</tr>
<tr>
<td>Segal 2003</td>
<td>120.2</td>
<td>15.9</td>
<td>82</td>
<td>117.6</td>
<td>14.9</td>
<td>73</td>
<td>7.2%</td>
<td>0.17 [-0.16, 0.48]</td>
</tr>
<tr>
<td>Jette 1999</td>
<td>-7.5</td>
<td>9.3</td>
<td>92</td>
<td>-9.8</td>
<td>12.1</td>
<td>104</td>
<td>0.1%</td>
<td>0.21 [0.08, 0.34]</td>
</tr>
<tr>
<td>Latham 2003</td>
<td>35.6</td>
<td>25.9</td>
<td>113</td>
<td>38.7</td>
<td>28.4</td>
<td>117</td>
<td>10.7%</td>
<td>-0.11 [-0.37, 0.15]</td>
</tr>
<tr>
<td>Ettinger 1997</td>
<td>-1.74</td>
<td>0.4</td>
<td>120</td>
<td>-1.9</td>
<td>0.3</td>
<td>127</td>
<td>11.3%</td>
<td>0.45 [0.26, 0.71]</td>
</tr>
</tbody>
</table>

Total (95% CI) = 1076

Heterogeneity: Chi² = 35.93, df = 52 (P = 0.29); I² = 11%
Test for overall effect: Z = 3.13 (P = 0.002)

Small, but significant effect of progressive resistance training on Physical performance

Gait speed, 14 trials, 798 participants, WMD 0.07 m/s, 95% CI 0.04 to 0.09)

Liu & Latham 2011
Results the Health ABC Cohort Study

Median total protein intake as a percentage of total energy intake (g.kg\(^{-1}\).d\(^{-1}\)) by quintile (from quintile 1 to quintile 5) was 11.2% (0.7 g.kg\(^{-1}\).d\(^{-1}\)), 12.7% (0.7 g.kg\(^{-1}\).d\(^{-1}\)), 14.1% (0.8 g.kg\(^{-1}\).d\(^{-1}\)), 15.8% (0.9 g.kg\(^{-1}\).d\(^{-1}\)), and 18.2% (1.1 g.kg\(^{-1}\).d\(^{-1}\)) \(N= 2066; \) Duration: 3 years

Houston DK AJCN 2008
Lesser muscle response with a small bolus of EAA

Mean (SEM) leg phenylalanine net balance 3.5 h after the ingestion of 7g EAA calculated by measuring the area under the phenylalanine net balance response curve in the elderly (n=11) and the young (n=8). Data were analyzed with a t test. *Significantly different from the young, P 0.010.

Katsanos CS AJCN 2005
Muscle Response to Feeding with Aging

Adequate quantity of EAA improves muscle protein synthesis

Mixed muscle fractional synthetic rate (FSR) in young and elderly before and after ingestion of 15 g of EAA. †Significant difference from corresponding postabsorptive values: young, $P < 0.012$; elderly, $P < 0.029$.

Paddon-Jones D Am J Physiol Metab 2004
Exercise training and protein supplementation (FFM)

Weighted mean difference: 0.69 kg; 95% CI: 0.47, 0.91 kg; P < 0.00001
Exercise training and protein supplementation (1-RM leg press)

Weighted mean difference: 13.5 kg; 95% CI: 6.4, 20.7 kg; P < 0.005

Protein supplementation in frail elderly

RCT of 15 g of protein supplementation BID, n=65

Treatment x Time interaction effect p<0.02
Protein supplementation in frail elderly

RCT of Resistance EX 2 sessions / week ± 15 g of protein BID

Tieland et al., JAMDA, 2012-B
Best fitting model using NuAge data with all paths significant

RMSEA: good
Chi-square: good
CFI: good
NFI: good
NNFI: good

Matta J & Morais JA, unpublished
What can we learn from the revised model

- Mobility and strength were significantly associated
  - For each unit increase in strength, there is a 0.37 unit increase in mobility
- Mobility significantly impacted on physical activity
- Fat mass & muscle mass *negatively* impacted on mobility
- Muscle mass *but* not fat mass was associated with strength
  - For each unit increase in muscle mass, there was a 6 unit increase in strength
- Muscle mass was *positively* associated with physical activity whereas fat mass was *negatively* associated
What can we learn from the revised model

- Greater muscle mass may not be the best target to enhance mobility, *and* since fat mass is also negatively associated with mobility, weight loss would be desirable in this population.

- However, weight loss should be directed exclusively towards fat mass and not muscle mass since our results suggest that muscle mass has a significant positive association with strength. What is needed is to improve muscle quality (strength/mass).
What can we learn from the revised model

- Containing fat mass while increasing strength (or muscle mass) could be achieved through physical activity
- Physical activity is the right approach to improve physical capacity. Indeed, physical activity was positively associated with mobility
Conclusions

- One cannot totally eliminate the effect of the “passage of time” on body composition and physical performance.
- Decreases in functional capacity with aging can be minimized by regular physical exercise and adequate nutrition.
- Even in the most frail person, some gains in function can be obtained.
  - Ex > protein supplementation
  - Better in combination
Thank you