Sarcopenie
Etiologie en aangrijpingspunten voor revalidatie

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Sarcopenia
Rosenberg J Nutr 1997
Age-related loss of muscle mass and muscle strength

Roubenoff R. J Gerontol 2003
\[ T\text{-score} = \frac{X - \text{mean}_\text{young}}{\text{SD}_\text{young}} \]

- Baumgartner ea. 1998
  - New Mexico, USA
    - N-Hisp: 205M, 173F
  - Reference group
    - N-Hisp, 107M, 122F aged 18-40yrs
  - >80 yrs = ♂ 53%, ♀ 43%

- Janssen ea. 2000
  - NHANES III, USA
    - 2224M, 2278F aged ≥60yrs
  - Reference group
    - 3116M, 3298F aged 18-39yrs
  - Class 1: -1 ≥ T ≤ -2
    - >80 yrs = ♂ 43%, ♀ 61%
  - Class 2: T < -2
    - >80 yrs = ♂ 7%, ♀ 11%

**Correction for weight or stature**
Table 1. Criteria for the diagnosis of sarcopenia

Diagnosis is based on documentation of criterion 1 plus (criterion 2 or criterion 3)

1. Low muscle mass
2. Low muscle strength
3. Low physical performance

European Working Group on Sarcopenia in Older People Age Ageing 2010

![Graph showing relative effort percentage for Ascent, Descent, and Chair rise with asterisks indicating significant differences.](Hortobagyı ea J Gerontol 2003)
Fatigue resistance

- Based on max. grip strength
- Time (seconds) until grip strength ↓ to 50%Max
- Reliability
  - Inter-observer ICC(3,1)= 0.77 – 0.91
  - Intra-observer ICC(3,1)= 0.82 – 0.94
Grip Work = 0.75 x Grip strength x Fatigue resistance
= area under the curve

STRENGTH ENDURANCE


N=291, age 20-93 yrs

**Muscle weakness & Fatigue**

**Underlying mechanisms**
## Table 2. Factors Contributing to Sarcopenia.

<table>
<thead>
<tr>
<th>Type</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Anabolism</td>
<td>↓ Hormonal stimulation (Growth Hormone, IGF-1, Testosterone, Oestrogen)</td>
</tr>
<tr>
<td></td>
<td>Loss of motorneurones, denervation of muscle fibres</td>
</tr>
<tr>
<td></td>
<td>↑ non-contractile tissue in muscle</td>
</tr>
<tr>
<td>Exogenous</td>
<td>↓ Physical activity</td>
</tr>
<tr>
<td></td>
<td>Bed rest, immobilisation</td>
</tr>
<tr>
<td>↑ Catabolism</td>
<td></td>
</tr>
<tr>
<td>Endogenous</td>
<td>↑ Basal inflammatory profile (IL-6, TNF-α)</td>
</tr>
<tr>
<td>Exogenous</td>
<td>Stress-induced inflammation: Life events, Depression</td>
</tr>
<tr>
<td></td>
<td>Disease</td>
</tr>
</tbody>
</table>

**Bautmans ea.** *Acta Clinica Belgica, 2009; 64-4*

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**Figure 1.** Plasma levels of tumor necrosis factor-receptor 1 (TNF-r1) and interleukin (IL)-6 (mean ± SE) by age (*n* = 1,411).

**Stowe ea.** *J Gerontol 2009; 65A: 429-433*
**N=79, age= 80 years, 5 years follow-up**

![Graph showing current periodontitis](image)

Figure 2. Percentage change in handgrip strength over 5 years among those with and without periodontitis at baseline ($p = 0.015$). Values are adjusted for gender, height, weight, number of chronic conditions and physical activity. Means with standard errors are shown.

*Hamalainen et al. Gerodontology 2004: 21; 155–160*

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**BED REST**

**N=680, non-disabled, aged >70 yrs, 18 months follow-up**

60% at least 1 episode bed rest!

*Gill et al., J Gerontol 2004*
**11 healthy subjects, aged 67±5 yrs, 10 days bed rest**

Table 2. Lower Extremity Muscle Performance and Aerobic Capacity

<table>
<thead>
<tr>
<th>Test</th>
<th>Pre-Bed Rest</th>
<th>Post-Bed Rest</th>
<th>% Change</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee extension (N = 11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isometric (N)</td>
<td>133.7 ± 15.1</td>
<td>117.6 ± 13.6</td>
<td>-11.2 ± 3.9</td>
<td>.017</td>
</tr>
<tr>
<td>Concentric 180° (N - m/s)</td>
<td>69.9 ± 8.1</td>
<td>60.1 ± 7.0</td>
<td>-13.5 ± 4.4</td>
<td>.011</td>
</tr>
<tr>
<td>Knee flexion (N = 11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isometric (N)</td>
<td>76.8 ± 10.0</td>
<td>68.1 ± 10.5</td>
<td>-14.2 ± 3.6</td>
<td>.003</td>
</tr>
<tr>
<td>Concentric 60° (N - m/s)</td>
<td>80.3 ± 8.8</td>
<td>71.6 ± 9.4</td>
<td>-11.8 ± 4.6</td>
<td>.03</td>
</tr>
<tr>
<td>Concentric 180° (N - m/s)</td>
<td>51.8 ± 7.7</td>
<td>46.6 ± 8.2</td>
<td>-13.2 ± 4.3</td>
<td>.01</td>
</tr>
<tr>
<td>Stair ascent power</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N - m/s) (N = 8)</td>
<td>403 ± 67</td>
<td>337 ± 48</td>
<td>-14.0 ± 4.1</td>
<td>.01</td>
</tr>
<tr>
<td>VO_{2max} (mL/kg/min) (N = 9)</td>
<td>22.7 ± 2.0</td>
<td>19.72 ± 1.7</td>
<td>-12.2 ± 4.5</td>
<td>.04</td>
</tr>
</tbody>
</table>

*Notes: All values are mean ± standard error of the mean.
1-RM = one repetition maximum; VO_{2max} = maximal oxygen uptake.*

Kortebein *et al.* *J Gerontol* 2008

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**Fig. 5.** Hypertrophy and atrophy signalling via Akt. Increases in RAS/RAF/MEK/ERK signalling results in an up regulation of cellular proliferation in response to IGF-I binding to its receptor. Activation of IRS-I/P70S6K/Akt1 pathway leads to an increase in hypertrophy via mTOR and p70S6K up regulation. Akt activation inhibits FOXO binding to DNA preventing MAFbx and MuRF1 activity and subsequent protein breakdown. NF-κB activation occurs following the degradation of its associated inhibitory protein IκB, leading to the nuclear transport of NF-κB transcription factors and MAFbx and MuRF1 activity, resulting in protein breakdown.

Saini *et al.* *Ageing Research Reviews* 2009;8:251–267
Acute accelerating factors

- Serious systemic inflammation
  - Inflammatory conditions (e.g. infection, surgery)
Inflammatory Patients No non-inflammatory Patients

N=63, Age=70-98 yrs
Bautmans ea. J Gerontol 2005

* Inflammatory Patients Significantly Weaker than Non-Inflammatory (p<0.05)
‡ Significant difference in evolution (p<0.05)

Hospitalized geriatric patients with acute infection, N=43, aged 84 ± 6 years
Mets, Bautmans ea. Am J Geriatr Pharmacother 2004

* Evolution FR significantly different between 3 groups (p=0.021) and improvement celecoxib group significantly better than acetaminophen group (p<0.05) control group (p<0.05)
**SURGERY**

N=66, age 24-91 yrs, elective abdominal surgery

Bautmans ea. *J Gerontology* 2010
Figure 2 - Evolution of post-surgical muscle fatigue resistance according to age. Patients aged >75 years (N=20, dotted line) worsened significantly more and recovered significantly less rapidly for fatigue resistance at day 4 post-surgery compared to the younger (age<50 years: N=29, plain line; aged 60-75 years: N=26, semi-dotted line) patients (Repeated measures ANOVA, interaction between age and fatigue resistance p<0.05).

Bautmans ea. J Gerontology 2010

N=66, age 24-91 yrs, elective abdominal surgery

Sarcopenia
Partly reversible
Cost of Sarcopenia USA 2000

<table>
<thead>
<tr>
<th>Group</th>
<th>Muscle Mass Range, kg/m²</th>
<th>Prevalence in Population, %</th>
<th>Relative Risk Dis­ability</th>
<th>Population Attributable Risk for Disability, %*</th>
<th>Cost, billion $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal muscle</td>
<td>≥ 10.75</td>
<td>35.7</td>
<td>1.00</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Moderate sarcopenia</td>
<td>8.51–10.75</td>
<td>53.1</td>
<td>3.48</td>
<td>56.8</td>
<td>7.18</td>
</tr>
<tr>
<td>Severe sarcopenia</td>
<td>≤ 8.50</td>
<td>11.2</td>
<td>4.60</td>
<td>28.7</td>
<td>3.63</td>
</tr>
<tr>
<td>Older women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal muscle</td>
<td>≥ 6.76</td>
<td>68.7</td>
<td>1.00</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Moderate sarcopenia</td>
<td>5.76–6.75</td>
<td>21.9</td>
<td>1.46</td>
<td>9.2</td>
<td>2.70</td>
</tr>
<tr>
<td>Severe sarcopenia</td>
<td>≤ 5.75</td>
<td>9.4</td>
<td>3.15</td>
<td>18.8</td>
<td>4.96</td>
</tr>
</tbody>
</table>

*[(prevalence (RR + 1)]/[(1 + prevalence (RR + 1)]).

Total 18.5 billion dollar!
10% reduction of sarcopenia = 1.1 billion dollar savings!

Countering Sarcopenia

Bautmans ea. 2000

Bennell ea. Gerontology 2008

Bautmans ea. BMC Geriatrics 2005

Strength training effective in elderly persons

• + 30-170% strength in 6 weeks
• Even in oldest old (age >90 yrs)

Latham ea. The Cochrane Library 2003
Fig. 4. Signalling pathways involved in hypertrophy. Akt activation leads to the deactivation of FOXO, its release from the DNA strand and exit from the nucleus and binding with the 14-3-3 transport protein to prevent it from becoming active and rebinding to DNA, resulting in a blockade of proteolysis.


12 weeks strength training (85-97 j)

Pre

Post

FIGURE 2. MRI images taken at the mid-thigh region of the male subject CC before (Pre) and after (Post) training (shown to the same scale). Quadriceps LCSA increased by 44% in this subject, who is represented by the triangle symbol with apex upwards in Figures 1, 5, and 6.

Fig. 1. Computer tomography images taken from the mid-thigh region of a female subject in the strength training (ST) group before and after training. The 2 images are shown at the same scale. Quadriceps muscle cross-sectional area of the operated side (op-leg) increased 33% in this subject; the nonoperated side (con-leg) did not change from pretraining to posttraining.


Non-frail elderly:
Strength training in fitness

Frail elderly:
supervised exercise
+ home-based program
All patients aged ≥70 years → Screening for muscle weakness:
- History: recent illness or hospitalization; difficulties with activities of daily life (walking stairs, raising from chair)
- Evaluation of grip strength and fatigue resistance

Muscle weakness

Medical screening, with attention for: neurologic & cardiovascular disorders, drug intake, laboratory

Risk assessment for complications during physical exercise

High risk → Low risk

No indication for muscle weakness → Risk assessment for complications during physical exercise

Low risk

(Preventive) exercise sessions: Fitness, seniors' sport activities, ...

High risk

(Preventive) exercise sessions under professional supervision (physical therapist); simultaneous home-based exercise program


Physical Capacity (Muscle Function)

* Trauma, Surgery, Infection

ADL

25-40 years  70 years

Bautmans et al. Acta Clinica Belgica, 2009; 64-4
Thank you.

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