Understanding sarcopenia: causes, mechanisms and consequences

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Muscle wasting is a problem

«Take an old person suffering a process of physiological atrophy due to advanced age, of his/her muscular elements, for instance of the muscles of the legs, where it usually happens, causing total or partial paraplegia. Why not calling it wasting, degeneration with no reincorporation?»

Starting point

• Sarcopenia is a medical condition not yet broadly recognized by the international medical community. Discussions on definition, diagnostic methods and interventions are ongoing.

• Sarcopenia is in the process to receive an ICD-10 code and is most certainly under-diagnosed.
Sarcopenia: first steps

• “No decline with age is as dramatic or potentially more significant than the decline in lean body mass. In fact, there may be no single feature of age-related decline more striking than the decline in lean body mass in affecting ambulation, mobility, energy intake, overall nutrient intake and status, independence and breathing.

• I suggested that if this phenomenon were to be taken seriously, we had to give it a name. I proposed that the name for this phenomenon should be derived from the Greek.”
Sarcopenia: the concept

Sarx
Flesh

Penia
Loss

Sarcopenia
Sarcopenia is a threat in old age

- Linked with the geriatric evolving concept of “frailty”
- Related with weight loss, malnutrition and cachexia
- The main consequences are disability, dependence and death
Human muscles

- 600 muscles in human body
- Skeletal muscles: 40-45% of total body mass
- 55% of skeletal muscle mass in lower limbs
- 50% of total body protein is in muscles

Low skeletal body mass and age

REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

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EWGSOP Definition of Sarcopenia

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.

CRITERIA FOR THE DIAGNOSIS OF SARCOPENIA

progressive

A lifelong model of sarcopenia

Birth weight and muscle strength

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.

CRITERIA FOR THE DIAGNOSIS OF SARCOPENIA

geriatric syndrome

### The complexity of geriatric syndromes

<table>
<thead>
<tr>
<th>ENTITY</th>
<th>ETIOLOGY</th>
<th>PATHOGENESIS</th>
<th>PRESENTING SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>Known</td>
<td>Known</td>
<td>Known, but variable in presentation</td>
</tr>
<tr>
<td>Syndrome 1</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Defined set of signs</td>
</tr>
<tr>
<td>Syndrome 2</td>
<td>Unknown</td>
<td>Known</td>
<td>Defined set of signs</td>
</tr>
<tr>
<td>Syndrome 3</td>
<td>Known</td>
<td>Unknown</td>
<td>Defined set of signs</td>
</tr>
<tr>
<td>Geriatric syndrome</td>
<td>Multiple etiological factors</td>
<td>Interacting pathogenetic pathways</td>
<td>Unified manifestation</td>
</tr>
</tbody>
</table>

Modeling geriatric syndromes

Congenital errors of metabolism
Cancer, ischemic heart disease
Geriatric syndromes

Sarcopenia is a geriatric syndrome

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.

Sarcopenia increases mortality

Table 2. Association between sarcopenia and all-cause mortality, after adjustment for various confounders (hazard ratios and 95% confidence intervals)

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarcopenia</td>
<td>2.95 (1.44–6.04)</td>
<td>2.89 (1.40–5.96)</td>
<td>2.40 (1.07–5.42)</td>
<td>2.32 (1.01–5.43)</td>
</tr>
<tr>
<td>Age</td>
<td>1.15 (0.93–1.42)</td>
<td>1.08 (0.85–1.36)</td>
<td>1.12 (0.87–1.43)</td>
<td></td>
</tr>
<tr>
<td>Gender (female)</td>
<td>0.55 (0.29–1.03)</td>
<td>0.49 (0.25–0.99)</td>
<td>0.49 (0.23–1.04)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>0.87 (0.72–1.04)</td>
<td>0.87 (0.72–1.05)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADL impairment</td>
<td>1.91 (1.29–2.83)</td>
<td>1.75 (1.20–2.56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.92 (0.86–0.99)</td>
<td>0.93 (0.86–1.01)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.60 (0.26–1.35)</td>
<td></td>
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<tr>
<td>Congestive heart failure</td>
<td>6.71 (0.70–64.1)</td>
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<tr>
<td>COPD</td>
<td>1.46 (0.50–4.21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of diseases</td>
<td>1.29 (0.92–1.80)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNF-α</td>
<td>0.99 (0.85–1.15)</td>
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</tbody>
</table>

Model 1: adjusted for age, gender.
Model 2: adjusted for age, gender, education, ADL impairment, body mass index.
Model 3: adjusted for age, gender, education, ADL impairment, body mass index, hypertension, congestive heart failure, chronic obstructive pulmonary disease (COPD), number of diseases, TNF-α.
Age, education, ADL impairment, body mass index, number of diseases, TNF-α was treated as a continuous variable.

Landi F et al. Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from iISIRENTE study. Age Ageing 2013
Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.

**CRITERIA FOR THE DIAGNOSIS OF SARCOPENIA**

- Low muscle mass
- Low muscle strength
- Low physical performance

Risk of poor physical performance or physical disability in older adults with low muscle mass

Risk of poor physical performance or physical disability in older adults with low muscle strength

Sarcopenia staging, which reflects the severity of the condition, is a concept that can help guide clinical management of the condition.

EWGSOP

Sarcopenia, cachexia, inflammation

- Systemic inflammation seems to be linked to muscle wasting
- Some degree of inflammation may be present in sarcopenia
- Inflammation is key in the pathogenesis of cachexia
  - CRP (>5.0 mg/l, IL-6 >4.0 pg/ml)
- Low muscle mass and strength are part of the definition of cachexia

Suggested measures to diagnose sarcopenia

**MUSCLE MASS**
- BIA
- DEXA
- CT
- MRI

**MUSCLE STRENGTH**
- Handgrip strength
- Knee flexion-extension
- PEF

**PHYSICAL PERFORMANCE**
- SPPB
- Gait speed
- Get up&Go
- Stair climbing

Sarcopenia with limited mobility is defined as a person with muscle loss whose walking speed is equal to or less than 1 m/s or who walks less than 400 m during a 6 minute walk.

Muscle loss: lean appendicular mass (corrected for height squared) >2 SD below healthy persons between 20 to 30 years of age of the same ethnic group.

Limitation in mobility not clearly attributable to the direct effect of specific disease such as peripheral vascular disease, or central or peripheral nervous system disorders, dementia, or cachexia.

Sarcopenia and physical frailty

<table>
<thead>
<tr>
<th>Shrinking: unintentional weight loss, sarcopenia</th>
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</thead>
<tbody>
<tr>
<td>Weakness</td>
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<tr>
<td>Poor endurance, exhaustion</td>
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<tr>
<td>Slowness</td>
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<tr>
<td>Low activity</td>
</tr>
<tr>
<td>Positive for frailty phenotype: 3 or more criteria present</td>
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<tr>
<td>Intermediate or prefrail: 1 or 2 criteria present</td>
</tr>
</tbody>
</table>

Sarcopenia may be a more practical concept than physical frailty in the quest to reduce disability