Sarcopenia in Older People

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Healthy Muscle & Body Composition (HMBC) Study
Overview

- Definition and assessment of muscle mass
- Prevalence
- Mechanism
- Consequences
- Management
Sarcopenia

Irwin Rosenberg (1989)
Sarcopenia: the observed age-related decline in muscle mass

- Age-related loss of muscle mass
- Age-related loss of muscle strength
- Low muscle mass in old age
- Loss of muscle mass
- Loss of muscle strength
- Low muscle strength in old age
- Low muscle mass, muscle strength and function in old age
Sarcopenia-Diagnostic Criteria

- The European Society of Parenteral and Enteral Nutrition Special Interest Groups
  - Low muscle mass – percentage of muscle mass > 2 SDs below the mean in individuals aged 18-39 in the National Health and Nutrition Examination Survey III Cohort
  - Walking speed <0.8 m/s in the 4-meter walk test or reduced performance in any functional test used to assess the geriatric population
- The European Working Group on Sarcopenia in Older People
  - Low muscle mass
  - Low muscle strength, eg, grip strength
  - Low physical performance, eg, gait speed
- The International Working Group on Sarcopenia
  - Gait speed < 1m/s
  - Objectively measured low muscle mass

Assessment of Muscle Mass

- The existing techniques of measurement could not be applied to day to day clinical practice
- Remains an important area of research
Under-water weighing

Air Displacement Plethysmograph (BodPod)
Dual Energy X-ray Absorptiometry (DEXA)

Total Body Potassium Counting

Prompt Gamma Activation Analysis
Computed Tomography (CT)  Magnetic Resonance Imaging (MRI)
Bioelectrical Impedance Analysis (BIA)

Skin Caliper
The prevalence of sarcopenia in the population above the age of 60 years varies between 10 and 60%.

Sarcopenia: Prevalence

Baumgartner et al., 1998

Janssen et al., 2002

Janssen et al., J Am Geriatr Soc 2002
Sarcopenia: Prevalence

Even with a conservative estimate of prevalence, sarcopenia affects >50 million people today and will affect >200 million people in the next 40 years

Cruz-Jentoft et al., Age Aging 2010
Mechanisms of Sarcopenia

Consequences of sarcopenia: Impaired ADLs and physical disability

<table>
<thead>
<tr>
<th></th>
<th>OR Men</th>
<th>OR Women</th>
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<tbody>
<tr>
<td>≥ 3 disabilities</td>
<td>3.7</td>
<td>4.1</td>
</tr>
<tr>
<td>&lt; 1 balance abnormality</td>
<td>3.2</td>
<td>1.8</td>
</tr>
<tr>
<td>&gt;1 gait abnormality</td>
<td>1.9</td>
<td>1.1</td>
</tr>
<tr>
<td>Use of can/walker</td>
<td>2.3</td>
<td>1.8</td>
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Sarcopenia is associated with a 3-4 fold increase in the risk of physical disability

Data from the Framingham Disability Study showed that older subjects are less able to perform everyday activities without difficulties.

Consequences of sarcopenia: Falls

- Fall Risk
  - Not much data on relationship between muscle mass in old age and risk of falls (2 major studies, retrospective, 12 months)
  - New Mexico, 883 elderly, sarcopenic Hispanic and Non Hispanic white males and females with mean age of 74
    - 22% of males and 31% of females reported a fall in the past year
    - After adjustment for confounding factors, the odds ratio for falls in males was statistically significant but not in females
  - MINOS study – 796 males aged 50 to 85
    - 25.4% reported falls in the past year
    - After adjustment for confounding factors, the odds ratio per SD lower of relative appendicular muscle mass (RAMM) was 1.31
    - Men in the highest tertile for RAMM were less likely to report falls in the previous year than those in the lower quartile for RAMM
Consequences of sarcopenia: Mortality

- Mortality
  - 1396 men and women aged 70 years and older
    - After confounding adjustments, low arm muscle area (≤21.4 cm² for men and ≤21.6 cm² for women) was associated with an 8 year mortality risk (hazard ratio (HR)=1.95)
  - 957 community-dwelling Japanese men and women aged 65 to 102 years old
    - Low arm muscle area (<23.5 cm²) was associated with a higher mortality risk (HR=2.03) compared to high muscle area (≥33.4 cm²)
    - 236 people died before the 2 year follow up
Consequences of sarcopenia: Mortality

- Mortality
  - Recently, large epidemiologic studies have been using more accurate measures of skeletal muscle mass
  - Health, Aging and Body composition study
    - 2292 well functioning men and women aged 70 to 79
    - Leg skeletal muscle mass measured with DXA and mid-thigh muscle cross-sectional area from CT scan
    - Confounding factors were adjusted for
    - Low mid-thigh muscle area was associated with increased mortality risk for men (per SD of 28.1 cm² lower muscle area the HR was 1.26)
    - This risk not found in women (HR=0.94)
    - Mean follow up was 4.9 years in which 286 people died
Consequences of sarcopenia: Financial Implications

- A 10% reduction in sarcopenia prevalence would save $1.1 billion per year.
- As the number of older persons is increasing, the economic burden of sarcopenia will continue to rise unless effective reduction of prevalence occurs.

Yearly costs (US)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yearly Cost (US)</th>
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<tr>
<td>Osteoporotic Fractures</td>
<td>$16.3 billion</td>
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<tr>
<td>Sarcopenia</td>
<td>$18.5 billion</td>
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Management of Sarcopenia

“Considerable evidence suggests that sarcopenia is a reversible cause of disability and could benefit from intervention, especially at the early stage of sarcopenia”

Prof Yves Rolland. et al., 2008
## Management of Sarcopenia: Physical Activity

Physical exercise should be recommended for all sarcopenic patients

<table>
<thead>
<tr>
<th>RECOMMENDATIONS</th>
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<tbody>
<tr>
<td>The American College of Sports Medicine</td>
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<td>The American Heart Association</td>
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<tr>
<td>(Nelson et al., 2007)</td>
<td>Resistance exercise</td>
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<tr>
<td></td>
<td>8 – 10 exercises (using the major muscle groups)</td>
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<tr>
<td></td>
<td>10 – 15 repetitions</td>
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<tr>
<td></td>
<td>Performed at 70-90% of one maximum repetition</td>
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<td></td>
<td>On 2 non-consecutive days per week</td>
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<tr>
<td>Society for Sarcopenia, Cachexia and Wasting Disease</td>
<td>Combination of resistance and aerobic exercise</td>
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<tr>
<td>(Morley et al., 2010)</td>
<td>20-30 minutes exercise</td>
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<td>3 times per week</td>
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<tr>
<td>Visvanathan and Chapman (2010)</td>
<td>Combination of resistance and aerobic exercise</td>
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<tr>
<td></td>
<td>Minimum 50% resistance exercise</td>
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<tr>
<td></td>
<td>30-45 minutes exercise</td>
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<td>3-5 times per week</td>
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Management of Sarcopenia: Physical Activity - Challenges

- Exercise programs need to be **relevant, effective, safe and realistic** for the frail elderly population they are targeted towards
- Organizing resistance training sessions in the elderly is **challenging**
- Requires motivation which may be difficult for some older subjects

Rolland et al., J Nutr Health Aging, 2008
Burton and Sumukadas, Clinical Interventions in Aging, 2010
Management of sarcopenia:
Nutritional management

- Contributory factors related to nutrition:
  - Inadequate protein intake
  - Increased splanchnic extraction of amino acids
  - Vitamin D deficiency
  - Decreased muscle response to anabolic stimuli

Cruz-Jentoft et al., Age Aging 2010
Nutritional management: Protein Intake

- Health ABC study:
  - Subjects in the highest quintile of protein intake lost ~40% less LM and aLM than those in the lowest quartile over 3 years
- Those in the lowest quartile of protein intake have a 2 fold higher risk of frailty

Nutritional management: Protein Intake

- The elderly have high protein requirements to maintain muscle mass and function
- The elderly have low protein intake
- A protein intake of 1.0-1.5g/kg/d is recommended in sarcopenic subjects

Campbell et al., J Gerontol 2001; Gaffney-Stromberg et al., J Am Geriatr Soc 2009; Morley et al., J Am Med Dir Assoc 2010; Feart et al., Br J Nut 2007
Nutritional management: Essential Amino Acid- Leucine

- Of EAAs, leucine is the most potent stimulator of muscle protein synthesis
- Supplementation of leucine (with EAA) significantly increases muscle strength and function in the elderly

Katsanos et al., Am J Physiol Endocrinol Metab 2006
Scognamiglio et al., Aging Clin Exp Res 2004;
Scognamiglio et al., Gerontology 2005; Borsheim et al., Clin Nutr 2008
Nutritional management of sarcopenia: Vitamin D

- Low vitamin D levels are associated with:
  - reduced muscle mass and strength
  - gait impairments
  - decreased balance
  - increased risk of falls
  - Long term decline in physical performance

- An independent association between low vitamin D levels and sarcopenia exists

Visser et al., J Clin Endocrinol Metab. 2003; Rolland et al., J Nutr Health Aging 2008; Bischoff-Ferrari, Best Pract Res Cl Rh. 2009; Visvanathan and Chapman, Maturitas 2010; Ceglia, Curr Opin Clin Nutr Metab Care. 2009; Wicherts et al., J Clin Endocrinol Metab 2007
Nutritional management of sarcopenia: Vitamin D

- Several randomized controlled trials have reported Vit. D supplementation improves muscle strength
  - In people aged 65 and above, 800 IU of Vit. D3 significantly improves lower extremity strength and function by 4% to 11% and body sway by 28% after 2 to 12 months of therapy
  - A recent meta-analysis reported that 700-1000 IU/day reduces fall risk by 19% in the elderly

Bischoff-Ferrari et al., BMJ 2009; Bischoff-Ferrari et al., Arch Intern Med 2009; Bischoff-Ferrari et al., J Bone Miner Res 2003; Pfeifer et al., J Bone Miner Res 2000; Pfeifer et al., Osteoporos Int 2008
Management of Sarcopenia: Pharmacologic Management

- **Hormonal Approach**
  - **Testosterone**
    - Increases the rate of muscle protein synthesis and # of muscle satellite cells
    - In hypogonadal elderly men, has been shown to increase muscle mass and strength and to decrease fat mass
    - BUT inconclusive results from studies evaluating effectiveness in muscle strength and functionality in community-dwelling populations
    - A 2006 meta-analysis of 11 studies suggested a moderate increase in muscle strength
    - Healthy men aged 60 to 80 with low testosterone
      - Testosterone replacement therapy over 6 months showed increases in lean muscle mass, but no improvement in strength and function
    - Large clinical trials are necessary
Project Title: The effect of testosterone and a nutritional supplement on hospital admissions in under-nourished, older people

- Investigators:
  - A/Prof Renuka Visvanathan – Geriatrician
  - Prof Ian Chapman – Endocrinologist
- 2 major centres:
  - Adelaide and Sydney
- Dr Cynthia Piantadosi on 82228818 or email:cynthia.piantadosi@adelaide.edu.au
Management of Sarcopenia: Pharmacologic Management

- **Hormonal Approach**
  - **Growth hormone (GH)**
    - Promotes muscle growth via insulin-like growth factor I (IGF-I)
    - 30% of men older than 60 years are GH deficient
    - In elderly men, many clinical trials show no additional benefit of GH in combination with exercise or testosterone therapy
      - Possibly due to small sample size, lack of pulsatile pattern of GH administration, high incidence of side effects
    - However, other studies report that a few months of GH therapy significantly increases lower extremity muscle strength and mass in healthy, elderly men and women
  - Further research needed
Management of Sarcopenia: Pharmacologic Management

• Hormonal Approach
  • Myostatin Inhibitors
    • Myostatin decreases protein synthesis leading to decreased muscle cell synthesis
    • Follistatin – myostatin-binding protein, recombinant Abs against myostatin, activin type IIB receptor (ActRIIB-Fc) - soluble myostatin decoy receptor
    • Animal models show promise, however experts report muscle tissue may be more susceptible to injury in mice with myostatin deficiency
    • A randomized, double-blind, phase I study on healthy post-menopausal women demonstrated a 2.4-2.6% increase in muscle mass after 15 days of treatment with ActRIIB-Fc
Management of Sarcopenia: Pharmacologic Management

- Statins
  - In a longitudinal study performed on community dwelling elderly adults, statin therapy was associated with declines in muscle strength and increased risk of falls
  - However, this was not confirmed by other authors
  - There is a consensus that statins increase appendicular lean muscle mass, especially after resistance training
    - Small tissue injury → local release of growth factors → muscle hypertrophy
  - Further studies are needed to assess the effect of statins on muscle strength and functionality
Management of Sarcopenia: Pharmacologic Management

- Creatine
  - Increases energy storage via increasing intramuscular phosphocreatine
  - Benefits on exercise performance in young adults are well-documented
  - Few trials on the elderly population
  - Mixed results on increases in muscle mass and strength
A working framework in development

Prevent/Delay Frailty
Health Promotion and Prevention

Life-course Determinants:
- Biological (including genetic)
- Psychological
- Social, Societal
- Environment

Sarcopenia
Kratopenia
Dynapenia

Adverse outcomes
- Disability
- Morbidity
- Hospitalization
- Institutionalization
- Death

Bergman H. 2004
Conclusion

- Sarcopenia is the age related decline in muscle mass, strength and function
- Sarcopenia is highly prevalent in the elderly
- The prevalence of sarcopenia will continue to grow significantly in an aging population
- Sarcopenia is associated with significant clinical consequences, physical disabilities, an increased risk of falls and fractures and loss of independence with an increased risk for institutionalisation and long term care
Conclusion

- Sarcopenia significantly impacts health care costs
- There is currently no useful bedside clinical tool to assist with early detection of sarcopenia
- Current evidence suggests that physical exercise and nutritional therapy are key to managing and reducing the risk of sarcopenia
- Physical exercise is effective in managing sarcopenia, but challenging to implement
- Nutritional support can play a key role in the management of sarcopenia
Thank You

LOVE MUSCLE
Acknowledgement

- Some slides taken from Prof Yves Rolland