Sarcopenia in Older People

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1. Introduction

It is well established that the aging process is associated with numerous changes in the human body. One of the most significant age-related anatomical changes is that which happens to the skeletal muscle mass. Aging process is associated with loss of muscle mass and strength. The term “sarcopenia” is used to indicate progressive reduction in muscle mass, muscle strength and function that affects older people. Sarcopenia is derived from the Greek word “sarx” for flesh and “penia” for loss (M.S. John Pathy 2006). This term was first used by Rosenberg in 1988 at a symposium on nutritional status and body composition to bring awareness and draw attention to this significant but then understudied problem of aging (M.S. John Pathy 2006). Sarcopenia is now acknowledged as an important geriatric syndrome and is considered one of the hallmarks of aging process (Cruz-Jentoft, et al. 2010b). Research on the process, causes, consequences, management and treatment of age-related muscle loss (mass, strength and quality) have exploded since the 1990’s (Janssen 2010; Schranger M 2003).

Sarcopenia results in unfavourable and detrimental effects on an older person’s physical function. Muscle mass decrease is probably the single most frequent cause of late-life disability among older people. It is directly responsible for functional impairment with loss of strength, and increased likelihood of falls and fractures (Y Rolland 2008). As muscles account for 60% of the body protein stores, the reduction in lean body mass has other health effects independent of its functional consequences (Y Rolland 2008). A number of physiological functions that take place within the muscle tissues have an essential role in human metabolism. For example, muscles are important body protein reserves and energy that can be used in extreme conditions such as stress or malnutrition; amino-acids can be mobilised during acute infections and are also used as building blocks for antibodies while hormones are produced and catabolised within the muscle tissue (M.S. John Pathy 2006). In other words, reduction in muscle mass has an adverse impact on metabolic adaptation and
immunological response to disease. Nevertheless, there remains considerable unexplained variation in muscle mass and strength among older people which may partly be explained by the observation that muscle mass and strength in later life reflect not only the rate of loss but also the peak attained earlier in life (A A Sayer 2008; M.S. John Pathy 2006). Thus, a life course model of sarcopenia will enable us to understand sarcopenia, its influences and develop effective interventions (A A Sayer 2008). This is shown in Figure 1.

Fig. 1. A life course model of sarcopenia.

Taking all these into account, sarcopenia is now one of the main focal points in aging research; drawing attention to its epidemiology, causes, consequences as well as health care costs. Increasing awareness of sarcopenia and promoting health enhancing strategies to overcome sarcopenia offers numerous benefits. This chapter provides an overview of the current literature on sarcopenia in older people.

2. Definition of sarcopenia

Sarcopenia is now defined as a geriatric syndrome characterised by progressive and generalised loss of skeletal muscle mass, strength and quality associated with ageing (Cruz-Jentoft, et al. 2010b). Sarcopenia is also associated with multiple contributing risk factors through a common and complex path, with a risk of adverse outcomes such as increased frailty and physical and mobility disability leading to loss of dependence, poor quality of life, increased healthcare costs and ultimately death (Cruz-Jentoft, et al. 2010b; M.S. John Pathy 2006; Y Rolland 2008).

Despite agreement in the conceptual definition of sarcopenia, the consensus on the operational definition of sarcopenia has yet to be reached. The definition of sarcopenia has been thoroughly discussed and the pooled consensus is that sarcopenia is mainly, but not only an age-related condition defined by the combined presence of reduced muscle mass and muscle function (Cruz-Jentoft, et al. 2010a; Muscaritoli, et al. 2010).

The European Working Group on Sarcopenia in Older People (EWGSOP) developed a practical clinical definition and consensus diagnostic criteria for age-related sarcopenia.

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(Cruz-Jentoft, et al. 2010a). The EWGSOP included representatives from four participant organisations i.e. the European Union Geriatric Medicine Society (EUGMS), the European Society for Clinical Nutrition and Metabolism (ESPEN), the International Associations of Gerontology and Geriatrics -European Region (IAGG-ER) and the International Association of Nutrition and Aging (Valderrama-Gama, et al.). The EWGSOP recommends using the presence of both low muscle mass and low muscle function (strength or performance) for the diagnosis of sarcopenia (Cruz-Jentoft, et al. 2010a). The diagnosis requires the presence of criterion 1 and the presence of either criterion 2 or 3 (see Table 1).

### Table 1. Criteria for the diagnosis of sarcopenia

<table>
<thead>
<tr>
<th>1.</th>
<th>Low muscle mass</th>
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<tbody>
<tr>
<td>2.</td>
<td>Low muscle strength</td>
</tr>
<tr>
<td>3.</td>
<td>Low physical performance</td>
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</table>


The EWGSOP report argues that the rationale in using two criteria is that muscle strength does not depend solely on muscle mass and the relationship between strength and mass is not linear (Cruz-Jentoft, et al. 2010a). Furthermore, defining sarcopenia in terms of muscle mass alone is too narrow and may be of limited clinical value. The EWGSOP report also categorised sarcopenia into three staging that reflects the severity of the condition: - a presarcopenia stage (characterised by low muscle mass without impact on muscle strength or physical performance), sarcopenia stage (characterised by low muscle mass and low muscle strength or low physical performance) and severe sarcopenia (characterised by low muscle mass, low muscle strength and low physical performance) (Cruz-Jentoft, et al. 2010a).

### 2.1 Measuring sarcopenia – The quantitative approach

The measurement variables include muscle mass, strength and physical performance. Age-related decline in muscle mass has been documented by lean body mass measurements with dual X-ray absorptiometry (DXA), muscle cross-sectional areas quantified by bioimaging methods such as X-ray computed tomography (CT) and magnetic resonance imaging (MRI), estimation of the volume of fat and lean body mass using bioimpedance analysis (BIA) and finally anthropometric measurements (i.e. calculations based on mid-upper arm circumference and skin-fold thickness) (M.S. John Pathy 2006). DXA is a better method for measuring muscle mass than bioelectric impedance and anthropometric measurements. DXA has the advantage of providing precise estimates of skeletal lean mass and being non-invasive compared to other accurate laboratory-based methods such as neutron activation and $^{40}K$ counting (M.S. John Pathy 2006). However, DXA is not portable and cannot be used in large-scale epidemiological studies. BIA may be considered as a portable alternative to DXA (Cruz-Jentoft, et al. 2010a). Muscle strength can be measured using isometric hand
grip. Muscle strength alone has been shown to be the most useful indicator of age-related changes in muscle for use in clinical practice (Hairi NN 2010). Grip strength is a good simple measure of muscle strength and correlates with leg strength (Cruz-Jentoft, et al. 2010a). Other measures of muscle strength include knee flexion/extension and peak expiratory flow (PEF) (Cruz-Jentoft, et al. 2010a). With regards to physical performance, a wide range of tests are available including Tinetti Performance Oriented Mobility Test, Gait Speed, Functional Independence Measure and the Timed Get-Up-and-Go (TGUG) test (Guralnik and Luigi 2003). Cut-off points depend upon the measurement technique chosen and on the availability of reference studies. The EWGSOP recommends the use of normative (healthy young adult) rather than other predictive reference populations (Cruz-Jentoft, et al. 2010a).

To date, sarcopenia has not been included in common classifications of disease (i.e. International Classification of Diseases), although some recent initiatives are trying to move in this direction.

3. Aetiology and pathogenesis of sarcopenia

The aetiology of sarcopenia is multifactorial (Cruz-Jentoft, et al. 2010b; Lang, et al. 2010; Y Rolland 2008). Multiple risk factors contribute to the development and progression of sarcopenia. These risk factors can be grouped into several categories such as constitutional factors, the aging process, certain life habits such as decreased protein intake, disuse or poor physical activity including lack of exercise, the use of tobacco and alcohol intake, changes in living conditions such as prolonged bed rest and immobility and chronic health conditions (Cruz-Jentoft, et al. 2010b). Table 2 shows the risk factors of sarcopenia.

The pathogenesis of sarcopenia is part of a complex process of age-related changes in musculoskeletal cellular as well as tissue structure and function (Doherty 2003; Lang, et al. 2010). Social and lifestyle behaviours such as physical inactivity, smoking, poor diet, being obese, as well as age-related hormonal, neurological, immunological and metabolic factors are important risk factors (M.S. John Pathy 2006). Genetic susceptibility also plays a role in sarcopenia formation (Muzcaritoli, et al. 2010). The putative causes of sarcopenia have been categorised into “intrinsic” and “extrinsic” factors (M.S. John Pathy 2006; Muscaritoli, et al. 2010). Reductions in anabolic hormones (testosterone, estrogens, growth hormones, insulin like growth factor-1), increases of apoptotic activities in the myofibers, increases of proinflammatory cytokines (e.g. TNF-α, IL-6), oxidative stress due to accumulation of free radicals, changes of the mitochondrial function of muscle cells and a decline in the number of α-motoneurons are some of the intrinsic factors involved (Lang, et al. 2010; Muscaritoli, et al. 2010). Deficient intake of energy and protein, reduced intake of vitamin D, acute and chronic co-morbidities and reduced physical activity are some of the extrinsic conditions leading to sarcopenia (Cruz-Jentoft, et al. 2010b; Muscaritoli, et al. 2010). Figure 2 shows the factors contributing to sarcopenia and its consequences.

What is not known is which factors or pathways are relatively more or less important with regards to the severity and rate of development of sarcopenia components; muscle mass, strength and quality. Each factor potentially contributes differently to the loss of muscle mass, strength and quality and it is likely that there is considerable individual variability in the interactions of these factors (M.S. John Pathy 2006).
### Factors, Aging Process, Chronic Health Conditions

<table>
<thead>
<tr>
<th>FACTORS</th>
<th>AGING PROCESS</th>
<th>CHRONIC HEALTH CONDITIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional</td>
<td><em>Increase muscle turnover</em></td>
<td>Cognitive impairment</td>
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<tr>
<td>Female</td>
<td>↑ Catabolic stimuli</td>
<td>Mood disturbances</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>↑ Protein degradation</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Genetic susceptibility</td>
<td>Low grade inflammation</td>
<td>Heart Failure</td>
</tr>
<tr>
<td></td>
<td>↓ Anabolic stimuli</td>
<td>Liver Failure</td>
</tr>
<tr>
<td></td>
<td>↓ Protein synthesis</td>
<td>Renal Failure</td>
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<tr>
<td></td>
<td></td>
<td>Respiratory Failure</td>
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<tr>
<td></td>
<td></td>
<td>Osteoarthritis</td>
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<tr>
<td></td>
<td></td>
<td>Chronic Pain</td>
</tr>
<tr>
<td>Lifestyle</td>
<td><em>Reduced number of muscle cells</em></td>
<td>Obesity</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>↑ Myostatin (↓ recruitment)</td>
<td>Catabolic effects of drugs</td>
</tr>
<tr>
<td>Low protein intake</td>
<td>↑ Apoptosis</td>
<td></td>
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<tr>
<td>Alcohol abuse</td>
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<td>Smoking</td>
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<tr>
<td>Physical inactivity</td>
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<tr>
<td>Living conditions</td>
<td><em>Hormonal deregulation</em></td>
<td></td>
</tr>
<tr>
<td>Starvation</td>
<td>↓ Testosterone, DHEA production</td>
<td></td>
</tr>
<tr>
<td>Bed rest</td>
<td>↓ Oestrogen production</td>
<td></td>
</tr>
<tr>
<td>Immobility deconditioning</td>
<td>↓ 1-25 (OH)₂ vitamin D</td>
<td></td>
</tr>
<tr>
<td>Weightlessness</td>
<td>↑ Thyroid Function</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ Growth hormone, IGF-1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ Insulin resistance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Changes in neuromuscular system</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ CNS input (loss of α- motor neurons)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuromuscular disjunction</td>
<td>Cancer ?</td>
</tr>
<tr>
<td></td>
<td>↓ Ciliary neurotrophic factor</td>
<td>Chronic inflammatory Disease?</td>
</tr>
<tr>
<td></td>
<td>↓ Motor unit firing rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Mitochondrial dysfunction</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ Peripheral vascular flow</td>
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</table>


Table 2. Risk factors of sarcopenia

### 4. Functional consequences of sarcopenia

Age-related loss of muscle mass and strength result in decreased functional limitation and physical disability among older people. Using the Nagi Model of Disablement pathology (e.g. sarcopenia) first leads to impairment such as lower extremity weakness (Steven M Albert and Vicki A Freedman 2010). When this crosses some threshold, functional impairment begins to show (which is measurable via gait speed below age-sex appropriate norm) and this in turn will lead to physical disability, e.g. needing help to cross the street (Steven M Albert and Vicki A Freedman 2010). This is as shown in Figure 3.
Recent cross sectional and longitudinal studies have shown that loss of muscle mass and/or strength increase the risk of poor physical function among older people (A.B. Newman, et al. 2003; I Janssen 2006; M.J. Delmonico, et al. 2007). However, due to the various operational definitions used, the relationship between age-related muscle mass and poor physical function has not been consistent. A recent study by Hairi et al. showed that in older men, low muscle strength, low muscle mass and low muscle quality (specific forces) are associated with physical disability in basic Activities of Daily Living (ADLs)(Hairi NN 2010) (Table 3).
The relationship between age-related muscle changes and poor physical function is complex. Muhlberg and Siber described three possible “vicious loops” that involve feedback from physiological and behavioural systems. The “vicious loops” are the immobilization loop, the nutritional loop and the metabolic loop (M.S. John Pathy 2006). The vicious loop between sarcopenia and immobilization is described as: sarcopenia → neuromuscular impairment → falls and fractures → immobilization → sarcopenia. The second loop is the “nutritional” vicious loop between sarcopenia and malnutrition: sarcopenia → immobilization → decline of nutrition skills (empty refrigerator) → malnutrition impaired protein synthesis → sarcopenia. Finally, the “metabolic” vicious loop between sarcopenia and the decline of protein reserve in the body: sarcopenia → decline of protein reserve of the body → diminished capacity to meet the extra demand of protein synthesis associated disease and injury → sarcopenia.

5. Prevention and treatments for sarcopenia

As sarcopenia (loss of muscle strength, muscle mass and quality) was found to be associated with poor physical function, improvements in muscle strength would prevent...
immobilization and break the cycle. Physical activity, especially resistance exercise attenuates and may reverse age associated decreases in muscle strength as well as improve physical agility. Other interventions such as combinations of exercise with dietary supplements, hormone replacement, anti-inflammatory and other pharmacological treatments are still being investigated.

5.1 The role of exercise and increased physical activity

Exercise stimulates the release of growth hormones that promotes healthy muscle mass (M.S. John Pathy 2006). Although any exercise is better than no exercise at all, in terms of preventing loss of lean muscle mass, resistance exercise is preferred (Y Rolland 2008). Resistance exercise increases muscle protein synthesis rate over proteolysis and results in a net increase in contractile protein mass and hypertrophy of muscle fibres. Strength training being part of resistance exercise remains highly effective in maintaining muscular strength throughout life (Mühlberg and Sieber 2004). However, in older people, strength levels fall far more rapidly, independent of training (Y Rolland 2008). This is due to the changes in hormones such as testosterone and growth hormones which decline more rapidly and dramatically after the age of 60 years. Reduction in the circulation of these hormones will result in a shift in the balance between muscle protein synthesis and protein breakdown (Borst 2004). The vast majority of the literature on prevention and treatment of sarcopenia is related to the effects of exercise. These studies have demonstrated that progressive resistance training in older people results in substantial improvements in muscle strength and mass (Borst 2004). The improvements in muscle strength are smaller in absolute terms but similar in relative terms, compared to the younger population. What remains unclear are issues such as optimal duration, frequency and type of resistive exercise, combinations of resistive and aerobic training, compliance and long term maintenance, adjuvant nutritional supplementation and/or pharmacologic treatment. A recent review by Borst SE suggested that resistance training is an effective intervention for increasing muscle mass and strength in older people (Borst 2004).

Additional benefits of resistance exercise include normalisation of blood pressure, improved insulin sensitivity, decreased total and abdominal fat, increased metabolic rate, prevention of bone loss, reduction of risk for falls, reduced pain and improved physical function. Other forms of exercise, such as aerobic exercises have well-established benefits on cardiovascular fitness, improving lipid profile and flexibility (M.S. John Pathy 2006). Therefore, engaging in some form of resistance training is essential to preserve and increase muscle mass and strength.

5.2 Nutritional strategies for prevention and treatment of sarcopenia

Aging is associated with a progressive reduction in food intake, which predisposes to energy-protein malnutrition. In other words, aging is associated with physiological anorexia, decrease in caloric intake and weight loss (Marcell 2003). The decline in food intake that happens even in healthy older people has been termed “anorexia of ageing” (M.S. John Pathy 2006). Studies have shown that low dietary energy intake is common among healthy older people. Other factors that influence food intake in older people include psychological state (e.g. depression or depressive symptoms), social support and network (e.g. loneliness) and physical change (poor dentition, impaired taste and smell). Changes in
food preferences with an increased liking for sweet and protein-poor foods have also been reported among older people. Dietary factors that contribute to sarcopenia include inadequate protein intake, insufficient calorie intake and low level metabolic acidosis (Paddon-Jones, et al. 2008). Metabolic efficiency in older people has been shown to be lower. Older people have a higher rate of protein catabolism and needing a higher requirement for dietary protein than their younger counterparts (Paddon-Jones, et al. 2008). There are research findings to support the ability of dietary protein to stimulate protein synthesis in older people. A review paper by Borst concludes that there is insufficient research to define an optimal value for protein ingestion (moderate intake or high intake) (Borst 2004). There are also uncertainties linking high protein intake to increased risk of impaired kidney function in healthy older people. This is further complicated by the fact that renal function decreases with age.

Older people have reduced food intake and increased protein requirements. Therefore, older people should strive to ensure adequate intake of protein (leucine-enriched amino acids and possibly creatine) from a variety of sources, accompanied by an increase in fruits and vegetables.

5.3 Hormone replacement and management of sarcopenia

Aging is accompanied by declining levels of many essentials hormones in the body, especially growth hormone (GH) and testosterone. The Reproductive-Cell Cycle Theory of Aging is a new theory explaining the process of aging (Bowen and Atwood 2004). This theory proposes that the rate of aging is synonymous with the rate of change. The rate of change/aging is most rapidly seen during the fetal period. Reproductive hormones are known to regulate mitogenesis (process by which a cell divides to form two daughter cells), and differentiation (process by which a cell becomes specialised to perform unique functions), hence aging is primarily regulated by these hormones (Bowen and Atwood 2004). In other words, the Reproductive-Cell Cycle Theory of Aging proposes that the hormones that regulate reproduction, promote growth and development early in life but in later life become dysregulated and drive senescence (Bowen and Atwood 2004).

Loss of testosterone is associated with loss of muscle mass and strength and decreased bone mineral density, thus increasing the risk of functional limitation, disability, fracture and falls (Lang, et al. 2010). Menopause is associated with loss of bone mass and also muscle strength (M.S. John Pathy 2006). GH stimulates growth during early life and is required for maintenance of muscle and bone in adulthood. GH exerts most of its action through insulin like growth factor (IGF-I). These are critical hormones in maintaining muscle and bone mass (Borst 2004). Without adequate levels it is impossible for anyone to maintain lean body mass, regardless of how well they eat or exercise. Secretion of GH is impaired in older people.

A recent review by Borst SE suggested that testosterone replacement in elderly hypogonadal men produces only modest increases in muscle mass and strength, which are observed in some and not all studies (Borst 2004). Furthermore, higher doses have not been given for fear of accelerating prostate cancer. With regards to GH, this review shows that growth hormone replacement in older people produces a high incidence of side effects, does not increase strength and does not augment strength gains resulting from resistance training (Borst 2004).

A review on hormone (testosterone or growth hormone) replacement to the older people produces only modest increases in muscle mass and strength in some but not all studies and
the risks associated with hormone replacements are still not clear (Borst 2004). To date, exercise and more importantly resistance training remains the most effective intervention for increasing muscle mass and strength in older people.

6. A diagnostic approach to sarcopenia

The EWGSOP proposed a practical approach to screen for sarcopenia in clinical practice (Cruz-Jentoft, et al. 2010a). This is as shown in Figure 4. This algorithm is based on gait speed measurement with a cut-off point of > 0.8 m/s.

7. Conclusion

Loss of muscle mass and strength with age is a slow but progressive process with undesirable consequences. The research in sarcopenia has shown that sarcopenia is linked to multiple causations: the aging process itself, genetic susceptibility, lifestyle practices, changes in living conditions and numerous chronic diseases. Sarcopenia also represents a set of unfavourable outcomes, such as the primary outcomes of loss of muscle mass, strength and quality, and secondary outcomes which cause further functional limitation, loss of mobility and increased risk of disability, falls and fractures. Current research has shown promising results on the assessment of sarcopenia and practical approach to the management of sarcopenic patients and/or patients at risk of sarcopenia in terms of prevention as well as its treatment. Sarcopenia is firmly on the agenda for research into ageing and needs to be recognised in routine clinical practice.


Fig. 4. EWGSOP suggested algorithm for screening and case finding of sarcopenia
8. Acknowledgements

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9. References


With the baby boomer generation reaching 65 years of age, attention in the medical field is turning to how best to meet the needs of this rapidly approaching, large population of geriatric individuals. Geriatric healthcare by nature is multi-dimensional, involving medical, educational, social, cultural, religious and economic factors. The chapters in this book illustrate the complex interplay of these factors in the development, management and treatment of geriatric patients, and begin by examining sarcopenia, cognitive decline and dysphagia as important factors involved in frailty syndrome. This is followed by strategies to increase healthspan and lifespan, such as exercise, nutrition and immunization, as well as how physical, psychological and socio-cultural changes impact learning in the elderly. The final chapters of the book examine end of life issues for geriatric patients, including effective advocacy by patients and families for responsive care, attitudes toward autonomy and legal instruments, and the cost effectiveness of new health care technologies and services.

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