SARCOPENIA

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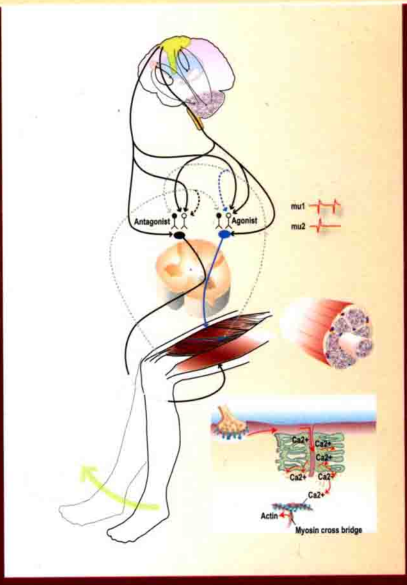
ALFONSO J. CRUZ-JENTOFT AND JOHN E. MORLEY



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Sarcopenia

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Preface

Over the past few years, sarcopenia has moved rapidly from being a concept used by a couple of academics to one that is widely explored in journals and scientific meetings. All aspects of sarcopenia, from basic science to clinical applicability, are now an extremely active area of research and clinical practice for those working in geriatric medicine, nutrition, epidemiology, basic biological research and many other disciplines. Its recent emergence, together with the conceptualization of frailty, is a step forward in the quest to identify and prevent the unwelcome disabilities that accompany many people in their last years of life.

Thus, the moment has come to summarize, to define where we are and where we are going, to stand on solid ground for the next step – or jump. This book is intended to be a clear and precise reference work for those physicians or researchers interested in having a global, yet detailed understanding of such a complex topic. Rooted in basic science and in the critical use of diagnostic tools, the book also covers clinical aspects, trying to identify the role of sarcopenia in the complex arena of age, disease, and physical disability.

To accomplish this task, we have carefully selected authors from both Europe and the United States, as the approach to sarcopenia differs slightly in each continent. This wide range of authors allows the reader a clearer picture of the issues involved. Of course, all of the authors, with no exception, are leading experts in the field. As editors we are extremely grateful for their enthusiastic acceptance to contribute to this book, the high quality of their submissions, and their patience in adapting their chapters to fit the book.

After describing the epidemiological challenge that sarcopenia brings to current geriatric care, and reviewing the definitions of the word, the first chapters, explore the biological aspects of muscle and the central nervous system and their relation with movement and function. Sarcopenia is then explored in the context of the individual, from a lifetime and a syndromic approach, looking at the adverse effects it has on health and function. An analysis of the intimate relations between sarcopenia, cachexia, frailty and bones opens the door to a description of the complexity of measuring different parameters linked to muscle mass and function. Finally, the door opens to intervention, from nutrition and exercise to drugs, ending with a difficult question: can sarcopenia (and thus disability) really be prevented?

We believe that we have produced a state-of-the-art textbook with a comprehensive approach to sarcopenia. We hope that it will be a valuable reference tool, not only for experts, but also for those who are interested in starting their own research in this area and those who wish to develop their own criteria about such a promising field within geriatric medicine.

Contents

CHAPTER 1

Epidemiology of Muscle Mass Loss with Age

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INTRODUCTION

The development of new body composition methods in the early 1970s and 1980s led to more research on this topic, including the study of differences in body composition between young and older persons. These initial studies were followed by much larger studies covering a wide age range investigating how body composition varied across the life span. Variations in lean body mass and fat-free mass were described between age groups. These studies served as the important scientific basis for developing the concept Sarcopenia. Sarcopenia was defined as the age-related loss of muscle mass [1]. The term is derived from the Greek words *sarx* (flesh) and *penia* (loss). The development of this concept further stimulated research in this specific body composition area. More recently, large-scale studies among older persons have included accurate and precise measurements of skeletal muscle mass. Moreover, these measurements have been repeated over time, enabling the sarcopenia process to be studied.

This chapter will discuss the results of epidemiological studies investigating the age-related loss of skeletal muscle mass. First, several cross-sectional studies will be presented comparing the body composition between younger and older persons. Then prospective studies will be discussed investigating the change in body composition with aging. The chapter will conclude with the results of more recent, prospective studies that precisely measured change in skeletal muscle mass in large samples of older persons.

MUSCLE MASS DIFFERENCES BETWEEN AGE GROUPS

Comparisons between young and older men and women with regard to muscle size have been made in several small studies. The results showed that healthy women in their 70s had a

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33% smaller quadriceps cross-sectional area as obtained by compound ultrasound imaging compared to women in their 20s [2]. Using the same methodology and age groups, healthy older men had a 25% smaller quadriceps cross-sectional area [3]. In a study investigating thigh composition using five computed tomography scans of the total thigh, smaller muscle cross-sectional areas were observed in older men compared to younger men even though their total thigh cross-sectional area was similar. The older men had a 13% smaller total muscle cross-sectional area, 25.4% smaller quadriceps and 17.9% smaller hamstring cross-sectional area [4]. Using magnetic resonance imaging of the leg anterior compartment, muscle area was measured in young and older men and women [5]. The older persons had a smaller area of contractile tissue; 11.5% less in women and 19.2% less in men; compared to the young persons. These data, obtained by different body composition technologies, clearly showed a smaller muscle size in older persons compared to young persons. The observed differences in muscle size between age 20 and age 70 suggested a loss of skeletal muscle mass of about 0.26% to 0.56% per year.

The amount of non-muscle tissue within the muscle was also assessed using five computed tomography scans of the thigh in 11 elderly men and 13 young men [4]. Older men had 59.4% more non-muscle tissue within the quadriceps and 127.3% within the hamstring muscle. In a similar study, the amount of non-muscle tissue in older men was 81% higher in the plantar flexors as compared to young men [6]. Thus, apart from the smaller muscle size in old age, these studies suggested that the composition of the muscle also changed with aging, leading to less 'lean' muscle tissue in old age.

With the greater availability of body composition methods such as bioelectrical impedance and dual-energy x-ray absorptiometry over time, cross-sectional data on muscle size in large study samples including a broad age range have been collected. Examples of these studies using lean mass from DXA (the non-bone, non-fat soft tissue mass) and fat-free mass from bioelectrical impedance, presented by 10-year age groups of men, are presented in Figure 1.1 [7,8]. Older age groups had a lower total body fat-free mass, lower

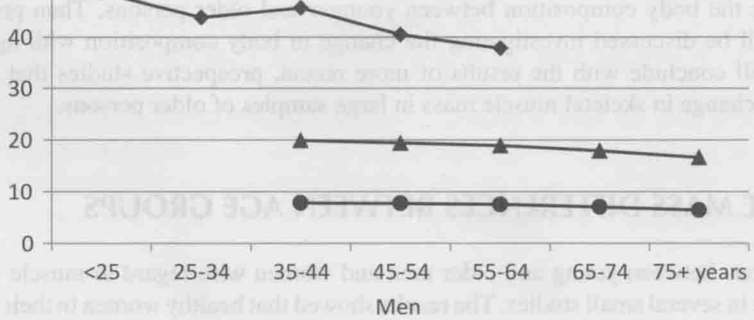

Figure 1.1 Differences in fat-free mass and lean mass using different body composition methodologies between men of different age groups. BIA = bioelectrical impedance. DXA = dual-energy x-ray absorptiometry. Based on references 7 and 8.

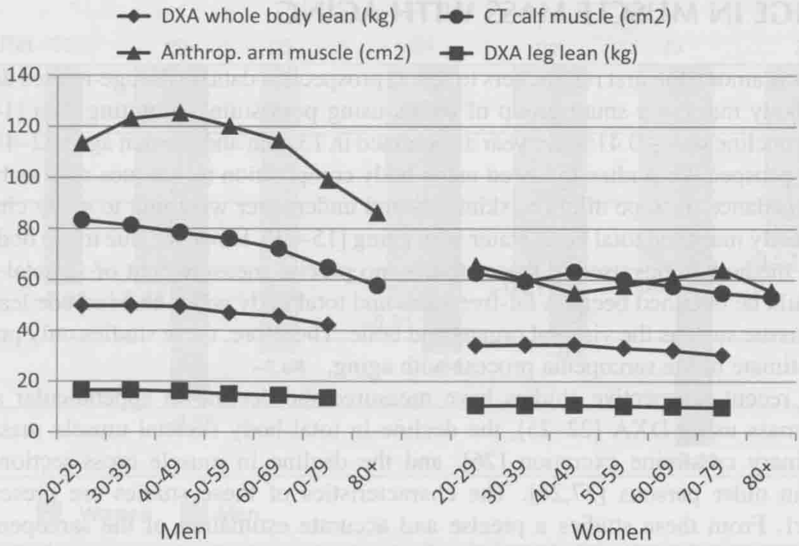

Figure 1.2 Differences in muscle cross-sectional area and lean mass using different body composition methodologies between men and women of different age groups. DXA = dual-energy x-ray absorptiometry. CT = computed tomography. Anthrop. = anthropometry, using arm circumference and triceps skinfold. Based on references 9–11.

total body lean mass, and lower arm and leg lean mass. Figure 1.2 presents the differences in muscle size between 10-year age groups in men and women. With increasing age group, the data suggested a lower whole body lean mass and leg lean mass as assessed by DXA [9], a smaller arm muscle cross-sectional area (from anthropometric measures [10]) and a smaller calf muscle cross-sectional area (from peripheral qualitative computed tomography [11]). These cross-sectional data derived from samples from Italy, Australia, India, Japan, and the USA consistently suggested a decline in muscle size with aging. These data also suggested a steeper decline in muscle size with aging in men compared to women.

Cross-sectional data from a sample of 72 women aged 18 years to 69 years suggested a strong correlation between age and the amount of low density lean tissue as assessed by a computed tomography scan of the mid-thigh. The density of muscle tissue as assessed by computed tomography is indicative of the amount of fat infiltration into the muscle [12]. Higher age was associated with greater amounts of low density lean tissue (correlation coefficient = 0.52 [13]). This result again suggested a greater fat infiltration into the muscle with increasing age.

These cross-sectional data, however, should be interpreted carefully as cohort and period effects, and not aging per se, may have caused the observed differences in muscle size and muscle composition between the age groups. For example, well-known cohort differences in body height, a strong determinant of muscle size, may partly explain the lower muscle mass in older persons compared to younger persons. In addition, period differences in lifestyle (e.g. sports participation and diet) and job demands may have differentially affected muscle size and muscle composition between age groups. Therefore, prospective data are preferred to investigate the change in muscle mass with aging.

CHANGE IN MUSCLE MASS WITH AGING

Forbes was among the first researchers to report prospective data on the age-related decrease in lean body mass in a small group of adults using potassium^{40} counting data [14]. The reported decline was −0.41% per year as obtained in 13 men and women aged 22–48 years.

Many prospective studies followed using body composition techniques such as bioelectrical impedance, isotope dilution, skinfolds and underwater weighing to study change in fat-free body mass and total body water with aging [15–21]. However, due to the body composition methodologies used in these studies, no precise measurement of skeletal muscle mass could be obtained because fat-free mass and total body water also include lean, non-muscle tissue such as the visceral organs and bone. Therefore, these studies only provide a crude estimate of the sarcopenia process with aging.

More recent prospective studies have measured the decline in appendicular skeletal muscle mass using DXA [22–25], the decline in total body skeletal muscle mass using 24-h urinary creatinine excretion [26], and the decline in muscle cross-sectional area by CT in older persons [27,28]. The characteristics of these studies are presented in Table 1.1. From these studies a precise and accurate estimation of the sarcopenia process can be obtained. The relative annual decline in skeletal muscle mass was estimated to be between −0.64 and −1.29 % per year for older men and between −0.53 and −0.84 % per year for older women (Figure 1.3). In older persons the absolute as well as the relative decline of skeletal muscle mass with aging was larger in men compared to women.

Table 1.1 Characteristics of prospective studies investigating the age-related change in skeletal muscle mass in older men and women

Reference	N and sex	Age (mean (SD)) or range (y)	Mean follow-up time (y)	Body composition method	Muscle measurement
27	12 men	71.1 (5.4)	8.9	CT	Mid-thigh total anterior muscle cross-sectional area
28	813 men 865 women	70–79	5	CT	Mid-thigh muscle cross-sectional area
25	26 women	75.5 (5.1)	2.0	DXA	Leg skeletal muscle mass
24	1129 men 1178 women	70–90	5	DXA	Leg skeletal muscle mass
22	24 men 54 women	60–90	4.7	DXA	Appendicular skeletal muscle mass
23	62 men 97 women	71.6 (2.2) 71.4 (2.2)	5.5	DXA	Appendicular skeletal muscle mass
26	52 men 68 women	60.4 (7.9) 60.4 (7.4)	9.7	24-h urinary creatinine excretion	Total body skeletal muscle mass

SD = standard deviation, CT = computed tomography, DXA = dual-energy x-ray absorptiometry

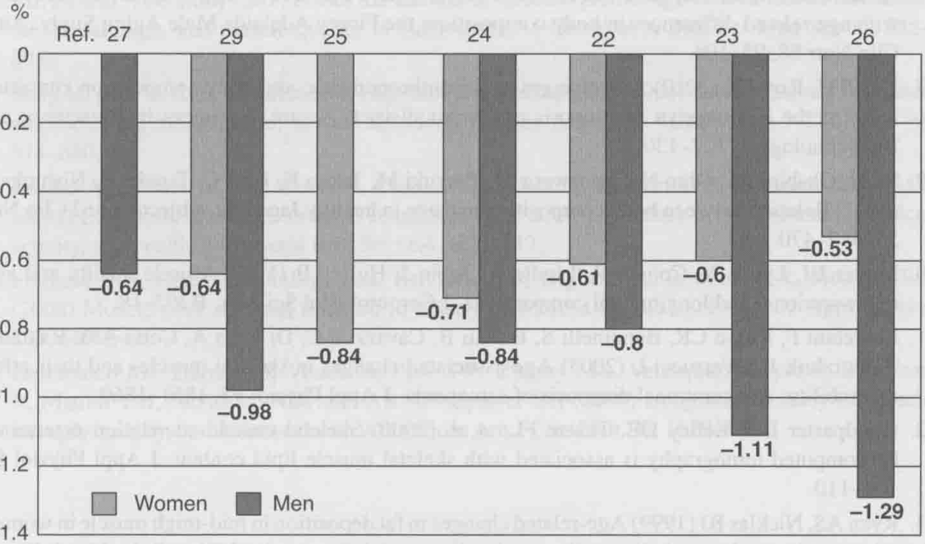

Figure 1.3 Annual decline (%) in skeletal muscle mass in older men and women from prospective studies with follow-up times from 2 to 9.7 years.

Limited data are available on the prospective change in muscle fat with aging. Data from the Health, Aging and Body Composition Study showed an increase in intermuscular fat at the mid-thigh of 3.1 cm^2 in older men and 1.7 cm^2 in older women during the 5-year follow-up [28]. This translated to an annual increase of 9.7% in men and 5.8% in women. This increase was paralleled by a decline in subcutaneous fat at the mid-thigh and shows specifically the increasing fat infiltration into muscle tissue with increasing age.

From these body composition studies it can be concluded that the amount of skeletal muscle mass declines substantially with aging. At the same time, the composition of the muscle changes and a greater fat infiltration into the muscle occurs. It is important to understand the potential impact of these changes on healthy aging.

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CHAPTER 2

Definitions of Sarcopenia

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THE ORIGINS OF THE WORD 'SARCOPENIA'

Sarcopenia has rapidly become a common term in geriatrics and gerontology, both in academic forums and in clinical practice. This is somehow surprising, as the word sarcopenia was introduced quite recently, trying to improve understanding of a previously eluding concept. In fact, while sarcopenia seems to be common and has huge personal and societal costs, sarcopenia still has no broadly accepted definition, diagnostic criteria, ICD-9 codes, or treatment guidelines. This chapter will review the still changing concept of sarcopenia, and recent efforts that are trying to agree on a definition that may reach wide consensus and be useful both for research and clinical practice.

In 1988, a meeting was convened in Albuquerque (USA) to discuss the assessment of health and nutrition in older populations. Rosenberg, who is accredited for the first use of the word, noted that 'no decline with age is more dramatic or potentially more functionally significant than the decline in muscle mass' and suggested that to provide recognition by the scientific community this phenomenon needed a name. He proposed a name derived from the Greek roots *sarx* for flesh and *penia* for loss [1].

Although the word chosen only described muscle mass, from the very beginning it was acknowledged that the consequences of muscle mass loss affected ambulation, mobility, nutrient intake and status, and functional independence.

DEFINITIONS BASED ON MUSCLE MASS

Availability and standards on techniques that measure muscle mass (or lean body mass) were initially far more advanced than measures of other parameters involved in sarcopenia. It is thus not surprising that most major epidemiological studies fixed to a strict definition of sarcopenia as loss of muscle mass.

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