Chapter 6
Skeletal Muscle Aging Atrophy: Assessment and Exercise-Based Treatment

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1 Introduction

In 2019, there were 703 million persons aged 65 years or over in the world. In 2050, the number of older persons will double to 1.5 billion. From 1990 to 2019, the number of people aged 65 years or over increased from 6% to 9%. This proportion will increase to 16%, meaning that one in six people in the world will be aged 65 years or over in 2050 [1].

Aging is associated with high cell damage occurrence. Aging leads to a decrease in physical and mental capacity and a growing risk of disease. These changes, however, are neither linear nor consistent, and they are only loosely associated with a

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person's age in years. While some 70 year-olds enjoy perfect health and functioning, other 70 year-olds are frail and require significant help from others [2].

With aging, there is a loss of skeletal muscle mass (skeletal muscle atrophy called sarcopenia) that decreases muscular strength and physical performance, that also influences cognitive status. Assessing these changes becomes vital in an older adult. In this line, there are several strategies which have been proposed to combat skeletal muscle atrophy due to aging, such as physical exercise, nutritional supplements, or drugs. Although some researchers showed the combination of these strategies, we will focus in this chapter only on the physical activity methods. This chapter aims to demonstrate the most used existing test/machines to evaluate the loss of skeletal muscle mass due to aging and, consequently, the decrease in muscle strength and physical performance. It will also propose physical exercise as an "effective drug" to counteract the effects produced by the loss of muscle mass and its consequences due to aging.

2 Skeletal Muscle Aging Atrophy

A young person has 48% muscle mass, 19% fat, and 33% non-muscle fat-free mass (FFM) at the age of around 22 years-old. On the other hand, a subject near the age of 78 years-old has a body composition of 25% muscle mass, 35% fat, and 40% of non-muscle FFM [3].

This decrease in global skeletal muscle mass (mainly reflected in the lower extremities) related by aging may be the product of a reduction in the synthesis pathways and through an increase in the degradation pathways of skeletal muscle proteins. In protein synthesis, the primary signaling networks that been investigate are the insulin-like growth factor 1 (IGF-1) axis and the protein kinase B/mammalian target of rapamycin/ribosomal S6 kinase (Akt/mTOR/S6) pathway. On the other hand, in protein degradation, there are several systems such as apoptosis, calpains, autophagy, ubiquitin-proteasome and oxidative stress. Also, there is interplay between sarcopenia and chronic inflammation [4–8].

At the level of muscle fibers, there are many cellular and molecular changes that contribute to muscle aging. For instance, reduced number of satellite cells, decreased number of muscle fibers (predominantly type II), reduced myosin protein content, reduced number of mitochondria, increased inter- and intra-muscular adipose tissue, disruption of excitation-contraction coupling, and others [9]. According to all of these changes in skeletal muscle due to aging, an older person shows a blunted muscle protein synthetic response to anabolic stimuli like amino acid administration and physical activity when compared with the effects seen in young persons. This condition is known as anabolic resistance [10]. Therefore, an older person will have to have a more significant anabolic stimulus to obtain beneficial responses at the muscular level.

The decrease in skeletal muscle mass loss due to aging is called sarcopenia. Irwin H. Rosenberg was the first to propose the sarcopenia term at a meeting in

1988. The sarcopenia Greek meaning is s*arx* for flesh and *penia* for loss [11]. Initially, the concept of sarcopenia was coined for the decrease of muscle mass and function [11], although most people associate it with only skeletal muscle mass loss.

Cruz-Jentoft and Sayer presented a reasonable timeline on the international definition of sarcopenia [12]. In 2010, the EWGSOP (European Working Group on Sarcopenia in Older People) defined sarcopenia using muscle mass, muscle strength, and physical performance (cut-offs not specified). In 2011, the International Working Group on Sarcopenia and Society of Sarcopenia, Cachexia, and Wasting Disorders (SSCWD) defined the disease using muscle mass and physical performance, with defined cut-offs. The SSCWD used the phrase sarcopenia with limited mobility. In 2014, the Asian Working Group on Sarcopenia gave the same definition as the EWGSOP and also defined cut-offs for Asia. In the same year, the Foundation for the National Institutes of Health described the disease using muscle mass and muscle strength, and also defined cut-offs, using physical performance as an outcome. The EWGSOP updated its definition in 2019 (EWGSOP2) with cut-offs determined, using physical performance to assess the severity of the condition [12].

3 Basic and Instrumental Activities of Daily Living Assessment

The geriatric assessment allows knowing the baseline situation of the subjects, evaluates the impact of diseases, and establishes specific treatments. The evaluation of the health condition of the older people includes assessment scales of basic Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL), physical and functional assessment scales, and instruments that assess the cognitive state (Table 6.1) [25].

3.1 Barthel Index

Mahoney and Barthel created this index in 1955 [13]. They measured the evolution of subjects with neuromuscular and skeletal muscle processes in a hospital for chronic patients in Maryland and published the results 10 years later. This was modified in 1979. The fundamental change occurs in the item of transfer by wheelchair to bed, which changes to the transfer of armchair to bed [13]. This index comprises 10 elements in their original version, with each item receiving a score of zero if the subject is unable to perform the task or a variable score between 5, 10, and 15 points, which reflect independence or intervals of relative autonomy for tasks. The values assigned to each activity are based on the time and amount of physical help required if the patient cannot perform that activity. Full credit is not granted for an activity if the subject needs help and/or minimal supervision [13].

Table 6.1 Valuation instruments in older people

Instrument	Parameters to evaluate	Interpretation
Barthel Index [13]	Basic Activities of Daily Living (ADL)	100 Independency ≥60 Slight dependency 40–55 Moderate dependency 20–35 Severe dependency <20 Total dependency
Katz Index [14]	Instrumental Activities of Daily Living (IADL)	6 = High (patient independent) 0 = Low (patient very dependent)
Lawton & Brody [15]	Instrumental Activities of Daily Living (IADL)	0 Dependent 8 Independent
Grip Strength [16]	Grip strength	In accordance with EWGSOP2∗, values <27 kg in men and <16 kg in women is associated with sarcopenia
Gait Speed [16]	Gait speed	In accordance with EWGSOP2∗, ≤0.8 m/s indicates low functional performance and association with sarcopenia
Timed Up and Go [17]	Dynamic balance	≤10 segments normal 11–19 segments slight risk of falls > 20 segments high risk of falls
Unipedal stance [18]	Dynamic balance	≥ 5 segments high risk of falls
Tinetti [19]	Dynamic balance	12 Independence
	Gait	16 Independence
Short Physical Performance Battery [20]	Static balance Dynamic balance Lower+ body strength	0–3 Severe limitations 4–6 Moderate limitations 7–9 Mild limitations 10–12 Minimal limitations The sum of the subtests has a maximum score of 12, indicates functional independence
Senior Fitness Test [21]	Lower body strength Upper body strength Aerobic capacity Superior train flexibility Superior train flexibility	Presents reference values by age range for each subtest
Mini Mental State Examination [22]	Cognitive state	30–35 Normal cognitive status 25–29 Slight deficit 20–24 Mild cognitive impairment 15–19 Moderate cognitive impairment 0–14 Severe cognitive impairment, dementia
Pfeffer Scale [23]	Cognitive state	0–2 errors: normal mental functioning 3–4 errors: mild cognitive impairment 5–7 errors: moderate cognitive impairment 8–10 errors: severe cognitive impairment
Geriatric Depression Scale [24]	Geriatric depression	0–5 Normal 6–9 Probable depression 10 or more established depression

aEWGSOP2: European Working Group on Sarcopenia in Older People 2

Environmental conditions can influence the index score since if the subject has special requirements to perform their ADL and the corresponding adaptations are not available, and therefore their score will be lower when they cannot be performed. Examples of this are the bars or handles in the bathroom, tub, and toilet. If needed and not available, the subject will not be able to perform the activity [13, 26].

Some authors have proposed reference scores to facilitate their interpretation. For example, it has been observed that an initial rating of more than 60 is related to a shorter duration of hospital stay and a higher probability of reintegrating into the community after discharge. This score seems to represent a limit [27–29].

The Barthel Index is a handy instrument in rehabilitation. Because of its validity and reliability, it is easy to apply and interpret. Its application is low cost and is useful for monitoring the evolution of subjects. It takes between 2 and 5 min, while the self-assessment is done in approximately 10 min. It can be applied by rehabilitation professionals or by other health professionals and by trained interviewers, who are trained in times requiring no longer than 1 h. It can also be self-administered, valued by third parties, or through a telephone interview [26].

3.2 Katz Index

The multidisciplinary team led by S. Katz created this index in 1958 at the Benjamin Rose Hospital in Ohio [30]. The purpose was to delimit dependence of subjects with hip fractures. It was published in 1959 under the name of the Index of Independence in Activities of Daily Living.

The purpose was to measure functionality in chronic patients and aging populations. It is a tool used to obtain important information about the prognosis and disability associated with aging [14]. In addition, it allows clinicians and researchers to assess the need for health care and determine treatment effectiveness, and it can be used as a therapeutic guide [25, 31].

The index considers performance in six essential activities: bathing, clothing, use of toilet, mobility, continence, and food consumption [30]. According to the assigned performance scores of A, B, C, D, E, F, or G, A is the most independent grade of the scale, and G is the most dependent grade. Through questions and/or observations, the evaluator forms a mental image of the patient's ADL status. The assessor determines if the patient performed his activities alone, with active personal assistance, directive assistance, or if he/she required supervision [31].

The Katz index describes a similarity between the patterns of loss and recovery of functions with the development of the infant, ordering dependence and the restoration of independence, and inverse processes, where the first capacity to recover is that of feeding and the latest are the ability to dress and bathe [30, 31].

3.3 Lawton and Brody Scale

The Lawton and Brody scale was first published in 1969 [15]. It was initially used at the Philadelphia Geriatric Center to evaluate physical autonomy and IADL in older people who may or may not be institutionalized. It is a widely used instrument internationally for IADL measurement, with the advantage of allowing analysis of each individual score used in the scale. It also allows evaluation of therapeutic plans used for older people, being sensitive in the detection of the first and most minimal signs of functional deterioration in this age group [15].

This index evaluates the functional capacity in 8 items: (i) use of the telephone, (ii) purchasing, (iii) ability to prepare food, (iv) home care, (v) doing laundry, (vi) use of means of transport, (vii) responsibility for medicines and (viii) management of economic affairs [15, 32]. The information is obtained by directly asking the subject or his/her usual caregiver. Each item is assigned a score of 0 if there is dependence and 1 point if there is independence for that activity. The total sum of points varies between 0 corresponding to maximum dependence and 8 points, which corresponds to complete independence for the operations [33].

4 Physical Performance Assessment

4.1 Grip Strength Test

The grip strength test is the simplest and recommended method for the evaluation of muscle strength in clinical practice due to its strong association with lower limb muscle strength [34]. This parameter is the maximum isometric contraction force generated around a dynamometer measured in kilograms, Newtons, pounds, or millimeters of mercury [34]. Older people commonly have difficulties with the operation of the hands and manual dexterity in tasks that require a delicate and precise grip, and the loss of the strength of the hands can affect simple everyday actions [35]. Impaired hand function occurs as a result of healthy aging and established disorders frequently found in older people, such as osteoporosis, osteoarthritis, and rheumatoid arthritis [35, 36].

For more details on this evaluation method, please see Sect. 6.2 in the hospital context."

4.2 Gait Speed Test

The gait is an intrinsic function in the human being, which is the reason why its deterioration determines the loss of dependence. The alteration in the gait speed in older people is also an indicator of increased risk of falls, fractures, and more significant morbidity and mortality [37]. Walking speed predicts the state of health and risk of future functional decline, including hospitalization and institutionalization [38]. This parameter requires a comparison with reference values that vary between 0.6 and 1.70 m/s. There is no standardized assessment consensus to evaluate this parameter. However, there are several physical performance assessment batteries that include the parameter “Short Physical Performance Battery and Senior Fitness Test”, which is described below.

4.3 Timed Up and Go Test

In the beginning, the Getup and Go test was used, which was designed as a screening instrument to detect balance changes in the population. The subject had to get up from a chair with armrests, walk 3 m, turn on himself, step back 3 m, and sit down again [39]. To make the measurement more objective, Podsiadlo and Richardson, in 1991, made a modified and timed version of the test, now called Timed Up and Go [17]. The time starts when the participant takes off from the straight back of the chair and ends when, after traveling, the circuit returns to the starting position. For its realization, the participant will use his usual or necessary technical help and will walk at a rapid pace, without running, walking at a light but safe speed [40].

Adults without neurological problems, who are independent in the natural balance and mobility tasks, perform the test in less than 10 s. Meanwhile, older people who need between 11 and 19 s to complete the activity present a slight risk of falls, and a high risk if they require more than 20 s to complete it [17].

4.4 Unipedal Stance Test

The Unipedal Stance test is used to assess static balance. For its realization, the older person must stand with his arms crossed on his chest, resting hands on shoulders, performing triple flexion of one leg at 90°, keeping in this position for as long as possible, to a maximum of 30 s. This activity is repeated 3 times, alternating the lower limb of support, considering the best time obtained [18]. An older person has a high risk of falls if he/she fails to maintain the position for a time shorter than or equal to 5 s [18, 41].

4.5 Tinetti Scale

The Tinetti scale was made in 1986 to assess the mobility of older people. Its main objective is to detect subjects with a high risk of falls, based on the two domains of gait and balance, composed of nine and seven items, respectively [42]. A zero score is assigned if the person does not achieve or maintain stability in position changes or has an inappropriate gait pattern according to the parameters established in the scale (considered abnormal). A score of 1 indicates that the individual achieves changes in position or gait patterns with compensations (the adaptive condition). A score of 2 indicates that the subject does not present difficulties for the different activities of the scale (the average condition). The maximum balance score obtained is 16 points, and the maximum gait score corresponds to 12 points. The sum of both tests provides a maximum total score of 28, with which the risk of falls is determined. Between 19 and 28 points is considered to represent a minimum risk of falls, while a score lower than 19 is regarded as a high risk of falls [19]. This instrument is mainly used in older people who live in the community and institutionalized, to assess the risk of falls and their consequent relationship with the functional alterations of each subject [43].

4.6 Short Physical Performance Battery

The Short Physical Performance Battery (SPPB), developed by Guralnik in 1994, is an instrument to be used safely in older people with or without underlying acute pathologies [20]. The SPPB consists of three tests: balance, gait speed, and getting up and sitting in a chair five times. In the first balance test, the subject must maintain three positions: feet together, semi-tandem, and tandem, following a hierarchical order of difficulty, for at least 10 s to obtain the full score of the item [20, 44]. The gait speed test is carried out so that the subject walks at his usual speed for a distance of 4 m twice, recording the shortest time. Finally, for the test to get up from the chair, the subject is asked to cross his arms over his chest and get up. If successful, the time is recorded from the moment when the subject stands for the first time until he sits at the fifth time. Each test is awarded a score in favor of the time used for each activity, where 0 corresponds to the worst performance and 4 to the best performance. A global test battery score ranging from 0 to 12 points is obtained. The low scores on this instrument have a high predictive value for a considerable amount of health consequences, including disability in the AVD, loss of mobility, disability, hospitalization, length of hospital stay, admission to nursing facilities, and mortality [45].

4.7 Senior Fitness Test

In 2001, Rikli and Jones designed the Senior Fitness Test battery to address the need to create tools that allow assessment of the physical condition of older people residing in the community [21]. It applies to older people from 60 years-old and over with different levels of physical and functional abilities. It does not require equipment or sophisticated spaces to be realized [46]. The tests that make up the battery include various components of functional capacity, this being the particularity of existing batteries that focus on only one component. It is composed of differentiated tests or evaluations: chair stand, arm curl, 6 min walk, 2 min step, chair-sit and reach, back scratch, foot up and go and body mass index [21, 47].

The chair stand test starts with the evaluation subject sitting in a chair with a straight back, feet flat on the floor and arms crossed on the chest. The subject should rise fully and return to the initial position as many times as possible during 30 s. It is essential for the examiner to consider the demonstration of the correct movement before starting the test and ask the subject to replicate it to ensure their understanding [21].

In the arm curl test, the participant starts sitting in a chair with a straight back, feet flat on the floor, with an extended elbow and then lifts a weight of 5 pounds in the case of women and 8 pounds in the case of men in the dominant hand, which is oriented towards the body. From that position, an elbow flexion and supination of the forearm is performed, and then the forearm returns to the initial position by extending the elbow and rotating the wrist. The score is assigned with the number of complete moves made in 30 s [21].

The 6 min walk test is used to evaluate aerobic endurance. This particular test requires ample space for its realization (30-m corridor). Ideally, it is done after finishing the other tests. The participant will walk as quickly as possible for 6 min in a marked circuit, and a score will be assigned to each return he/she makes. For each elapsed min, the subject will be informed of the remaining evaluation time associated with the pace of walking. The participant will stand sideways performing leg lift movements alternately at the end of the 6 min [21].

Before starting the 2 min step test, it is necessary to measure the height at which the participant should raise the knee. The average distance between the iliac crest and the upper part of the patella is calculated, thus marking the midpoint of the thigh corresponding to the height of the knee while walking. To visualize this mark, it must be transferred to the wall so that the participant has a reference. Start the test when the signal is given, and the subject begins to march in place as many times as possible for 2 min. Both knees must reach the indicated height. The number of times the right knee reaches the reference height is considered. If it does not reach the stated level, the speed should be reduced so that the test is valid without stopping the time. The final score will be awarded according to the number of steps taken and the right knee has reached the set height [21].

The chair-sit and reach test assesses the flexibility of the lower extremities, mainly the biceps femoris. The participant sits in the chair with the gluteal fold at the front edge of the chair. One leg will be with the knee in flexion and the foot resting on the ground, while the other leg will be extended forward as much as possible. With the arms extended and the hands together, the participant will flex the hip slowly to touch the tip of the foot with both middle fingers or beyond this point. If the extended leg begins to flex, the subject should return to the starting position. The score is assigned according to the remaining cm to reach the tip of the foot or the amount by which it is exceeded [21].

The back scratch test evaluates the flexibility of the upper body, mainly shoulders. The participant starts standing with his favorite hand on the same shoulder with the palm facing down. In this position, he/she will bring the hand towards the middle of the back as far as possible while keeping the elbow towards the ceiling. The other arm is located on the back around the waist, trying to take it as far as possible, trying to touch both hands. The middle fingers should be oriented as close as possible, and the distance between them or, failing that, the number of cm that are exceeded is measured [21].

The foot up and go test assesses agility and dynamic balance. The participant will be placed in a chair with a straight back, hands on the thighs and feet resting on the floor with one more advanced. At the signal, the subject will rise from the chair without supporting their hands to push themselves and will quickly walk towards a cone located at an established distance and then return to sit down and position themselves in the initial position [21].

The body mass index of each subject is measured using the formula: body weight (kg) divided by height (m^2).

Finally, the scores obtained in each of the tests that make up the battery are added to a standardized record sheet and are compared with the existing reference values for each age group within the elderly population [47].

5 Cognitive Assessment

5.1 Mini Mental State Examination

The Mini Mental State Examination (MMSE) is an instrument created in 1975 to assess cognitive status systematically and thoroughly. It consists of 11 questions that analyze areas of cognitive functioning, including orientation, registration, attention, calculation, memory, and language. This tool requires 5 min of application, so it is considered practical in its administration in older people [22]. The performance of this evaluation has variables, which may or may not influence the final result. Among these variables, we can find the educational level of the participant and the sensory deficit, such as difficulty in hearing or sight [48]. The maximum score is 19 points, and a value less than or equal to 13 points is considered suggestive of cognitive deficit [49].

5.2 Pfeffer Scale

The Pfeffer scale has been used since 1982 and applies to the companion of the older person who obtained a score less than or equal to 13 in the MMSE. It is used to complement the assessment of cognitive status with information obtained from a relative or caregiver of the participant [22, 23]. This scale measures the ability to perform IADL, designed for studies in the community in individuals with good health or with mild alterations. The instrument evaluates 11 functional activities scored on a scale of 0–33 points, with score of 0 being an ideal performance [50]. This instrument has a high correlation with the Lawton and Brody scale [15].

5.3 Geriatric Depression Scale

Brink and Yesavage created this instrument in 1983 to assess depression in older people with or without cognitive impairment and as a measure of symptom evolution [24]. It can be used in older people who have an optimal state of health, with medical illness, and in those with mild to moderate cognitive impairment. The scale is a self-report, brief, and dichotomous (yes/no). It has 30 questions, although there is an abbreviated version with 15 questions to avoid fatigue and loss of concentration that are sometimes associated with longer instruments. The score is the sum of all positive responses with a cut-off point of 11. A score from 0 to 11 is considered healthy, while a score between 21 and 30 is associated with moderate to severe depression [24, 51].

6 Skeletal Muscle Atrophy: Aging and Hospitalization Combined

The process of skeletal muscle atrophy in the context of hospitalization, a consequence of bed rest, disuse, and decreased physical activity, is a critical factor that relates to the deterioration of functionality in hospitalized patients [52, 53]. In this context, and as compared to their state of fragility before hospital admission, older patients have a high risk of loss of autonomy, worsening of their physical capacity, and a decrease in their primary and instrumental ADL [54]. Additionally, hospital stay leads to a reduction of muscle strength and aerobic capacity. In this sense, the presence of skeletal muscle atrophy is associated with an increase in the days of mechanical ventilation (MV), stay in intensive care units (ICUs), stay in hospital, and risk of mortality [55–57]. In the short-term, the hospitalization effects of older people have a more significant negative impact on the generation of strength and skeletal muscle mass loss compared to young adults. This fact suggests a higher vulnerability of the older age groups, especially in variables such as functional independence [58, 59]. This latter is an indicator of short-term disability and, consequently, a high risk in the deterioration of the quality of life of these patients after the hospitalization stage [60].

6.1 Sarcopenia and Costs Associated with Hospitalization

Due to the increased prevalence in the development of sarcopenia, its effects significantly affect older adults causing an increased risk of suffering a disability, more significant functional impairment, high risk of falls, a high incidence of hospitalization, and a high mortality rate compared to a healthy older adult. The above varies according to age from 4.6% between 70 and 74 years to 31.9% in people over 85 years [61, 62]. For these purposes, the costs associated with this condition in the home environment, outpatient care, and in-hospital services should be considered. In European countries, the total costs related to sarcopenia were estimated at € 1125.3 ± 1367.2 compared to € 561.4 ± 762.6 for non-sarcopenic older people. This has led us to consider sarcopenia as a public health problem [62, 63]. Also, this condition is associated with multiple comorbidities such as osteoporosis, obesity, and type 2 diabetes mellitus, so the economic impact is probably even higher than reported. Older adults with sarcopenia significantly increase their hospital stay compared to non-sarcopenic older adults (13.4 days versus 9.4 days, respectively) [64]. Along the same lines, the average costs per day of hospitalization reach € 68 for people with sarcopenia and € 40 for those who do not suffer from the syndrome, which equals total expenses during hospital stays of € 11,294 and € 6878, respectively [65]. Currently, in the health systems of the USA, data are reported showing a total hospitalization cost of USD 40.4 billion in individuals with sarcopenia, an average of USD 260 per person, and for those over 65 years old, the cost was USD 19.1 billion [66].

6.2 Decrease in Skeletal Muscle Mass and Strength: Clinical Evaluation in the Hospital Context

There is a series of factors to be considered when selecting an element for the evaluation of the decrease in skeletal muscle mass and strength in older people. The factors include: A) the purpose of the measurement, B) the clinical utility that represents decision making, C) the patient's ability to collaborate in the procedure, and D) the validity properties of each instrument [67]. Thus, researchers have made several recommendations based on the tools that provide accurate information regarding the evaluation in the hospital setting of the skeletal muscle mass loss in older patients. The tools to assess skeletal muscle mass and volume are: ultrasonography, computed tomography (CT) or magnetic resonance imaging (MRI). Assessment of muscle strength requires the Medical Research Council sum-score scale (MRC-SS), and grip strength through dynamometry [67–69].

The current changes in the definition of sarcopenia include the loss of muscle function associated with a skeletal muscle mass loss. The management of this condition needs to identify preventive interventions that may delay, improve, reverse, or eliminate the changes produced in muscle strength, muscle mass, and quality. This will allow us to define and to standardize parameters that include a large percentage of the population [70]. In ICUs, the skeletal muscle mass loss occurs between 25% and 40% in adult patients who are under mechanical ventilation for periods longer than 48 h, with a percentage of skeletal muscle atrophy that reaches 21% during the first 10 days of hospitalization. Additionally, in a study conducted in Asia, the entire hospitalized older adult population showed a severe decrease in muscle strength, and all recorded values located below the cut-off score for the diagnosis of sarcopenia. Currently, the prevalence of sarcopenia in hospitalized older adults reaches between 22% and 26% [68, 69, 71, 72].

Regarding the evaluation methodology, the moment of the measurements should be considered [70]. Accordingly, a delayed measure could mean errors in the actual identification of skeletal muscle atrophy [73]. In this regard and considering the rate of skeletal, muscular atrophy in hospitalized patients, researchers have proposed serial evaluation during the first weeks of hospitalization. During days 1, 3, 5, 7, and 10, it has been proposed to collect quantitative and qualitative dates of the muscle state, standardize the measurements and be able to guide the decision-making regarding specific therapeutic behaviors [74, 75].

MRC-SS

The MRC-SS scale has become the main measuring instrument in hospitalized patients to assess muscle strength [76]. For the application of this scale, there must be an active patient collaboration, both to understand the therapist's instruction and to perform the requested movement. This degree of cooperation is measured by applying the Standardized 5 Questions (S5Q) scale, in which the patient must be able to answer 3 of 5 questions favorably to determine an adequate cognitive state [67–73, 77]. The MRC-SS scale has been used mainly in critically ill patients for the assessment and diagnosis of ICU-acquired weakness (ICUAW). The scores have a range between 0 (complete paralysis) and 60 (normal force) points and a cut-off score below 48 points sets the basis for diagnosis [78]. The scale has an excellent level of reliability in the total sum of scores at the time of assessing all muscle groups. However, it may vary depending on the context of the patient hospitalized in the ICU, or surgical medical services [79].

Regarding the correlation degree with functional scales, the MRC-SS scale obtains adequate correlation degrees with the Barthel index and the elderly mobility scale [80]. Besides, those patients that have a measurement below 48 points, the use of mechanical ventilation could be more prolonged, or the individual could have a more extended stay in the ICU and hospital, and even higher mortality after hospital discharge [79, 81–83].

The MRC-SS scale has predictive value and a higher score in the sum of muscle forces is associated with better physical performance [76]. Due to this, the latest reports include the MRC-SS scale within the tools for assessing muscle strength, which has allowed a therapeutic approach to the physical performance of the subject [84].

Grip Strength in the Hospital

The assessment of grip strength, using dynamometry, is aimed at assessing isometric grip performance in patients who can collaborate and who have a score > 3 on the MRC-SS scale [85]. It is a straightforward application tool with essential clinical utility. The cut-off values for weakness in adult patients hospitalized in ICU, with high levels of sensitivity and specificity, are 7 kg for women and 11 kg for men. In addition, grip strength shows a high level of correlation with the MRC scale [84]. Along the same lines, hospitalized adults with grip strength value less than 5 kg have a high percentage of mortality in the ICU. In addition, it is considered as an independent variable associated with more days of connection to MV, increased hospital stay, and death [83–86]. On the other hand, for patients hospitalized in medicine-surgery services, values lower than 11.52 kg for women and 13.89 kg for men during hospital stay is related to a longer hospitalization time and may be used to predict the degree of functional capacity impairment in older adults after discharge [87].

Regarding the ways to evaluate grip strength, there is a standardized form of evaluation which often uses the right hand, the dominant hand or both sides [49]. However, the ideal way to perform the test consists of having a seated patient, with the elbow at 90°, and the prehensile effort made must be maintained for at least 3 s and with a 30 s pause between each attempt. The best value of three tries is the final record [88–90]. Therefore, grip strength could help to identify potential candidate patients for intervention to mitigate the exposure risk. According to the above, the use of this evaluation technique has advantages over the evaluation of the global strength in limbs, since it uses less time, and it is not necessary to reposition the patient for the measurements and deliver a more objective numerical value [87].

In general, in the context of the older patients hospitalized in medical-surgical units, the assessment of grip strength has been used to determine variables such as mortality, survival, disability, hospital complications, and increased hospital stay [87–91]. In clinical practice, the assessment of grip strength is an easy and quick method to execute, which means that it is an excellent tool for the recognition and diagnosis of skeletal muscular atrophy. This makes it a potential gold standard for measurement for assessment of this medical condition [92].

Ultrasonography

Ultrasonography allows confident quantification of skeletal muscle atrophy. This exam is a validated tool to determine the changes in skeletal muscle mass in the hospital context [93]. This includes the measurement of muscle thickness as well as quality concerning the degree of echogenicity. The association between muscle thickness and strength has not demonstrated with an adequate correlation in this method [94, 95]. The ultrasound image does not have the necessary information regarding the neuromuscular properties. The ultrasound image underestimates the strength loss in critical patients [73]. Despite the above, the application of this technique has an excellent level of reliability in variables such as echogenicity, independent of the level of experience of the evaluator. It gives added value in the quantification of skeletal muscle atrophy [96].

The measurement of the quadriceps muscle and its rectus femoris and vastus lateral portions, in addition to being performed in full extension position, can be executed in 10°, 50° and 115° knee flexion, in semi-Fowler position, seated position with knee and hip flexion at 90°, and even in a standing position. Before measurement, the subject should remain at rest for 30 min and preferably the same amount of time in the position where the test will be performed, and the muscle should be completely relaxed [97].

On the other hand, in older hospitalized patients in units of low complexity, the reality regarding skeletal muscular atrophy does not differ concerning the data obtained in the ICU. The incidence in the development of sarcopenia is higher in those who remain in the hospital for an average 5 days of bed rest. In hospitalized older adults, the use of ultrasound allows us to measure parameters such as muscle architecture and its association with functional capacity. This tool gives advantages when identifying patients at risk of disability and also to prescribe rehabilitation programs during hospitalization. Thus, it avoids the deterioration of physical capacity, the increase in falls, and even a decrease in the quality of life [98, 99]. The quantification of skeletal muscle atrophy through the use of ultrasonography also allows identification of stages of sarcopenia. Varying degrees of echogenicity and decreased quadriceps muscle thickness relate to physical performance, specifically with the decrease in gait speed and lower limb strength [80].

In summary, ultrasonography is a tool that allows clinicians and researchers to detect changes in skeletal muscle mass before and after intervention programs. It is easy to apply, will enable examinations next to the patient bed, and does not generate damage associated with the measurement technique. It has a high degree of validity and reliability when comparing the measurements with more specific tools such as CT and MRI, and even with the electrical bioimpedance technique (methods described in Sect. 7) [68, 69].

7 Techniques of Skeletal Muscle Mass Assessment

Changes in body composition occur as part of the normal aging process and are associated with important effects on health and function [100]. The decrease in age-related skeletal muscle mass is widely known as one of the main components for the diagnosis of sarcopenia [16]. As mentioned earlier, the main aspects of interest in body composition during the aging process are the content and distribution of body fat and FFM [100]. It is necessary to use valid, precise, and accurate methods to identify high-risk groups of age-related muscle loss and monitor the potential efficacy of health interventions. The methods for the analysis of the body composition are fundamental for an in-depth assessment of the body state [101].

7.1 Body Composition

Wang et al. developed a widely accepted five-level model of body composition research [101]. They divided the human body into different compartments using the following levels: atomic, molecular, cell, tissue system, and the whole body. This model provides a structural framework to explain the relationships between the main compartments of the body.

7.2 Multi-compartment Model

The atomic level is characterized by 11 main elements that comprise more than 99% of body mass including oxygen, carbon, hydrogen, nitrogen, calcium, phosphorus, potassium, sulfur, sodium, chlorine, and magnesium [101]. On the other hand, the molecular level is the most studied level in the field of body composition research. The classic two-component model consisting of fat and FFM is a molecular level model. The molecular level is one level above the atomic scale in body composition and, therefore, has close links with the elements of the nuclear level. Some units of the molecular level such as proteins, fats, bone minerals and water are, in turn, composed of elements of the atomic level such as nitrogen, calcium, carbon, and oxygen [102]. Also, the cellular level consists of three main components: cells, extracellular fluids, and extracellular solids. The extracellular solids component is mainly composed of bone minerals and, to a lesser extent, other solid components such as collagen. This level has been critical in physiological studies [103]. The multi-component model of the tissue system includes adipose tissue and its subcomponents. It also includes various organs such as the brain, heart, liver, kidneys, spleen, lung, and skeletal muscle [104].

7.3 Body Imaging Techniques

Multiple and varied technological evaluation methods have been developed to measure the quantity and quality of skeletal muscle mass, which have revolutionized the current understanding of abnormalities in body composition. Imaging technologies used to detect skeletal muscle mass loss include MRI, CT, and dual-energy x-ray absorptiometry (DXA). These methods differ in terms of costs, reliability, radiation exposure, and availability. Qualitative changes in muscle fibers can only be investigated by histochemical analysis and microscopy using invasive quantification techniques, such as skeletal muscle biopsy.

The following sections describe the main characteristics of the imaging techniques used to assess skeletal muscle mass loss.

MRI

MRI is an imaging technique that estimates the volume of body components. The main advantage of MRI over other technologies is that it does not involve exposure to ionizing radiation and is based on the interaction between hydrogen nuclei in the human body [105]. Data acquisition is based on the generation of a magnetic field that focuses on the alignment of hydrogen nuclei. Then, a radiofrequency pulse is applied, which leads to the absorption of energy by hydrogen protons, which release energy as the pulse goes off. Then, the protons return to the original position. A receiver detects the energy released in the form of a radio frequency signal used to create whole-body or regional images [106].

Using analysis software, the images generated in grayscale can be determined based on the voxel information (volume and pixels) and the area (calculated based on cm^2). Using specific configurations, the sizes of the whole body and/or regions can be calculated based on a three-dimensional formula that represents the area of the tissue, the thickness of the cut, the distance between consecutive images, and the number of images [106]. The tissue mass (kg) can be calculated based on the assumed constant density values for skeletal muscle (1.04 g/cm^3) and adipose tissue (0.92 g/cm^3) [105].

From the skeletal muscle point of view, MRI has been a powerful non-invasive technique with which the structure and function of the skeletal muscle has been evaluated *in vivo*. Beyond the evaluation of the anatomical characteristics of the tissue using conventional MRI techniques, biochemical and physiological properties of the tissue have been studied [107], such as the presence of intramuscular lipids [108], the presence of edema and changes in the mitochondrial metabolism [109]. This latter makes muscle MRI a potent tool in the diagnosis and follow-up of patients with muscle disorders/conditions such as aging [110].

CT

CT is based on an X-ray beam that crosses the body. The intensity of X-ray output transmission is controlled by a series of detectors, which results in the visual production of cross-sections of approximately 10 mm thick. The output transmission is used to calculate the average attenuation coefficient along the length of the X-ray beam. Attenuation coefficients occur in terms of Hounsfield units (HUs), in which bone and other dense materials are equal to +1000, water is equal to zero, and the air is equivalent to −1000 [111]. Visceral organs, bone, skeletal muscle, and adipose tissue have ranges of specific HUs, allowing their identification in cross-sectional images [106, 112].

CT has been used to measure the quality of several tissues, particularly skeletal muscle tissue. CT analysis of latter can distinguish between different types of tissues based on their attenuation characteristics, which in turn can be presented according to tissue density and chemical composition. A typical density for skeletal muscle is defined as having attenuation values in a range of 40–100 HUs [113]. Low mean values of attenuation will have higher lipid infiltration into the muscle [114].

Typical anatomical locations for measurements of skeletal muscle mass with CT are the thigh, the proximal femur, and the trunk [115]. However, the abdominal area at the level of the third lumbar vertebra is commonly used in most studies, as it relates well to the skeletal muscle mass throughout the body [116]. Also, researchers have used a single-slice CT of the total transverse psoas muscle area to identify sarcopenia [105].

DXA

One of the popular techniques today for estimating body composition is DXA. The principle of using DXA to measure body composition at the molecular level is based on the notion that when an X-ray beam is passed through a complex material, the beam is attenuated in proportion to the composition of the material [117]. The DXA scanner emits two X-ray beams composed of photons at two different energy levels and, as a result of the interaction within the human body, the energy of the X-ray photon undergoes an attenuation that is directly related to the specific chemical compounds with which interacts. By knowing how many photons are transmitted with respect to the detected number, the amount of mineral can be determined, as well as soft tissues (fat mass and FFM) at the level of the whole body or body region (although it does not distinguish visceral and subcutaneous fat in the abdominal region) [118]. Skeletal muscle and adipose tissue mainly consist of water and organic compounds, which restrict the flow of X-rays less than bone [111], so DXA will reflect changes in hydration as a change in lean tissue [100].

The radiation dose varies by model and manufacturer, but is generally small, which makes DXA a safe option for repeated measurements of body composition [119]. In addition, DXA allows the measurement of three compartments of body composition and can provide regional estimates for each of them. This last property has been used to estimate the mass of the appendicular skeletal muscle (ASM) by measuring the amount of lean soft tissue in the upper and lower extremities, which is mainly skeletal muscle [118]. ASM is largely used in the study of sarcopenia and a low ASM is one of the parameters on which all available definitions of sarcopenia are based [16].

However, one should be aware that DXA does not measure skeletal muscle mass directly since some percentage of the mass identified as lean is not muscular and probably includes connective or fibrotic tissue, water and organic mass [120]. There are many ways to represent body composition, but a popular approach in recent years has been the use of indexes normalized by height of the subject. Such as the lean mass index (LMI: total lean mass/height^2), appendicular lean mass (ALM: arms lean mass + legs lean mass) and skeletal muscle mass index (SMI: ALM/height^2) [121, 122]. These have been proposed as parameters for the evaluation of a reduction in skeletal muscle mass which, in turn, is critical in the sarcopenia diagnosis.

Bioelectrical Impedance Analysis (BIA)

The use of BIA to measure the composition is based on the notion that tissues rich in water and electrolytes are less resistant to the passage of an electric current compared to adipose tissue, which is rich in lipids. The accuracy of the estimation of BIA muscle mass is specific to the device and the test population [123]. The best results are obtained when the equation is validated for both the BIA device and the population. The most used equation for the estimation of skeletal muscle was developed by Janssen et al. and is presented below [124]:

$$\text{Skeletal muscle mass}\left(\text{kg}\right) = \left[\begin{array}{l}\left(\text{height}^2 \,/\, \text{bioelectrical resistance} \times 0.401\right) + \\ \left(\text{gender} \times 3.825\right) + \left(\text{age} \times -0.071\right)\end{array}\right] + 5.102$$

The SMI (kg/m^2) is obtained by dividing the absolute muscle mass by the squared height [125], being used as a variable for the diagnosis of sarcopenia [126]. However, it has been shown that BIA results are confused by fluid retention. Hydrostatic abnormalities, peripheral edema, and the use of diuretic medications may affect the validity of BIA measurements in older people [127].

The main concern about this tool is that BIA does not measure any compartment of the body and is considered a doubly indirect method. BIA does not measure anything beyond impedance or its two components, resistance and reactance [128]. By using these variables, in combination with other covariates such as sex, weight and height, BIA can estimate several body compartments that are used as a substitute measure of skeletal muscle mass, according to the reference method used to develop the equations/algorithms [129].

Anthropometry

The imaging equipment mentioned above is not available in low-income clinical settings, such as primary health care centers, which represent the first point of access for the majority of older people with muscle disorders [130]. In such situations, the estimation of body composition and skeletal muscle mass through anthropometric measurements may allow a safe and effective initial evaluation [131]. Anthropometry is a technique that offers excellent portability, applicability, and economy in its use for various environments, being also a non-invasive tool with which the health professional can evaluate size, proportions, and body composition. In contrast to some body imaging techniques, it does not employ ionizing radiation [132].

The inherent errors overshadow the clear advantages of anthropometric techniques. These errors at the level of the evaluator, the instrument, and changes in the body composition of the tissue. The evaluator mistake can be minimized by proper training and by performing several measurements on the same subject. On the other hand, to reduce the error of the instrument, it is necessary to use high quality measuring devices, developed for anthropometric purposes. Regarding changes in the composition or physical properties of tissues, alterations in muscle tone or fluctuations in hydration are factors that can alter the results [132]. Changes in body water lead to changing the proportion of muscle area, such as can occur in the arm [133]. These same effects are caused by the infiltration of fat or connective tissue in lean mass [132].

Among the anthropometric measurements that can be found to measure skeletal muscle mass are arm circumference and calf circumference (CC) [134]. CC has been recommended for several years [135, 136] as a more sensitive measure than other anthropometric measurements (e.g., arm circumference) to assess the global muscle mass loss in the elderly. The first studies that used the measurement of CC reported a correlation between the decrease in CC and the decrease in physical activity, as well as the fact that CC has a significant relationship with the FFM in the elderly [135].

The World Health Organization (WHO) published a report in 1995 developed by a committee of experts in which it describes the use and interpretation of anthropometry. These reinforce the idea of previous studies recommending CC as the most sensitive measure of skeletal muscle mass in older people, capable of indicating changes in FFM that occur with aging and by decreased physical activity [137].

At present, this measurement has been widely investigated around the world, obtaining a significant variability of values in terms of ethnicity and geographical distribution. A correlation between CC and the appendicular skeletal muscle mass index (ASMI) [138] and skeletal appendicular muscle mass [139] has been described. It is also used in the diagnosis of sarcopenia [138–141].

7.4 Invasive Evaluation of Skeletal Muscle Mass

Skeletal Muscle Biopsy

The percutaneous biopsy technique is used to obtain skeletal muscle samples, this being a minimally invasive and relatively safe procedure. Most subjects undergoing skeletal muscle biopsy report few changes in their ability to perform their daily living activities [142]. Duchenne was the first to build a needle with a trocar to obtain a skeletal muscle sample from living subjects through a percutaneous biopsy [143]. In the 1960s, Bergström introduced a percutaneous biopsy needle similar to that described by Duchenne [144, 145]. This technique has encouraged the diagnosis of myopathies and the understanding of the structure and function of skeletal muscle. Molecular and cellular studies in skeletal muscle require samples obtained primarily from the vastus lateralis muscle. Classically, a muscle biopsy is described as an open procedure in which the skin is cut so that a needle connected to a vacuum pump can be inserted to aspirate skeletal muscle tissue [144]. The procedure takes 15–20 min, most of which to prepare the incision. In studies based on interventions such as physical exercise, muscle samples are often taken before and after the activity, with one or two samples collected during recovery [146]. Alternatively, when shorter periods of physical activity are investigated, an incision can be made before exercise, covered with a sterile bandage and secured with surgical tape, thus allowing the biopsy sample to be taken quickly after completing a series of exercises [147]. The relative speed of the procedure allows the researcher to capture cellular and molecular events before, during, and after an intervention.

The collected muscle samples can be used to observe a large number of variables, such as the determination of the type and proportion of muscle fibers [148], muscle damage quantification [148, 149], capillary density of muscle tissue [150], enzymatic and oxidative activity [151], protein synthesis [152, 153], inflammatory response markers [154] and oxidative stress [155], among others.

8 Physical Exercise as a Drug to Combat Skeletal Muscle Atrophy in the Older Population

During aging, there is a reduction in physical activity levels, which contributes to the loss of functionality [156]. However, the regular practice of exercise can minimize the harmful effects of a sedentary lifestyle, increase active and independent life expectancy and control the development or progression of chronic diseases, which are characteristic of the aged population [157].

For such effects, the combination of aerobic and muscular strength activities seems to be more effective than any form of training alone, to counteract the detrimental effects on health, general well-being, and the functioning of the cardiovascular and skeletal muscle systems. In addition, it is recommended to include modalities of flexibility and balance to the prescription of exercises for older people to improve problems of joint range and stability. Therefore, an ideal physical intervention plan is one that comprehensively addresses the components that make up physical fitness (Table 6.2) [158].

8.1 Modalities of Physical Exercise in Older People

Resistance Exercise Training (RET) or Muscle Strength

RET is an excellent intervention tool to combat skeletal muscle disuse, sarcopenia, frailty and consequently improve the functional capacity of older people [167], by increasing strength, FFM) and cross-sectional areas of muscle and muscle fiber [168]. RET is defined according to the type of exercise, characterized by repeated muscle contractions against an external load [169]. The contractions can be static (isometric), producing strength without joint movement or changes in muscle length. This is useful in older people when joint movement is restricted due to pain

Table 6.2 Recommendations to practice physical exercise in older people

Exercise type	Recommendations	Doses	Examples
Resistance exercise training (RET) or muscle strength [158–160]	The development of muscle strength and endurance is progressive over time. This means that gradual increases in the amount of weight and the days per week of exercise should be planned so that sessions are not held on consecutive days	*Frequency:* 2–3 days/week *Workload:* Progressive training, low (40% 1RM), moderate (60% 1RM) and high (80% 1RM) load and power exercises (20% –40% 1RM) *Repetitions:* 2–3 sets of 8–12 repetitions that address major muscle groups (it is suggested to include stabilizing spine and core muscles) A specific amount of time for muscle strengthening is not recommended	Exercises using exercise bands, weight machines, hand weights or calisthenic exercises (body weight provides resistance to movement)
Aerobic exercise training (AET) or endurance [159, 170, 173]	Continuous exercise Prefer aerobic activity or endurance that do not impose excessive joint stress The increases should be gradual of cardiorespiratory resistance and preferably distribute the exercise to non-consecutive days, depending on the intensity of the training	*Frequency:* 3–5 days/week *Intensity:* Start with moderate load (50% –60% VO_{2max}) to progress to high load (70% –80% VO_{2max}) *Training time:* 30 min (moderate) or 20 min (vigorous), or divided into 3 series of 10 min Older adults should do at least 150 min a week of moderate intensity, according to the effort perception scale (PSE) 5 or 6/10, or 75 min/week of vigorous intensity (PSE) 7 or 8/10 to obtain substantial benefits for aerobic health.	Walking, dancing, swimming, water aerobics, jogging, aerobic exercise classes, bicycle riding (stationary or on a path)
Stretching or flexibility training [159, 164, 165]	Defined as any activity that maintains or increases flexibility using sustained stretches for each major muscle group Static mode is preferred over ballistic stretching This type of exercise is recommended to maintain the normal range of motion for daily activities, and is usually combined with warm-up or calm-down activities	*Frequency:* ≥ 2–3 days/week They generally complement aerobic or strength training sessions *Intensity:* stretch to the point of tightness or slight discomfort *Repetitions:* 2–4 for each stretch, maintaining the technique for 30–60 s	Static and dynamic elongations are the most used in the older population Achieving an improvement in ROM, regardless of the type of stretch chosen The use of ballistic stretching is not promoted, due to its complexity and associated risks

(continued)

Table 6.2 (continued)

Exercise type	Recommendations	Doses	Examples
Balance training [159, 166]	Older adults at risk of falls should do balance training ≥3 days/week and do standardized exercises of a strengthening program shown to reduce falls Progressively difficult postures that gradually reduce the support base, with dynamic movements that disturb the center of gravity and stress the postural muscle groups	Frequency: ≥2–3 days/week. Training with proprioceptive characteristics, agility, walking With progressive complexity, around postures, disturbance exercises, reduction of sensory input (eyes closed)	Walking backwards, sideways, on heels, on toes, and standing from a sitting position Exercises can increase in difficulty by progressing from holding to a stable support (such as furniture) while performing the exercises to doing so without support Tai Chi and yoga are alternatives that can help prevent falls

or injury. There are also dynamic contractions, which can be divided in concentric or eccentric [169].

Another form of RET is high-speed resistance training, or also known as power. This involves the use of rapid contractions with low external resistances at approximately 40% of the 1 repetition maximum (1RM). In older adults, it may be relevant to practice this modality because the disproportionate reduction of type II muscle fibers, translates into a rapid and progressive loss of muscle power [163, 170]. Other improvements attributed to the RET act on the muscular quality especially during the first phases of the training, increasing the rates of recruitment and/or discharge of the motor units. The benefits of this are observed in a similar way between older and younger people [170].

Regarding the prescription of this type of physical exercise, some reports show favorable changes on muscular endurance, the FFM, and body fat [171]. However, for increases in lean body mass in older people, training volume and age are vital determinants of therapeutic effectiveness, suggesting that higher doses result in a more significant adaptive response. Given this context, the current recommendations, which recommend a sequential increase in the load, should be modified towards the control of the total dose. This means the series performed, as well as the repetitions and weight lifted, to generate significant improvements in the physical condition [161].

In summary, the intervention of RET should be progressive in the total volume load, that is from 60% to 70% of 1RM towards high intensity (80% of 1RM), controlling the number of repetitions and series, with a physical work applied to the whole body, 2 or 3 times a week [159].

Most of the research applied in older people is carried out using strength training machines, such as leg press, chest press, knee extension, and lat pulldown devices.

All of these are chosen because they represent the totality of muscles associated with functionality. It should be noted how essential the incorporation of the exercises for the lower extremities is because the decrease in strength and skeletal muscle atrophy during aging is superior in this region when compared to the upper extremities. For these reasons, the intervention of the lower extremities provides an excellent means of improving the capacity of locomotion and reduction of the risk of falling [160].

Aerobic Exercise Training (AET) or Endurance

Aerobic training involves the participation of large muscle groups, which move rhythmically and steadily for prolonged periods [170]. The aerobic capacity measured using the maximum oxygen consumption (VO_{2max}) shows a constant decrease with age of up to 10% per decade after 25 years. This decrease is mainly due to the reduction in cardiac output caused by an increase in peripheral circulatory resistance [172]. Therefore, it is important to incorporate aerobic exercise in older adults to mediate age-related circulatory system detriments, such as elastic arterial stiffness and endothelial vascular dysfunction. Favorable adaptations occur including lower heart rate at rest or at any submaximal workload, decrease in systolic, diastolic and mean blood pressure during exercise or improvements in vasodilation and oxygen absorption capacity in trained muscle groups [162].

Similarly, AET programs contribute to protective metabolic cardiovascular effects. These effects include reductions in atherogenic levels (reduced triglycerides and higher concentrations of HDL), increased transport of glucose in skeletal muscle, and improved insulin action throughout the body, which ultimately leads to the reduction of cardiovascular risk [173]. This type of exercise also improves body composition, such that at moderate intensity (≥60% of VO_{2max}), it is useful for the loss of total body fat and fat of the intra-abdominal region (>10%), both in a young or older population who are overweight. Also, it has effects on FFM by stimulating protein synthesis in healthy older individuals, so that it can lead to skeletal muscle growth, mainly of the slow myofibers [174]. Despite this, the statistical power of the effect of muscular hypertrophy is significantly higher for resistance training, which also benefits the population suffering from chronic diseases such as diabetes, obesity, and heart failure [175, 176].

Supervised programs that seek to improve aerobic capacity should be executed at a sufficient intensity (≥60% VO_{2max}), frequency (≥3 days/week), and adequate duration (≥16 weeks), both in healthy middle-aged and older adults [159].

Stretching or Flexibility Training

Flexibility corresponds to the ability to move a joint through a full range of motion (ROM) and is mainly dependent on tendons, bones, and muscle length [170, 177].

During aging the ROM changes, triggering a loss that varies in each individual. From the age of 71, flexibility decreases on average by 20–30% in the hip and spine and 30–40% in the ankle, especially in women [164]. These effects result in a limited range of movement in the joints, which can lead to an increased risk of skeletal muscle injuries, falls, and less efficiency in the gait due to the reduction in stride length, speed, and balance, typical of the elderly [178].

Given this context, stretching can maintain and/or improve musculoskeletal flexibility and increase the quality of body movement [179, 180]. There are different modalities, such as treating this component of physical fitness, among which static stretching (SS) exercises stand out. SS is defined as the most effective alternative to improve joint range and prevent damage to muscles and tendons. Its application is recommended after an aerobic training of resistance or muscular power. The contractile capacity of the musculoskeletal tissue is not altered, unlike the dynamic stretching (DS) that can also be used as an alternative to warming or in preparation to the movement and is recommended before the main training phase [181].

Despite the link between functionality and this type of training in older people, there is little research dedicated to examining dosage, types of elongations, timing of application, and regarding the impact on flexibility around health outcomes in general [165, 182].

Concerning dosage in older people, there are more significant gains in the ROM with longer durations of stretching (30–60 s). The repetition of each elongation exercise is most effective when done 2–4 times. Improvements after 3–12 weeks of training are observed if performed at a frequency of at least 2–3 times weekly, with more significant progress if done daily. The main objective is to reach 60 s of total stretching time per flexibility exercise, resting between stretches for approximately 30–60 s [159].

Balance Training

The balance gives the possibility of maintaining the center of mass of the body within the limits of the support base. For this purpose, the postural control synchronizes several systems including sensory (i.e., vestibular, visual, somatosensory), cognitive (central nervous system), and skeletal muscle ones [183].

Balance disorders increase in the geriatric population, as a result of multifactorial causes, presenting weakness in the core stabilizing muscles, alteration in muscle activation patterns, loss of proprioception and the ability to control central processing and normal muscular effectors, which contributes to deficiencies in stability and balance. This exposes older people to the risk of falls in situations that demand balance [184]. Consequently, many older adults are at risk of falling during their ADL. In most cases, falls and associated injuries impair the quality of life and cause physical limitations, anxiety, loss of confidence, and fear of movement [185]. For these reasons, adapted physical activity programs have been suggested to improve the balance control of older participants. Among the components of this type of training, of the main challenge is to integrate the sensory and neuromuscular systems in accordance with the information and adaptation to the needs of the environment. This must consider changes in the direction of travel, orientation in space, speed or height of the center of mass and thus allow the overcoming of challenges such as double or multiple tasks improving the stability and speed of walking [186, 187].

Following the beneficial effects of the inclusion of balance exercises to a training program in the older people, the combination of movements that include balance and coordination are recommended, such as tai chi and yoga, that incorporate motor skills, agility, and proprioceptive training [188–191]. For balance exercises, it is recommended to perform 2–3 sessions per week, for periods of at least 8 weeks, as a tool to improve part of physical fitness, agility, quality of life, and reduce the risk of falling [159, 161, 170, 171].

Final Considerations

Aerobic and resistance exercises should be applied to restore or maintain independence in ADLs, where mainly activities that involve the muscle strength component prevent, delay or modulate frailty, along with regulating the disproportionate increase in sarcopenia. Increasing muscle protein synthesis, skeletal muscle mass, improvement of neural recruitment, and muscle strength ensure more positive effects. The combination of these components of physical fitness (cardiorespiratory capacity and muscular strength) [158, 165, 171] has produced beneficial effects on body composition [161, 168, 174, 175] and functionality, as well as in general well-being among elderly users [159, 166].

It should be kept in mind that older people have a high risk of falling, due to difficulties in their motor capacity and locomotion, resulting from reduced flexibility, balance, or coordination. Therefore, among the variety of modalities of physical exercise are the tools to improve the detriments of older people. It is essential, also consider each component of the physical condition decreased or altered, in the development of a training program for older adults along with adequate planning around dosing and periodization, to achieve improvements in physical performance and quality of life.

9 Conclusions

The best way to evaluate an older person is through their muscular strength, skeletal muscle mass and physical performance. There are several ways to assess these parameters, which will depend on the clinician or researcher on which one to choose according to the context in which it is found and the available economic resources. Among the strategies we have to combat skeletal muscle atrophy due to aging (or sarcopenia) is physical exercise, which has shown greater beneficial effects compared to other strategies such as nutritional or pharmacological ones. Therefore, different training modalities have been carried out to counteract the problems associated with decreased muscle strength, skeletal muscle mass loss, and decreased physical performance. Among these, aerobic and resistance training have been shown to have more significant benefits over those of balance and flexibility, with resistance training being the most effective due to its ability to increase skeletal muscle mass and muscle strength in older people and, consequently, improve physical performance. Funding Supported by FONDECYT - Chile (Grant Number 11180949) and Dirección de Investigación (DIUFRO) of Universidad de La Frontera (Grant Number DI18-0068). FAPESP, CNPq, and CAPES support the Rui Curi Research team.

References

1. United Nations, Department of Economic and Social Affairs PD. World Population Ageing 2019: Highlights https://www.un.org/development/desa/family/wp-content/uploads/sites/23/2018/05/BACKGROUND-PAPER.SDGs1611.FINAL_.pdf
2. World Health Organization (2018) Ageing and health. https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
3. Short KR, Nair KS (2000) The effect of age on protein metabolism. Curr Opin Clin Nutr Metab Care 3(1):39–44
4. Giovannini S, Marzetti E, Borst SE, Leeuwenburgh C (2008) Modulation of GH/IGF-1 axis: potential strategies to counteract sarcopenia in older adults. Mech Ageing Dev 129(10):593–601
5. Jackman RW, Kandarian SC (2004) The molecular basis of skeletal muscle atrophy. Am J Physiol Cell Physiol 287(4):C834–C343
6. Kudryavtseva AV, Krasnov GS, Dmitriev AA, Alekseev BY, Kardymon OL, Sadritdinova AF et al (2016) Mitochondrial dysfunction and oxidative stress in aging and cancer. Oncotarget 7(29):44879–44905
7. Fan J, Kou X, Jia S, Yang X, Yang Y, Chen N (2016) Autophagy as a potential target for sarcopenia. J Cell Physiol 231(7):1450–1459
8. Dalle S, Rossmeislova L, Koppo K (2017) The role of inflammation in age-related sarcopenia. Front Physiol 8:1045. https://doi.org/10.3389/fphys.2017.01045
9. Miljkovic N, Lim JY, Miljkovic I, Frontera WR (2015) Aging of skeletal muscle fibers. Ann Rehabil Med 39(2):155–162
10. Burd NA, Gorissen SH, Van Loon LJC (2013) Anabolic resistance of muscle protein synthesis with aging. Exerc Sport Sci Rev 41(3):169–173
11. Rosenberg IH (1997) Sarcopenia: origins and clinical relevance. J Nutr 127(5):990S–991S
12. Cruz-Jentoft AJ, Sayer AA (2019) Sarcopenia. Lancet 393(10191):2636–2646
13. Mahoney FI, Barthel DW (1965) Functional evaluation: the Barthel index. Md State Med J 14:61–65
14. Katz S, Heiple KG, Downs TD, Ford AB, Scott CP (1967) Long term course of 147 patients with fracture of the hip. Surg Gynecol Obstet 124(6):1219–1230
15. Lawton MP, Brody EM (1969) Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 9(3):179–186
16. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T et al (2019) Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 48(1):16–31
17. Podsiadlo DRS (1991) The timed "up & go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 39(2):142–148

18. Eladio Mancilla S, José Valenzuela H, Máximo Escobar C (2015) Timed up and go right and left unipodal stance results in Chilean older people with different degrees of disability. Rev Med Chil 143(1):39–46
19. Tinetti ME, Franklin Williams T, Mayewski R (1986) Fall risk index for elderly patients based on number of chronic disabilities. Am J Med 80(3):429–434
20. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB (1995) Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med 332(9):556–561
21. Rikli RE, Jones CJ (2000) Senior fitness test manual. Human Kinetics Publishers, Champaign. ISBN-10: 9780736033565
22. Folstein MF, Folstein SE, McHugh PR (1975) "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12(3):189–198
23. Pfeffer RI, Kurosaki TT, Harrah CH, Chance JM, Filos S (1982) Measurement of functional activities in older adults in the community. J Gerontol 37(3):323–329
24. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M et al (1982) Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 17(1):37–49
25. Stuck AE, Siu AL, Wieland GD, Rubenstein LZ, Adams J (1993) Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet 342(8878):1032–1036
26. González N, Bilbao A, Forjaz MJ, Ayala A, Orive M, Garcia-Gutierrez S et al (2018) Psychometric characteristics of the Spanish version of the Barthel index. Aging Clin Exp Res 30(5):489–497
27. Granger CV, Hamilton BB, Gresham GE (1988) The stroke rehabilitation outcome study--part I: general description. Arch Phys Med Rehabil 69(7):506–509
28. Granger CV, Hamilton BB, Gresham GE, Kramer AA (1989) The stroke rehabilitation outcome study: part II. Relative merits of the total Barthel index score and a four-item subscore in predicting patient outcomes. Arch Phys Med Rehabil 70(2):100–103
29. Mahoney FI, Wood OH, Barthel DW (1958) Rehabilitation of chronically ill patients: the influence of complications on the final goal. South Med J 51(5):605–609
30. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW (1963) Studies of illness in the aged: the index of ADL: a standardized measure of biological and psychosocial function. JAMA 185(12):914–919
31. Katz S, Downs TD, Cash HR, Grotz RC (1970) Progress in development of the index of ADL. Gerontologist 10(1):20–30
32. Jiménez-Caballero PE, López-Espuela F, Portilla-Cuenca JC, Pedrera-Zamorano JD, Jiménez-Gracia MA, Lavado-García JM et al (2019) Evaluation of the instrumental activities of daily living following a stroke by means of the Lawton and Brody scale. Rev Neurol 55(6):337–242
33. Graf C (2008) The Lawton instrumental activities of daily living scale. Medsurg Nurs 17(5):343–344
34. Massy-Westropp NM, Gill TK, Taylor AW, Bohannon RW, Hill CL (2011) Hand grip strength: age and gender stratified normative data in a population-based study. BMC Res Notes 4:127. https://doi.org/10.1186/1756-0500-4-127
35. Carmeli E, Patish H, Coleman R (2003) The aging hand. J Gerontol A Biol Sci Med Sci 58(2):146–152
36. Kong YK, Lee JH, Shin JM, Shim HH, Kim JK, Cho MU et al (2019) Evaluation of subjective perceived rating for grip strength depending on handedness for various target force levels. Work 62(1):21–26
37. Sanders JB, Bremmer MA, Comijs HC, van de Ven PM, Deeg DJH, Beekman ATF (2017) Gait speed and processing speed as clinical markers for geriatric health outcomes. Am J Geriatr Psychiatry 25(4):374–385
38. Hackett RA, Davies-Kershaw H, Cadar D, Orrell M, Steptoe A (2018) Walking speed, cognitive function, and dementia risk in the English longitudinal study of ageing. J Am Geriatr Soc 66(9):1670–1675

39. Hofheinz M, Mibs M (2016) The prognostic validity of the timed up and go test with a dual task for predicting the risk of falls in the elderly. Gerontol Geriatr Med 2:2333721416637798. https://doi.org/10.1177/2333721416637798
40. Barry E, Galvin R, Keogh C, Horgan F, Fahey T (2014) Is the timed up and go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. BMC Geriatr 14:14. https://doi.org/10.1186/1471-2318-14-14
41. Ortega A (2016) Prevention of falls in the elderly: a review of new concepts based on the evidence. Eur J Investig Heal Psychol Educ 6(2):71–82
42. Guevara CR, Lugo Validez LH (2012) Validity and reliability of Tinetti Scale for Colombian people. Revista Colombiana de Reumatología 19:213–233
43. Curcio F, Basile C, Liguori I, Della-Morte D, Gargiulo G, Galizia G et al (2016) Tinetti mobility test is related to muscle mass and strength in non-institutionalized elderly people. Age (Omaha) 38(5–6):525–533
44. Stookey AD, Katzel LI, Steinbrenner G, Shaughnessy M, Ivey FM (2014) The short physical performance battery as a predictor of functional capacity after stroke. J Stroke Cerebrovasc Dis 23(1):130–135
45. Volpato S, Cavalieri M, Sioulis F, Guerra G, Maraldi C, Zuliani G et al (2011) Predictive value of the short physical performance battery following hospitalization in older patients. J Gerontol Ser A Biol Sci Med Sci 66(1):89–96
46. Langhammer B, Stanghelle JK (2015) The senior fitness test. J Physiother 61(3):163. https://doi.org/10.1016/j.jphys.2015.04.001
47. Rikli RE, Jones CJ (2013) Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. Gerontologist 53(2):255–267
48. Creavin ST, Wisniewski S, Noel-Storr AH, Trevelyan CM, Hampton T, Rayment D et al (2016) Mini-mental state examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. Cochrane Database Syst Rev 1:CD011145. https://doi.org/10.1002/14651858.CD011145.pub2
49. Muñoz Silva CA, Rojas Orellana PA, Marzuca-Nassr GN (2015) Criterios de valoración geriátrica integral en adultos mayores con dependencia moderada y severa en centros de atención primaria en chile. Rev Med Chil 143(5):612–618
50. Pfeffer RI, Kurosaki TT, Chance JM, Filos S, Bates D (1984) Use of the mental function index in older adults: reliability, validity, and measurement of change over time. Am J Epidemiol 120(6):922–935
51. Brink TL (1989) Proper scoring of the geriatric depression scale. J Am Geriatr Soc 37(8):819–819
52. Covinsky KE, Palmer RM, Fortinsky RH, Counsell SR, Stewart AL, Kresevic D et al (2003) Loss of independence in activities of daily living in older adults hospitalized with medical illnesses: increased vulnerability with age. J Am Geriatr Soc 51(4):451–458
53. Kortebein P, Symons TB, Ferrando A, Paddon-Jones D, Ronsen O, Protas E et al (2008) Functional impact of 10 days of bed rest in healthy older adults. J Gerontol A Biol Sci Med Sci 63(10):1076–1081
54. Bodilsen AC, Pedersen MM, Petersen J, Beyer N, Andersen O, Smith LL et al (2013) Acute hospitalization of the older patient: changes in muscle strength and functional performance during hospitalization and 30 days after discharge. Am J Phys Med Rehabil 92(9):789–796
55. Kramer CL (2017) Intensive care unit–acquired weakness. Neurol Clin 35(4):723–736
56. Schreiber A, Bertoni M, Goligher EC (2018) Avoiding respiratory and peripheral muscle injury during mechanical ventilation: diaphragm-protective ventilation and early mobilization. Crit Care Clin 34(3):357–381
57. Ferrante LE, Pisani MA, Murphy TE, Gahbauer EA, Leo-Summers LS, Gill TM (2016) Factors associated with functional recovery among older intensive care unit survivors. Am J Respir Crit Care Med 194(3):299–307
58. Dos Santos C, Hussain SNA, Mathur S, Picard M, Herridge M, Correa J et al (2016) Mechanisms of chronic muscle wasting and dysfunction after an intensive care unit stay: a pilot study. Am J Respir Crit Care Med 194(7):821–830

59. Rossi AP, Rubele S, Pelizzari L, Fantin F, Morgante S, Marchi O et al (2017) Hospitalization effects on physical performance and muscle strength in hospitalized elderly subjects. J Gerontol Geriatr Res 06(02). https://doi.org/10.4172/2167-7182.1000401
60. Guidet B, Vallet H, Boddaert J, de Lange DW, Morandi A, Leblanc G et al (2018) Caring for the critically ill patients over 80: a narrative review. Ann Intensive Care 8(1):114. https://doi.org/10.1186/s13613-018-0458-7
61. Beaudart C, Zaaria M, Pasleau F, Reginster JY, Bruyère O (2017) Health outcomes of sarcopenia: a systematic review and meta-analysis. PLoS One 12(1):e0169548. https://doi.org/10.1371/journal.pone.0169548
62. Steffl M, Sima J, Shiells K, Holmerova I (2017) The increase in health care costs associated with muscle weakness in older people without long-term illnesses in the Czech Republic: results from the survey of health, ageing and retirement in Europe (SHARE). Clin Interv Aging 12:2003–2007
63. Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff R (2004) The healthcare costs of sarcopenia in the United States. J Am Geriatr Soc 52(1):80–85
64. Beaudart C, Rizzoli R, Bruyère O, Reginster J-Y, Biver E (2014) Sarcopenia: burden and challenges for public health. Arch Public Health 72(1):45. https://doi.org/10.1186/2049-3258-72-45
65. Van Vugt JLA, Buettner S, Levolger S, Coebergh Van Den Braak RRJ, Suker M, Gaspersz MP et al (2017) Low skeletal muscle mass is associated with increased hospital expenditure in patients undergoing cancer surgery of the alimentary tract. PLoS One 12(10):e0186547. https://doi.org/10.1371/journal.pone.0186547
66. Goates S, Du K, Arensberg MB, Gaillard T, Guralnik J, Pereira SL (2019) Economic impact of hospitalizations in US adults with sarcopenia. J Frailty Aging 8(2):93–99
67. Parry SM, Huang M, Needham DM (2019) Evaluating physical functioning in critical care: considerations for clinical practice and research. Crit Care 21(1):249. https://doi.org/10.1186/s13054-017-1827-6
68. Looijaard WGPM, Molinger J, Weijs PJM (2018) Measuring and monitoring lean body mass in critical illness. Curr Opin Crit Care 24(4):241–247
69. Mijnarends DM, Meijers JMM, Halfens RJG, ter Borg S, Luiking YC, Verlaan S et al (2013) Validity and reliability of tools to measure muscle mass, strength, and physical performance in community-dwelling older people: a systematic review. J Am Med Dir Assoc 14(3):170–178
70. Gruther W, Benesch T, Zorn C, Paternostro-Sluga T, Quittan M, Fialka-Moser V et al (2008) Muscle wasting in intensive care patients: ultrasound observation of the M. quadriceps femoris muscle layer. J Rehabil Med 40(3):185–189
71. Yamanouchi A, Yoshimura Y, Matsumoto Y, Jeong S (2016) Severely decreased muscle mass among older patients hospitalized in a long-term care ward in Japan. J Nutr Sci Vitaminol (Tokyo) 62(4):229–234
72. Welch C, Hassan-Smith ZK, Greig CA, Lord JM, Jackson TA (2018) Acute sarcopenia secondary to hospitalisation – an emerging condition affecting older adults. Aging Dis 9(1):151–164
73. Parry SM, Granger CL, Berney S, Jones J, Beach L, El-Ansary D et al (2015) Assessment of impairment and activity limitations in the critically ill: a systematic review of measurement instruments and their clinimetric properties. Intensive Care Med 41(5):744–762
74. Parry SM, El-Ansary D, Cartwright MS, Sarwal A, Berney S, Koopman R et al (2015) Ultrasonography in the intensive care setting can be used to detect changes in the quality and quantity of muscle and is related to muscle strength and function. J Crit Care 30(5):1151.e9–1151.e14
75. Puthucheary ZA, Phadke R, Rawal J, McPhail MJW, Sidhu PS, Rowlerson A et al (2015) Qualitative ultrasound in acute critical illness muscle wasting. Crit Care Med 43(8):1603–1611
76. Connolly B, Thompson A, Moxham J, Hart N (2012) Relationship of Medical Research Council sum-score with physical function in patients post critical illness. Am J Respir Crit Care Med 185:A3075–A3075

77. Parry SM, Berney S, Granger CL, Dunlop DL, Murphy L, El-Ansary D et al (2015) A new two-tier strength assessment approach to the diagnosis of weakness in intensive care: an observational study. Crit Care 19(1):52. https://doi.org/10.1186/s13054-015-0780-5
78. Stevens RD, Marshall SA, Cornblath DR, Hoke A, Needham DM, De Jonghe B et al (2009) A framework for diagnosing and classifying intensive care unit-acquired weakness. Crit Care Med 37(10 Suppl):S299–S308
79. Brunello AG, Haenggi M, Wigger O, Porta F, Takala J, Jakob SM (2010) Usefulness of a clinical diagnosis of ICU-acquired paresis to predict outcome in patients with SIRS and acute respiratory failure. Intensive Care Med 36(1):66–74
80. Yamada M, Kimura Y, Ishiyama D, Nishio N, Abe Y, Kakehi T et al (2017) Differential characteristics of skeletal muscle in community-dwelling older adults. J Am Med Dir Assoc 18(9):807.e9–807.e16
81. Sharshar T, Bastuji-Garin S, Stevens RD, Durand MC, Malissin I, Rodriguez P et al (2009) Presence and severity of intensive care unit-acquired paresis at time of awakening are associated with increased intensive care unit and hospital mortality. Crit Care Med 37(12):3047–3053
82. Ali NA, O'Brien JM, Hoffmann SP, Phillips G, Garland A, Finley JCW et al (2008) Acquired weakness, handgrip strength, and mortality in critically III patients. Am J Respir Crit Care Med 178(3):261–268
83. Lee JJ, Waak K, Grosse-Sundrup M, Xue F, Lee J, Chipman D et al (2012) Global muscle strength but not grip strength predicts mortality and length of stay in a general population in a surgical intensive care unit. Phys Ther 92(12):1546–1555
84. Vanpee G, Hermans G, Segers J, Gosselink R (2014) Assessment of limb muscle strength in critically ill patients: a systematic review. Crit Care Med 42(3):701–711
85. García-Peña C, García-Fabela LC, Gutiérrez-Robledo LM, García-González JJ, Arango-Lopera VE, Pérez-Zepeda MU (2013) Handgrip strength predicts functional decline at discharge in hospitalized male elderly: a hospital cohort study. PLoS One 8(7):e69849. https://doi.org/10.1371/journal.pone.0069849
86. Roberson AR, Starkweather A, Grossman C, Acevedo E, Salyer J (2018) Influence of muscle strength on early mobility in critically ill adult patients: systematic literature review. Hear Lung J Acute Crit Care 47(1):1–9
87. Bohannon RW (2008) Hand-grip dynamometry predicts future outcomes in aging adults. J Geriatr Phys Ther 31(1):3–10
88. Mohamed-Hussein AAR, Makhlouf HA, Selim ZI, Gamaleldin Saleh W (2018) Association between hand grip strength with weaning and intensive care outcomes in COPD patients: a pilot study. Clin Respir J 12(10):2475–2479
89. Cottereau G, Dres M, Avenel A, Fichet J, Jacobs FM, Prat D et al (2015) Handgrip strength predicts difficult weaning but not extubation failure in mechanically ventilated subjects. Respir Care 60(8):1097–1104
90. Syddall H, Cooper C, Martin F, Briggs R, Sayer AA (2003) Is grip strength a useful single marker of frailty? Age Ageing 32(6):650–656
91. Schmidt D, Coelho AC, Vieira FN, Torres VF, Savi A, Vieira SRR (2019) Critical illness polyneuromyopathy in septic patients: is it possible to diagnose it in a bedside clinical examination? Arq Neuropsiquiatr 77(1):33–38
92. Bragança RD, Ravetti CG, Barreto L, Ataíde TBLS, Carneiro RM, Teixeira AL et al (2019) Use of handgrip dynamometry for diagnosis and prognosis assessment of intensive care unit acquired weakness: a prospective study. Hear Lung 48(6):532–537
93. Reid CL, Campbell IT, Little RA (2014) Muscle wasting and energy balance in critical illness. Clin Nutr 23(2):273–280
94. Baldwin CE, Bersten AD (2014) Alterations in respiratory and limb muscle strength and size in patients with sepsis who are mechanically ventilated. Phys Ther 94(1):68–82

95. Grimm A, Teschner U, Porzelius C, Ludewig K, Zielske J, Witte OW et al (2013) Muscle ultrasound for early assessment of critical illness neuromyopathy in severe sepsis. Crit Care 17(5):R227. https://doi.org/10.1186/cc13050
96. Sarwal A, Parry SM, Berry MJ, Hsu FC, Lewis MT, Justus NW et al (2015) Interobserver reliability of quantitative muscle sonographic analysis in the critically ill population. J Ultrasound Med 34(7):1191–1200
97. Perkisas S, Baudry S, Bauer J, Beckwée D, De Cock AM, Hobbelen H et al (2018) Application of ultrasound for muscle assessment in sarcopenia: towards standardized measurements. Eur Geriatr Med 9(6):739–757
98. Aubertin-Leheudre M, Martel D, Narici M, Bonnefoy M (2019) The usefulness of muscle architecture assessed with ultrasound to identify hospitalized older adults with physical decline. Exp Gerontol 125:110678. https://doi.org/10.1016/j.exger.2019.110678
99. Martone AM, Bianchi L, Abete P, Bellelli G, Bo M, Cherubini A et al (2017) The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. J Cachexia Sarcopenia Muscle 8(6):907–914
100. Woodrow G (2009) Body composition analysis techniques in the aged adult: indications and limitations. Curr Opin Clin Nutr Metab Care 12(1):8–14
101. Wang ZM, Pierson RN, Heymsfield SB (1992) The five-level model: a new approach to organizing body-composition research. Am J Clin Nutr 56(1):19–28
102. Wang ZM, Heshka S, Pierson RN, Heymsfield SB (1995) Systematic organization of body-composition methodology: an overview with emphasis on component-based methods. Am J Clin Nutr 61(3):457–465
103. Pietrobelli A, Heymsfield S, Wang Z, Gallagher D (2019) Multi-component body composition models: recent advances and future directions. Eur J Clin Nutr 55(2):69–75
104. Gallagher D, Belmonte D, Deurenberg P, Wang Z, Krasnow N, Pi-Sunyer FX et al (1998) Organ-tissue mass measurement allows modeling of REE and metabolically active tissue mass. Am J Phys 275(2):E249–E258
105. Prado CMM, Heymsfield SB (2014) Lean tissue imaging: a new era for nutritional assessment and intervention. J Parenter Enter Nutr 38(8):940–953
106. Ross R, Janssen I (2005) Human body composition. 2nd ed. Heymsfield SB, Lohman T, Wang Z GS (eds) Human kinetics (ADVANTAGE) (Consignment), Leeds, United Kingdom, 2nd revised edition, pp 89–108. ISBN-10: 0736046550
107. Chang G, Wang L, Cárdenas-Blanco A, Schweitzer ME, Recht MP, Regatte RR (2010) Biochemical and physiological MR imaging of skeletal muscle at 7 Tesla and above. Semin Musculoskelet Radiol 14(2):269–278
108. Alizai H, Chang G, Regatte RR (2015) MRI of the musculoskeletal system: advanced applications using high and ultrahigh field MRI. Semin Musculoskelet Radiol 19(4):363–374
109. Parida GK, Roy SG, Kumar R (2017) FDG-PET/CT in skeletal muscle: pitfalls and pathologies. Semin Nucl Med 47(4):362–372
110. Juras V, Mlynarik V, Szomolanyi P, Valkovič L, Trattnig S (2019) Magnetic resonance imaging of the musculoskeletal system at 7T: morphological imaging and beyond. Top Magn Reson Imaging 28(3):125–135
111. Lustgarten MS, Fielding RA (2011) Assessment of analytical methods used to measure changes in body composition in the elderly and recommendations for their use in phase II clinical trials. J Nutr Heal Aging 15(5):368–375
112. Mattsson S, Thomas BJ (2006) Development of methods for body composition studies. Phys Med Biol 51(13):R203–R228
113. Kelley DE, Slasky BS, Janosky J (1991) Skeletal muscle density: effects of obesity and non-insulin-dependent diabetes mellitus. Am J Clin Nutr 54(3):509–515
114. Ross R (2003) Advances in the application of imaging methods in applied and clinical physiology. Acta Diabetol 40(Suppl 1):S45–S50
115. Engelke K, Museyko O, Wang L, Laredo JD (2018) Quantitative analysis of skeletal muscle by computed tomography imaging – state of the art. J Orthop Translat 15:91–103

116. Shen W, Punyanitya M, Wang ZM, Gallagher D, St. Onge MP, Albu J et al (2004) Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. J Appl Physiol 97(6):2333–2338
117. Lukaski HC (1993) Soft tissue composition and bone mineral status: evaluation by dual-energy X-ray absorptiometry. J Nutr 123(2 suppl):438–443
118. Heymsfield SB, Adamek M, Gonzalez MC, Jia G, Thomas DM (2014) Assessing skeletal muscle mass: historical overview and state of the art. J Cachexia Sarcopenia Muscle 5(1):9–18
119. Damilakis J, Adams JE, Guglielmi G, Link TM (2010) Radiation exposure in X-ray-based imaging techniques used in osteoporosis. Eur Radiol 20(11):2707–2714
120. Cawthon PM (2015) Assessment of lean mass and physical performance in sarcopenia. J Clin Densitom 18(4):467–471
121. Shepherd JA, Ng BK, Sommer MJ, Heymsfield SB (2017) Body composition by DXA. Bone 104:101–105
122. Guglielmi G, Ponti F, Agostini M, Amadori M, Battista G, Bazzocchi A (2016) The role of DXA in sarcopenia. Aging Clin Exp Res 28(6):1047–1060
123. Offord NJ, Witham MD (2017) The emergence of sarcopenia as an important entity in older people. Clin Med (Lond) 17(4):363–366
124. Janssen I, Heymsfield SB, Baumgartner RN, Ross R (2000) Estimation of skeletal muscle mass by bioelectrical impedance analysis. J Appl Physiol 89(2):465–471
125. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R (2004) Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. Am J Epidemiol 159(4):413–421
126. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F et al (2010) Sarcopenia: European consensus on definition and diagnosis. Age Ageing 39(4):412–423
127. Haapala I, Hirvonen A, Niskanen L, Uusitupa M, Kröger H, Alhava E et al (2002) Anthropometry, bioelectrical impedance and dual-energy X-ray absorptiometry in the assessment of body composition in elderly Finnish women. Clin Physiol Funct Imaging 22(6):383–391
128. Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J (2015) Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. Proc Nutr Soc 74(4):355–366
129. Sergi G, De Rui M, Veronese N, Bolzetta F, Berton L, Carraro S et al (2015) Assessing appendicular skeletal muscle mass with bioelectrical impedance analysis in free-living Caucasian older adults. Clin Nutr 34(4):667–673
130. Landi F, Martone AM, Calvani R, Marzetti E (2014) Sarcopenia risk screening tool: a new strategy for clinical practice. J Am Med Dir Assoc 15(9):613–614
131. Landi F, Onder G, Russo A, Liperoti R, Tosato M, Martone AM et al (2014) Calf circumference, frailty and physical performance among older adults living in the community. Clin Nutr 33(3):539–544
132. Heymsfield SB, Casper K (1987) Anthropometric assessment of the adult hospitalized patient. J Parenter Enter Nutr 11(5 suppl):36S–41S
133. Heymsfield SB, Stevens V, Noel R, McManus C, Smith J, Nixon D (1982) Biochemical composition of muscle in normal and semistarved human subjects: relevance to anthropometric measurements. Am J Clin Nutr 36(1):131–142
134. Tosato M, Marzetti E, Cesari M, Savera G, Miller RR, Bernabei R et al (2017) Measurement of muscle mass in sarcopenia: from imaging to biochemical markers. Aging Clin Exp Res 29(1):19–27
135. Patrick JM, Bassey EJ, Fentem PH (1982) Changes in body fat and muscle in manual workers at and after retirement. Eur J Appl Physiol Occup Physiol 49(2):187–196
136. Pearson MB, Bassey EJ, Bendall MJ (1985) The effects of age on muscle strength and anthropometric indices within a group of elderly men and women. Age Ageing 14(4):230–234
137. http://www.who.int/childgrowth/publications/physical_status/en/

138. Ukegbu PO, Kruger HS, Meyer JD, Nienaber-Rousseau C, Botha-Ravyse C, Moss SJ et al (2018) The association between calf circumference and appendicular skeletal muscle mass index of black urban women in Tlokwe City. J Endocrinol Metab Diabetes 23(3):86–90
139. Kim M, Won CW (2019) Prevalence of sarcopenia in community-dwelling older adults using the definition of the European Working Group on Sarcopenia in Older People 2: findings from the Korean Frailty and Aging Cohort Study. Age Ageing 48(6):910–916
140. Kusaka S, Takahashi T, Hiyama Y, Kusumoto Y, Tsuchiya J, Umeda M (2017) Large calf circumference indicates non-sarcopenia despite body mass. J Phys Ther Sci 29(11):1925–1928
141. Pagotto V, Santos KFD, Malaquias SG, Bachion MM, Silveira EA (2018) Calf circumference: clinical validation for evaluation of muscle mass in the elderly. Rev Bras 71(2):322–328
142. Andrew Shanely R, Zwetsloot KA, Travis Triplett N, Meaney MP, Farris GE, Nieman DC (2014) Human skeletal muscle biopsy procedures using the modified Bergström technique. J Vis Exp 91:51812. https://doi.org/10.3791/51812
143. Duchenne GB (1868) Recherches sur la paralysie musculaire pseudo-hypertrophique ou paralysie myoo-sclerosique. Archs Gen Med 6(5)
144. Bergström J (1962) Muscle electrolytes in man determined by neutron activation analysis on needle biopsy specimens. Scand J Clin Lab Invest 14(Supp 68):7–110
145. Bergström J, Hultman E (1967) A study of the glycogen metabolism during exercise in man. Scand J Clin Lab Invest 19(3):218–228
146. Coyle EF, Coggan AR, Hemmert MK, Ivy JL (1986) Muscle glycogen utilization during prolonged strenous exercise when fed carbohydrate. J Appl Physiol 61(1):165–172
147. Utter AC, Kang J, Nieman DC, Dumke CL, McAnulty SR, Vinci DM et al (2004) Carbohydrate supplementation and perceived exertion during prolonged running. Med Sci Sports Exerc 36(6):1036–1041
148. Horstman AMH, Backx EMP, Smeets JSJ, Marzuca-Nassr GN, Van Kranenburg J, De Boer D et al (2019) Nandrolone decanoate administration does not attenuate muscle atrophy during a short period of disuse. PLoS One 14(1):e0210823. https://doi.org/10.1371/journal.pone.0210823
149. Langer HT, Senden JMG, Gijsen AP, Kempa S, van Loon LJC, Spuler S (2018) Muscle atrophy due to nerve damage is accompanied by elevated myofibrillar protein synthesis rates. Front Physiol 9:1220. https://doi.org/10.3389/fphys.2018.01220
150. Holloway TM, Snijders T, Van Kranenburg J, Van Loon LJC, Verdijk LB (2018) Temporal response of angiogenesis and hypertrophy to resistance training in young men. Med Sci Sports Exerc 50(1):36–45
151. Niemeijer VM, Snijders T, Verdijk LB, Van Kranenburg J, Groen BBL, Holwerda AM et al (2018) Skeletal muscle fiber characteristics in patients with chronic heart failure: impact of disease severity and relation with muscle oxygenation during exercise. J Appl Physiol 125(4):1266–1276
152. Kilroe SP, Fulford J, Holwerda AM, Jackman SR, Lee BP, Gijsen AP et al (2019) Short-term muscle disuse induces a rapid and sustained decline in daily myofibrillar protein synthesis rates. Am J Physiol Endocrinol Metab 19. https://doi.org/10.1152/ajpendo.00360.2019. [Epub ahead of print]
153. Dirks ML, Smeets JSJ, Holwerda AM, Kouw IWK, Marzuca-Nassr GN, Gijsen AP et al (2019) Dietary feeding pattern does not modulate the loss of muscle mass or the decline in metabolic health during short-term bed rest. Am J Physiol Endocrinol Metab 316(3):E536–E545
154. Tsintzas K, Stephens FB, Snijders T, Wall BT, Cooper S, Mallinson J et al (2017) Intramyocellular lipid content and lipogenic gene expression responses following a single bout of resistance type exercise differ between young and older men. Exp Gerontol 93:36–45
155. Whitfield J, Ludzki A, Heigenhauser GJF, Senden JMG, Verdijk LB, van Loon LJC et al (2016) Beetroot juice supplementation reduces whole body oxygen consumption but does not improve indices of mitochondrial efficiency in human skeletal muscle. J Physiol 594(2):421–435

156. Wullems JA, Verschueren SMP, Degens H, Morse CI, Onambélé GL (2016) A review of the assessment and prevalence of sedentarism in older adults, its physiology/health impact and non-exercise mobility counter-measures. Biogerontology 17(3):547–565
157. Watson KB, Carlson SA, Gunn JP, Galuska DA, O'Connor A, Greenlund KJ et al (2014) Physical inactivity among adults aged 50 years and older – United States, 2014. MMWR Morb Mortal Wkly Rep 65(36):954–958
158. Mora JC, Valencia WM (2018) Exercise and older adults. Clin Geriatr Med 34(1):145–162
159. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, American College of Sports Medicine et al (2009) American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc 41(7):1510–1530. https://doi.org/10.1249/MSS.0b013e3181a0c95c
160. Peterson MD, Rhea MR, Sen A, Gordon PM (2010) Resistance exercise for muscular strength in older adults: a meta-analysis. Ageing Res Rev 9(3):226–237
161. Peterson MD, Sen A, Gordon PM (2011) Influence of resistance exercise on lean body mass in aging adults: a meta-analysis. Med Sci Sports Exerc 43(2):249–258
162. Seals DR, DeSouza CA, Donato AJ, Tanaka H (2008) Habitual exercise and arterial aging. J Appl Physiol (1985) 105(4):1323–1332
163. Sayers SP, Gibson K (2010) A comparison of high-speed power training and traditional slow-speed resistance training in older men and women. J Strength Cond Res 24(12):3369–3380
164. Stathokostas L, McDonald MW, Little RMD, Paterson DH (2013) Flexibility of older adults aged 55–86 years and the influence of physical activity. J Aging Res 2013:743843. https://doi.org/10.1155/2013/743843
165. Montero-Fernández N, Serra-Rexach JA (2013) Role of exercise on sarcopenia in the elderly. Eur J Phys Rehabil Med 49(1):131–143
166. Dunsky A (2019) The effect of balance and coordination exercises on quality of life in older adults : a mini-review. Front Aging Neurosci 11:318. https://doi.org/10.3389/fnagi.2019.00318
167. Fragala MS, Cadore EL, Dorgo S, Izquierdo M, Kraemer WJ, Peterson MD et al (2019) Resistance training for older adults: position statement from the national strength and conditioning association. J Strength Cond Res 33(8):2019–2052
168. Binder EF, Yarasheski KE, Steger-May K, Sinacore DR, Brown M, Schechtman KB et al (2011) Effects of progressive resistance training on body composition in frail older adults: results of a randomized, controlled trial. J Gerontol Ser A Biol Sci Med Sci 60(11):1425–1431
169. Kraemer WJ, Ratamess NA, Flanagan SD, Shurley JP, Todd JS, Todd TC (2017) Understanding the science of resistance training: an evolutionary perspective. Sport Med 47(12):2415–2435
170. Galloza J, Castillo B, Micheo W (2017) Benefits of exercise in the older population. Phys Med Rehabil Clin N Am 28(4):659–669
171. Phu S, Boersma D, Duque G (2015) Exercise and Sarcopenia. J Clin Densitom 18(4):488–492
172. Seals DR, Walker AE, Pierce GL, Lesniewski LA (2009) Habitual exercise and vascular ageing. J Physiol 587(Pt 23):5541–5549
173. Rivera-Brown AM, Frontera WR (2012) Principles of exercise physiology: responses to acute exercise and long-term adaptations to training. PM R 4(11):797–804
174. Harber MP, Konopka AR, Douglass MD, Minchev K, Kaminsky LA, Trappe TA et al (2009) Aerobic exercise training improves whole muscle and single myofiber size and function in older women. Am J Physiol Regul Integr Comp Physiol 297(5):R1452–R1459
175. Sipilä S, Elorinne M, Alen M, Suominen H, Kovanen V (1997) Effects of strength and endurance training on muscle fibre characteristics in elderly women. Clin Physiol 17(5):459–474
176. Liu Y, Ye W, Chen Q, Zhang Y, Kuo CH, Korivi M (2019) Resistance exercise intensity is correlated with attenuation of HbA1c and insulin in patients with type 2 diabetes: a systematic review and meta-analysis. Int J Environ Res Public Health 16(1). pii: E140. https://doi.org/10.3390/ijerph16010140
177. Micheo W, Baerga L, Miranda G (2012) Basic principles regarding strength, flexibility, and stability exercises. PM R 4(11):805–811

178. Seco J, Abecia LC, Echevarría E, Barbero I, Torres-Unda J, Rodriguez V et al (2013) A long-term physical activity training program increases strength and flexibility, and improves balance in older adults. Rehabil Nurs 38(1):37–47
179. Behm DG, Blazevich AJ, Kay AD, McHugh M (2015) Acute effects of muscle stretching on physical performance, range of motion, and injury incidence in healthy active individuals: a systematic review. Appl Physiol Nutr Metab 41(1):1–11
180. Zhou WS, Lin JH, Chen SC, Chien KY (2019) Effects of dynamic stretching with different loads on hip joint range of motion in the elderly. J Sport Sci Med 18(1):52–57
181. Reid JC, Greene R, Young JD, Hodgson DD, Blazevich AJ, Behm DG (2018) The effects of different durations of static stretching within a comprehensive warm-up on voluntary and evoked contractile properties. Eur J Appl Physiol 118(7):1427–1445
182. Stathokostas L, Little RMD, Vandervoort AA, Paterson DH (2012) Flexibility training and functional ability in older adults: a systematic review. J Aging Res 2012:306818. https://doi.org/10.1155/2012/306818
183. Horak FB (2006) Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? Age Ageing 35(Suppl 2):ii7–ii11
184. Dunsky A, Zeev A, Netz Y (2017) Balance performance is task specific in older adults. Biomed Res Int 2017:6987017. https://doi.org/10.1155/2017/6987017
185. Kojima G (2015) Frailty as a predictor of future falls among community-dwelling older people: a systematic review and meta-analysis. J Am Med Dir Assoc 16(12):1027–1033
186. Silsupadol P, Shumway-Cook A, Lugade V, van Donkelaar P, Chou LS, Mayr U et al (2009) Effects of single-task versus dual-task training on balance performance in older adults: a double-blind, randomized controlled trial. Arch Phys Med Rehabil 90(3):381–387
187. Azadian E, Torbati HRT, Kakhki ARS, Farahpour N (2016) The effect of dual task and executive training on pattern of gait in older adults with balance impairment: a randomized controlled trial. Arch Gerontol Geriatr 62:83–89
188. Zhong D, Xiao Q, He M, Li Y, Ye J, Zheng H et al (2019) Tai Chi for improving balance and reducing falls: a protocol of systematic review and meta-analysis. Medicine (Baltimore) 98(17):e15225. https://doi.org/10.1097/MD.0000000000015225
189. Huang ZG, Feng YH, Li YH, Lv CS (2017) BMJ open systematic review and meta-analysis: Tai Chi for preventing falls in older adults. BMJ Open 7(2):e013661. https://doi.org/10.1136/bmjopen-2016-013661
190. Saravanakumar P, Higgins IJ, Van Der Riet PJ, Marquez J, Sibbritt D (2014) The influence of tai chi and yoga on balance and falls in a residential care setting: a randomised controlled trial. Contemp Nurse 48(1):76–87
191. Sivaramakrishnan D, Fitzsimons C, Kelly P, Ludwig K, Mutrie N, Saunders DH et al (2019) The effects of yoga compared to active and inactive controls on physical function and health related quality of life in older adults- systematic review and meta-analysis of randomised controlled trials. Int J Behav Nutr Phys Act 16(1):33. https://doi.org/10.1186/s12966-019-0789-2