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Examination methods in sarcopenia

Vyšetrovacie metódy u sarkopénie

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Abstract
The age-dependent loss of muscle, termed sarcopenia, is virtually omnipresent in the elder population. As it carries great health hazards along, like increased risk of falls, immobility and higher mortality rates, it is important to identify and diagnose people at risk to embank the possible complications they might have to face. This article deals with the algorithm founded by the EWGSOP for the diagnosis of sarcopenia, consisting of three successive approaches, namely the measurement of physical performance, measurement of muscle strength and the measurement of muscle mass. Even though some of those methods are more precise than others, each one of them has their own limitation and therefore a correct selection of an accurate technique is needed for reliable outcomes.

Key words: muscle mass – muscle strength – physical performance – sarcopenia

Abstrakt
Úbytok svaloviny v závislosti na veku, nazývaný sarkopénia, je u staršej populácie skutočne všadeprítomný. Keďže s sebou nesie veľké zdravotné riziká, ako je zvýšené riziko pádu, neschopnosti pohybu a vyššej miery úmrtnosti, je dôležité identifikovať a diagnostikovať ohrozené osoby s cieľom zamedziť možným komplikáciám, ktoré by u nich mohli nastať. Tento článok sa zaoberá algoritmom, ktorý bol vytvorený skupinou EWGSOP pre diagnostiku sarkopénie a zostáva z troch po sebe idúcich postupov, menovito meraní fyzickej výkonnosti, meraní svalovej sily a meraní svalovej hmoty. Aj kedy niektoré z týchto metód sú presnejšie než iné, každá z nich má svoje vlastné obmedzenia, a preto je pre dosiahnutie spoľahlivých výsledkov treba správne zvoliť presnú techniku.

Kľúčové slová: fyzická výkonnosť – sarkopénia – svalová hmota – svalová sila

Introduction

Sarcopenia has been introduced as the term describing an age- related loss in skeletal muscle mass and strength by Rosenberg in 1989. This term is derived from the Greek language 'sarx', meaning flesh, and 'penia' meaning loss. Even though this seems to be an accurate description of the condition, finding a widely accepted definition is still a problem [1]. Due to the lack of this clearly defined border, finding precise prevalence values in epidemiological studies is extremely hard as the results cannot be compared due to differently used definitions of sarcopenia. Nevertheless, it can be said that the loss of skeletal muscle starts around the 40th to 50th year of life and accelerates at approximately 70 years of life. If the definition stating that sarcopenia is a skeletal muscle mass change in all extremities more than two standard deviations from the mean value of a young and healthy reference group, gets used, it can be generalized said that around 50% of all healthy people over 80 years are affected by sarcopenia. According to these facts can be stated that skeletal muscle mass and strength decline continuously and with an increasing rate that can lead to a reduction of 3% of muscle strength in one year [2], and annual reductions of muscle mass ranging between 1 and 2%. Those rates are even higher in people having a sedentary lifestyle, and they are two times higher in

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men than women. Indeed, men have a higher total skeletal muscle mass and a shorter life expectancy in average [3]. Still, it should be kept in mind that sarcopenia is not only a condition affecting older people, if a closer look is taken into its underlying mechanisms, an acceleration of its development in people suffering from chronic diseases with inflammatory elements will be found. Studies have shown that 20 to 50% of chronic heart insufficiency patients also suffer from sarcopenia [2]. The exact pathophysiology of this condition has not been cleared yet, and it has been stated that the loss of muscle force and power is mainly a result of the decline in muscle mass. After estimation of muscle mass with various examination methods, it got clear that it's loss is not enough to explain the decrease in muscle strength, and it can also be attributed to an age-dependent increase of non-contractile muscle compartments, resulting from muscle fiber atrophy and increasing intramuscular fat and fibrosis of skeletal muscles [4]. Therefore, it can be said that until now it is not clear whether the reduction of skeletal muscle's functional capacity is a result of the loss of muscle mass and/or its qualitative alterations [3]. This loss of muscle strength and mass can have devastating effects on the life of affected individuals, starting with impaired mobility and increased risk of falls, fractures and metabolic disturbances and leading to a higher mortality and making it therefore an important health condition that needs more attention drawn to it [4].

Definition and cut-off points

For a long time, a huge problem regarding sarcopenia was the missing clinical definition that was broadly accepted, together with consensus diagnostic criteria, ICD9 codes and guidelines for treatment. Therefore, in 2009 the European Working Group on Sarcopenia in Older People (EWGSOP) was founded, which would develop diagnostic criteria and definitions that could be deployable in clinical practice as well as in research studies [1].

In the early years, definition of sarcopenia was based on the calculation of appendicular fat- free muscle mass of all extremities, measured with dual energy X- ray absorptiometry scans, divided by the body height squared. If the result of this appendicular skeletal muscle mass index was more than 2 standard deviations below the average of a young and sex- specific reference group, sarcopenia was indicated. Using this definition, sarcopenia has had a prevalence of 53% in men and 43% in women over 80 years [1]. Additionally, a gait speed lower, or as low as, 1 m/s, or a covered distance less than 400 m during a 6 minute walk, were also parts of those criteria [2]. Since the year 2005, there have been more approaches on finding a clear definition for sarcopenia, together with appropriate cut-off point criteria which are based on combinations of different measurements around sarcopenia. The International Working Group on Sarcopenia defined the condition as:

- The age-associated loss of skeletal muscle mass and function. The causes of sarcopenia are multifactorial and can include disuse, altered endocrine function, chronic disease, inflammation, insulin resistance, and nutritional deficiencies. While cachexia may be a component of sarcopenia, the two conditions are not the same.

With criteria being a gait speed lower than, or as low as, 1 m/s and an objectively measured low muscle mass, for example the appendicular muscle mass index under, or as low as, 7,23 kg/m^2 in men and 5,67 kg/m^2 in women.

Another definition is the one suggested by the European Working Group on Sarcopenia in Older People (EWGSOP):

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

Moreover, they divide the term into a "primary sarcopenia" if the primary cause is increasing age, or into "secondary sarcopenia" if other causative factors like malnutrition, inactivity or any comorbidity contribute to its development [5]. Set criteria from EWGSOP are formulated as:

- The diagnosis of sarcopenia requires the presence of low muscle mass (estimated by the ratio of appendicular lean mass over the height squared, ≤ 8.0 kg/ht^2 for men and ≤ 6.0 kg/ht^2 for women), in the presence of low physical performance (a gait speed < 0.8 m/s and/or a grip strength < 26–30 kg for men and < 16–20 kg for women) [6].

The cut- off points used are more than 2 standard deviations below the mean of a young and healthy reference population [5].

Adding up to those definitions and criteria, the International Working Group on Sarcopenia has found four recommendations to identify sarcopenia more easily in clinical practice [5]:

1. assess patient for reduced physical capability (or weakness)
2. consider sarcopenia in patients who are non-ambulatory or who cannot rise from a chair unassisted
3. assess usual walking pace (habitual gait speed) over a 4-m course, and
4. patients with a habitual gait speed 1.0 m/s should be considered for quantitative measurement of body composition by DXA

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Measurement of physical performance

According the diagnostic method established by the EWGSOP, for sarcopenia assessment three parameters have to be measured: physical performance, muscle strength and muscle mass. For the measurement of physical performance, usually measure standing balance, sit-to stand time and gait speed get measured, which are included in the Short Physical Performance Battery (SPPB). Those three parameters all rely on motor and strength control, and, with the exception of standing balance, on muscle power [3].

When measuring standing balance, the patient has to take three different positions, the first of them being standing straight with placing both feet directly beside each other. In the second position, the semi- tandem stand, the patient has to place on foot beside the other with its heel being in one level with the middle of the inner face of his other foot. If the patient is able to do so for 10 seconds, he will get one point for each position. The third position is called the tandem stand. Here the patient has to stand with his feet being lined up behind each other for 10 seconds. If he succeeds, he will get two points, and if the patient fails to stay in any of those three positions for 10 seconds, he will get zero points for said position. For the gait speed test, the patient is asked to walk 4 m in his normal walking speed. Walking aids in any form are allowed for this step. Once the patient starts walking, the stopwatch is started, and then stopped again at the moment the patient surpasses the finish line. Depending on the time it took points will be given, for example a duration of under 4,82 seconds will account for four points, over 8,7 seconds one point, and if the distance is not manageable it will yield zero points. The sit-to-stand test is used to assess the leg strength by having the patient stand up and sit down five times on a normally-sized chair for five times. His arms have to be crossed in front of the chest to inhibit possible aid by stabilization. Again, the time it takes for the patient to complete the task is measured and according to the result points are given: a time of under 11.19 seconds equals four points, a result longer than 16,7 seconds is 1 point, and if it takes the patient longer than 60 seconds or he is not able to complete the task, zero points are given. So, in total, a patient can reach a sum of 12 points with those three tests.

With the help of this evaluation system the degree of limitation that a person has to face during his normal daily life, ranging from minimal to no limitation with a result of 10 to 12 points, a mild restriction between 7 to 9 points, a moderate limitation in the range of 4 to 6 points, and a heavy limitation with a result from 3 points down, can get estimated. According to these test results a prognosis can be made. It has been shown that patients over 65 years of age with a test result of 4 to 6 points showed a clear deterioration of mobility in their everyday life in the following four years. Furthermore, patients with such low results showed also an increased probability to get admitted to a nursing home, and the mortality risk increased to 5,7- 12,3% in the next four years [7]. Additionally, low scores are predictive of an elevated risk to fall, lower mobility, disabilities and longer stays in hospitals [8]. Patients with higher results, on the other hand, had lesser probabilities for those outcomes.

The SPPB shows a great reliability and has an intraclass coefficient of 0,88 to 0,92 (the optimum is 1), and therefore can help us not only to assess the fitness level of a geriatric patient, but also to discover changes in people with possible sarcopenia [7].

Measurement of muscle strength

Muscle strength is shown to be superior in the prediction of muscle function in the common population than muscle mass. Muscle strength is the maximal capacity for force generation a muscle has, and it is in a positive relationship with muscle mass, the muscle fiber cross- sectional area, and myonuclear and satellite cell amount in elderly men. In older people of both sexes, muscle strength is declining earlier than muscle mass, even though those two events are connected with each other. Moreover, it can be stated that low muscle strength is associated with an increased mortality, autonomously from a low muscle mass [5].

The isokinetic dynamometer is useable for the measurement of three different types of muscle contractions. During an isometric muscle contraction, the muscle length stays the same, whilst during an isokinetic muscle contraction, the muscle length changes. Such an isokinetic contraction can be further divided into an eccentric one, where the active muscles increase in length, and into a concentric one, during which the active muscles get shorter.

The unique features of isokinetic dynamometry are optimal loading of the muscles in dynamic conditions and constant preselected velocity of movement. These features provide safety in the rehabilitation of patients with muscular and ligaments injuries, for this reason is recognized as a good standard for measuring muscle strength in old people.

In clinical practice, and also in research, muscle strength can be assessed by measuring knee extension strength with the isokinetic dynamometer [3]. Hereby the quadriceps muscle most commonly gets measured. Even though this is a good technique of strength measurement, it is still limited in many cases in clinical practice due to its costs, the necessity of buying the needed equipment, the absence of practiced staff and the limited amount of data in the elder population. The repeated chair stand

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test, in which the patient has to stand up and sit down unassisted from a chair for five times as fast as possible, is a good alternative for measuring muscle strength of lower body as it has been shown to be reliable and yield valid results.

Nevertheless, handgrip strength measurement is still the most widely used method for muscle strength assessment.

In general, isometric handgrip strength shows a good correlation with leg strength and also with lower extremity power, knee extension torque and calf cross- sectional muscle area.

In addition to that, it has the great advantage that it is easy to perform and does not need a specialised staff to be executed, and it is a lot cheaper than other methods. For the hand grip strength measurement, the patient has to sit on a chair with his arms lying on the armchairs whilst six measurements are taken, three on each hand. The patient has to squeeze the dynamometer as tightly and hard as possible for 3–5 seconds, and the highest result is taken into account as the definite one. The Jamar dynamometer is the commonest instrument used, but it's design can be a limitation in patients with rheumatoid arthritis, in which cases the Martin vigorimeter is an appropriate alternative as the patient has to squeeze rubber balls here. Different threshold values have been proposed for grip strength, ranging from 26- 30 kg in men and from 16–20 kg in women [9]. Lowered hand- grip strength clinically indicates poor mobility and can predict clinical outcomes better than a lowered muscle mass [3].

Measurement of muscle mass

Anthropometric measurements

There are many ways on how to measure the appendicular muscle mass. Anthropometric methods include the body mass index, arm or calf circumference, arm muscle cross- sectional area as part of arm muscle circumference and skinfold thickness. Those methods are simple to apply but are not very precise, even though some may highly match with appendicular muscle mass, big predictions errors tend to occur as well [5].

Bioimpedance measurement

Bioimpedance analysis is another cheap, non-invasive and often used method for body composition measurement, including the measurement of muscle mass, as well as the assessment of a patient's clinical condition.

Bioimpedance or biological impedance is defined as the ability of biological tissue to impede electric current [10].

Therefore, the use of bioimpedance to measure the body composition is based on the identification of body volume with the help of resistance measurement [10].

The body is made up from two different resistances (R) to electric currents: the capacitative R, or reactance, and the resistive R, simplified called resistance. Impedance describes those two terms combined [11]. In the human body, reactance is caused by the capacitance of cell membranes, and resistance is made from the total water in the body [10].

The relationship between capacitance and R is interesting because it reflects different electrical properties of tissues that are affected in various ways by disease and nutritional status and hydration status [11].

Additionally, the body is composed of fat mass (FM), which is does not conduct electric charge, and fat free mass (FFM), which does conduct electrical charge due to the fact that electrolytes dissolved in body water are conductive. This body water, also described as total body water (TBW), is the main component of FFM and makes about 73.2% of it in a normally hydrated person. When using bioimpedance to measure a body's composition, the five-compartment module gets used, in which the body is divided into five segments consisting of the two upper extremities, the two lower extremities, and the trunk. In addition to that, here the segments are split into their components, which are the FM and the FFM, which consists of bone minerals, TBW and body cell mass (BCM) which includes protein. In addition to that, the TBW can be further divided into intracellular fluid (ICF) and extracellular fluid (ECF) [12].

Furthermore, BIA can be used to assess other factors defining muscularity, for example the total body skeletal muscle mass (SM), being located to 73- 75% in the extremities where it is termed as the appendicular skeletal muscle mass (ASMM). The skeletal muscle index, being defined as the SM in kg divided by the height in m squared, and the appendicular skeletal muscle index, being calculated with the same formula as the skeletal muscle index, are being used to normalize the gained values and to be able to compare them with pre- set cut-off values [12].

The, above mentioned, impedance depends on the frequency at which the current is applied [10]. If a low frequency is used, the current flows only through extracellular fluid because it is not able to penetrate cell membranes as they act as insulators, and therefore shows the resistance of extracellular fluid. A very high frequency, on the other hand, reflects the resistance of extracellular and intracellular fluid combined. The perfect frequencies for usage in measurements are predicted using Cole-Cole plots [11].

Single frequency bioimpedance analysis

Single Frequency Bioimpedance Analysis (SF-BIA) – here, the frequency used is 50 KHz. It is one of the ear-

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liest methods and also one of the mostly used ones for body compartment estimation. The principle on which this method is based is, that impedance and TBW are inversely proportional to each other. SF-BIA is used in measurement of TBW and FFM in normally hydrated individuals, as it is not available in patients with changed hydration status [10].

Multiple frequency bioimpedance analysis

Multiple Frequency Bioimpedance Analysis (MF-BIA) uses at least 2 different frequencies and is based upon the fact that with the help of low and high frequency electric currents ECF and TBW can be assessed once exposed to them. This method evaluated ECF more exact than SF-BIA, but it is less useful in the detection of shifts in ICF and ECF in older and ill patients [10].

Bioimpedance spectroscopy

Bioimpedance Spectroscopy (BIS) uses the resistance occurring at zero frequency (R_0) and the one occurring at infinite frequency (R_{inf}) to project the ECF and TBW. It uses either an equation modules approach or an analytically derived equations approach [10].

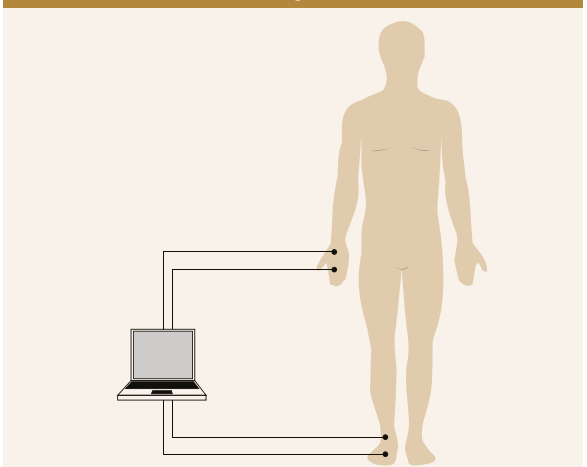
Whole body bioimpedance measurement

This method is the method of choice for whole body compartment estimation. There are three different application forms: the hand to food method, being the most common one, the foot to foot method, and the hand to hand method [10].

Body segment bioimpedance measurement

In segmental – Body Segment Bioimpedance Measurement (BIA), there are four protocols according to which electrodes get placed on different placed on the body for measurement. It is very precise in the detection of changes of ECF due posture differences, and also has better results in the assessment of TBW and skeletal muscle mass (SMM) than whole body bioimpedance measurement [10], Figure 1.

Figure 1 | Two electrodes are placed on the right hand and foot for bioimpedance measurement. Modified according to [13]



Bioimpedance vector analysis method

Bioimpedance Vector Analysis Method (BIVA) has been established to assess a patient's hydration status. Therefore, a height indexed resistance reactance data from bioimpedance measurement is used.

Using 8,022 normal subjects Piccoli et al. formulated 50%, 75% and 95% tolerance ellipses that determine increasing and decreasing body mass if the minor vector falls in the left and right half of the 50% ellipse, along with increasing and decreasing hydration ratio if the major vector falls in the lower and upper half of the 50% ellipse [10].

After measurement, the gained values have to be used in appropriate equations to yield usable and standardized results. This still stays a main problem in BIA usage, as an equation has to be adjusted to the people assessed [11]. The reason behind this are the many factors that can influence and lead to a wrong outcome if not being acknowledged. Anthropometric measurements, like height, weight, circumferences, skinfold thickness, lead to lot more precise results if being included. There is also a big difference between the two genders, as women possess a higher FM and TBW than

Figure 2 | DXA scan of a whole body composition measurement. Modified according to [13]



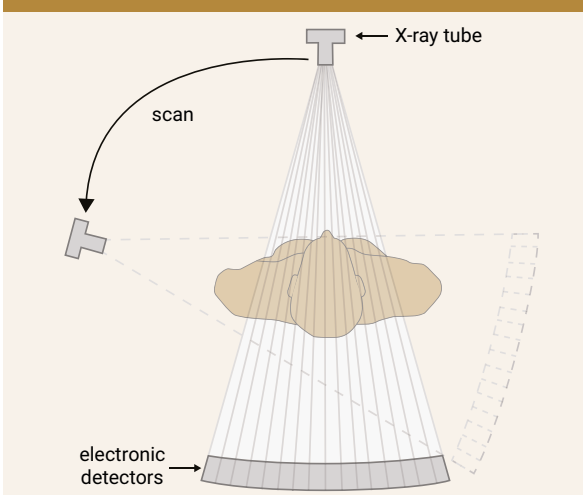
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men, whilst the latter have more FFM. Normal aging of a person causes an alteration of a body's composition, meaning an increase in FM and a decline in lean mass. There is also a discrepancy of body composition amongst different ethnic groups being explained by variable nutritional factors, culture and environment in addition to other body conformations affecting limb length, body size and body fat percentages. Moreover, the use of alternating protocols and electrode sizes, as well as movement during measurement or miss- positioning can also lead to errors during the examination [10]. Furthermore, out of the many reference methods that can be chosen, including dual- energy X- ray absorptiometry, densitometry and many more, each one of them is limited by a different factor having to be included in the whole process. Therefore, chosing a correct equation for measurement of a specific population or person requires a multifactorial approach [11].

Dual energy X-ray absorptiometry

Dual Energy X-Ray Absorptiometry (DXA) is named to be the gold- standard method for body composition measurement as it is highly precise, quick, non- invasive and uses only a low amount of radiation. It is used for the assessment of lean mass, fat mass and bone mineral content, therefore based on a three-compartment model, and for the differentiation between a physiological muscle mass loss or a pathological one. One can either use it for a specific body region or for measurement of the whole body. The principle behind DXA is the scattering or absorption of X- rays that are transmitted through the body beforehand (Figure 2 and Figure 3). This depends of the thickness and density of the tissue and the energy intensity used: low density tissue, like soft tissue, readily lets the photons pass through and therefore scatters only little transmitted rays, whilst, on the other hand, tissue with a high density attenuates the X- rays to a great deal. DXA is able to distinguish soft tissue and bone, and fat mass and lean mass can be calculated from the pixels seen in the acquired picture that are not bone. Still, a big problem in using DXA for measurement is the missing standardization [14]. Moreover, it is not possible to measure intramuscular fat with this method [3].

Figure 3 | DXA scan of a whole body composition measurement. Modified according to [13]



Computed tomography

Computed Tomography (CT) works similar to the DXA meaning it is also based on the attenuation of X-rays that are sent through the body. This attenuation of rays happens to different degrees in different tissues due to their varying densities. The CT number represents this phenomenon and Hounsfield units are used to express it. The CT number and density of tissue are in a linear proportion to each other [15]. It is a highly accurate method with great image resolution and the possibility to assess the amount of intramuscular fat. Nevertheless, there are also some negative aspects of CT examination, as the high radiation exposure, it's high cost and the required technical skills of the operator and patient compliance needed for the execution [14].

Magnetic resonance imaging

Magnetic Resonance Imaging (MRI) offers, like the CT, a high reproducibility, accuracy and image resolution, as well as also the greatest accuracy in differentiation of various tissues at anatomical levels. In addition to that it also provides the most precise assessment of intramuscular fat [14]. MRI can be used for measurement of the whole body's composition or just for one region. This technique works through the interaction between a magnetic field and hydrogen atom nuclei. The patients is put inside the MR imager and as it produces a magnetic field, the patient's proton's magnetic moments align themselves with it. Then, a pulsed radiofrequency is released whose energy gets absorbed by the protons. Once the radiofrequency is turned off again, the protons go back to their original state and the stored energy gets set free from the protons as another radiofrequency impulse which is measured by the machine to produce an image [15]. Even though this technique is very precise, it is expensive, not everywhere available and needs great patient compliance and special skills for operation [14].

Conclusion

Sarcopenia is an increasingly occurring, geriatric syndrome that needs more attention drawn to it in com-

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bination with further research. The three approaches used for diagnosis, the measurement of physical performance, muscle strength and muscle mass, are appropriate methods giving more or less reliable results, still, they each have their own limitations and negative aspects that need to be figured out. Furthermore, unified definitions and cut-off values are needed to set general criteria on decision making when a person is said to be sarcopenic or not.

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