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Revisão de Literatura

Review: Sarcopenia and Pre-Sarcopenia: Evaluation Methods in Clinical Practice

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ABSTRACT

In recent years the population has been experiencing an increase in life expectancy. With these years gained later in life, problems such as sarcopenia and pre-sarcopenia arise. Sarcopenia, defined as the loss of muscle mass and strength, acts directly on individual health and well-being, eventually leading to limitations and dependence on caregivers. Pre-sarcopenia is an earlier preceding step, defined as low muscle mass alone. This review aims to describe and critically analyze the methods that can be used for screening and early diagnosis of sarcopenia and pre-sarcopenia, selecting the most cost-effective in clinical practice to detect, prevent and monitor affected individuals.

Keywords: sarcopenia; aging; muscle; strength; diagnosis

INTRODUCTION

Sarcopenia can be broadly understood as the loss of strength and muscle mass. Muscle mass starts to decline from ~40 years onwards[1] thus sarcopenia prevalence increases with age. Current United Nations projections estimate[2] that adults aged 60 and over will increase from 1 in 8 now to 1 in 5 people by 2050, leading to an increased prevalence of age-related sarcopenia and its potential consequences: limitation in daily life activities, loss of autonomy, dependance, depression, falls, fractures, hospitalization, and death[3]. Metabolic consequences such as increase in insulin resistance and metabolic syndrome[4], worse prognosis in cancer or surgical patients[5] have also been reported. Despite its importance, sarcopenia is not routinely screened in individuals at risk, either older or with predisposing conditions. And most important, sarcopenia can be partially reversed with the correct intervention and treatment!

There are at least seven different definitions for sarcopenia[6]. The most used one is from the EWGSOP2[1] (*European Working Group on Sarcopenia in Older People)*, stating that sarcopenia is suspected when there is low muscle strength and confirmed by low muscle quantity (two standard deviations below a healthy population muscle mass) or low muscle quality, in overweight individuals who may have intramuscular fat, for example. The same group had previously defined pre-sarcopenia as low muscle mass alone and severe sarcopenia when physical performance is impaired.

Questionnaires have low to moderate sensitivity for sarcopenia detection[7] and there isn't a single and simple exam available in clinical practice for the diagnosis[8]. Low muscle strength and mass can be assessed through different tests and cut-offs according to different populations. In a recent meta-analysis of 151 studies, the overall prevalence of sarcopenia using the most common criteria could range from 0.3–91.2% in women and 0.4–87.7% in men[8]! Sarcopenia prevalence varied by diagnostic criteria from 10-27% in those > 60 years old; by geographic region and ethnicity, being lower in Europe; by gender, depending on the diagnostic method[8]; and by age, varying more in those < 60 years old than in those above 60 years old. However few studies were performed in individuals < 60 years old. Beyond that,the current obesity epidemics may change the cut-offs for muscle mass, making the pre-sarcopenia or sarcopenia diagnosis in unsuspected individuals even more difficult.

The objective of this review is to describe and critically analyze the methods that can be used for screening and early diagnosis of sarcopenia and pre-sarcopenia, selecting the most cost-effective in the clinical practice to detect, prevent and follow affected individuals.

METHODS

A literature review was carried out on methods for assessing pre-sarcopenia and sarcopenia in clinical practice. The search was performed in the PubMed databases, using the keywords: "sarcopenia diagnosis", "sarcopenia diagnosis method", "sarcopenia and SARC-F", "bioimpedance (BIA) and sarcopenia", "sarcopenia -ray absorptometry of energy double (DXA)", "sarcopenia and computed tomography"

and "EWGSOP". We included all books and documents, meta-analyses, clinical trials, randomized tests and review articles published in the last five years, between January 2018 and January 2023, using as strata those who discussed at least one of the diagnostic methods of pre-sarcopenia and sarcopenia, to systematize the assessment tools for this pathology, aiming to provide a better path for early intervention.

DISCUSSION

In whom to look for sarcopenia and pre-sarcopenia?

Sarcopenia is a physiological process in which there is loss of muscle mass and consequent decrease in muscle strength. It affects mainly individuals within a higher age group, that is, in the aging spectrum. However, there are also data that confirm the incidence of sarcopenia preceding the age of 60. Recent studies indicate a higher incidence of sarcopenia in hospitalized younger populations, in nursing homes or hospitals. A review of several studies revealed a prevalence of sarcopenia from 9.9% to 40.4% in hospitalized populations, according to the diagnostic criteria used[8].

Also noteworthy is the muscle fragility disorder linked to sarcopenia in patients with chronic diseases, such as diabetes, demonstrated by a cross-sectional study to be more predisposed to the development of sarcopenia, as well as individuals who regularly used more than four daily medications. The chances of developing sarcopenia were 3.6 and 2.6 times higher, respectively[9].

In addition, sarcopenia may be related to the reduction in the functionality of the skeletal muscles, due to inactivity because of a sedentary lifestyle or upon prolonged mobility arrests due to orthopedic or neurological illnesses[5], like stroke for example. A nutritional relationship with the development of sarcopenia was also observed. Healthy eating habits, intake of proteins and vitamin D evidence a positive effect for the non-occurrence of sarcopenia, as well as the frequent practice of physical exercises. Thus, being sedentary and poor nutrition are associated with the development of sarcopenia[10].

Besides, studies demonstrate the evolutionary association of muscle weakness and the development of sarcopenia in patients with dementia of various etiologies. Several factors can influence the sarcopenia process in dementia, including poor nutrition, inactivity, cognitive decline, but there are also reports about the anatomical decrease in brain volume in the hippocampal region in moderate stages of dementia associated with the reduction of muscle capacities for these individuals[11].

Finally, we highlight the increased incidence of sarcopenia in females, probably due to the earlier hormonal and metabolic variations present in women compared to men. As women age, there is a hormonal decline due to the cessation of reproductive activity around 50 years old, which results in a more advanced loss of muscle mass. In men hormonal levels suffer a slow decline usually after 60 years old, overlapping with the aging process. Estimates to date indicate that 14.5% to 26.75% of postmenopausal women between 57 and 69 years of age are considered pre-sarcopenic and sarcopenic respectively[12.]

In summary, sarcopenia is a muscle disorder of multifactorial development, affecting different

groups, in which multiple factors may trigger the process of muscle loss, weakness, slowness and low muscle strength. A higher incidence of sarcopenia is observed in individuals aged over 60 years, hospitalized population, people with chronic diseases, sedentary or with mobility disorders, and malnourished individuals, patients with dementia and women.

Screening for sarcopenia

Sarcopenia diagnosis depends on a comprehensive assessment of strength, function and muscle quality. Most of these assessments, in addition to being time-consuming, are also laborious, difficult to implement, and often unsuitable for large-scale population surveys[13]. Therefore, if people with favorable scenarios for developing sarcopenia could be identified at an early stage and only then widely evaluated, it would save time, costs, and the detection rate would be improved. The appropriate intervention could be carried out in the case of a possible sarcopenia or pre-sarcopenia, to prevent the development of this pathology and thus strongly improve the quality of life of individuals. So, screening for sarcopenia is crucial to public health; therefore, to detect, maintain and improve sarcopenia at an early stage, it is relevant to select an easily measurable and clinically validated screening tool[14].

When the EWGSOP2 updated the diagnostic criteria for sarcopenia (2018), it also recommended a screening questionnaire called SARC-F to determine whether individuals should be further evaluated for sarcopenia [1]. The SARC-F questionnaire was announced by John E. Morley as a method for sarcopenia screening at the EU/US Committee on Sarcopenia in the Elderly at the International Conference on Sarcopenia Research (ICSR) held in Orlando in 2012[15,16].

The SARC-F Questionnaire

The SARC-F questionnaire was developed as a possible quick test with the main objective of filtering the probable cases of sarcopenia, before taking measurements of strength and muscle mass. This survey tracks sarcopenia through data described by the patients about daily difficulties, such as falls, climbing stairs, getting up from a chair, need for assistance in walking and physical strength. It is a simple, practical, and easy-to-apply screening instrument, for both the test giver and the patient[17].

Sarcopenia screened by SARC-F alone was shown to increase the diagnostic accuracy (predictive value) in people undergoing adverse pathologies[18], as is the case with the possibility of applying SARC-F in postmenopausal women[19], people who need long-term care[20] or older adults[21], that can be related to sarcopenia.

The SARC-F is composed of five questions graded from 0 to 2 points, where 0 corresponds to "no difficulty" and 2 is considered "very difficult" regarding:

- Strength (S)
- Assistance to walk (A)
- Rising from a chair (R)
- Climbing stairs (C)
- Presence of falls (F)

The total calculated maximum score is 10 points; the cut-off value $\geq$ 4 points is recommended as suggestive of a probable risk of sarcopenia (Figure 1).

Figure 1. The SARC-F questionnaire

Components	Questions	SARC-F Score
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None = 0 Some = 1 A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0 Some = 1 A lot, use aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0 Some = 1 A lot or unable without help = 2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None = 0 Some = 1 A lot or unable = 2
Falls	How many times have you fallen in the past year?	None = 0 1–3 falls = 1 4 or more falls = 2

Adapted from Yang M, et *al.*[21]

If, on the one hand, the SARC-F questionnaire is characterized by having high specificity and a relatively good overall predictive value, on the other hand, its sensitivity is low[22-25]which is an important limitation of the SARC-F questionnaire as a screening tool[26]. Sensitivity determines the ability of a test to correctly identify those who have the disease. This low sensitivity would possibly result from the absence of low muscle mass evidence in the questionnaire[27-29]. So, in 2016, to increase the sensitivity of the SARC-F test, Barbosa-Silva et al. suggested a new test model: the "SARC-CalF circumference" or "SARC-F + CC"[28], by claiming that the SARC-CalF had considerably improved the screening performance and sensitivity of the "simple SARC-F" for sarcopenia, finally enabling the test to be used in clinical practice.

SARC-CalF or SARCF + CC

Basically, the SARC-CalF adds the calf circumference (CC) to the SARC-F, being a modified version of the SARC-F, that's why it was also called as SARC-F + CC (or SARC-CalF score). The introduction of the CC measurement to the SARC-F aims to incorporate an anthropometric measurement (CC) as a marker of muscle mass to the muscular functional categories assessed by the original questionnaire. Calf circumference assessment is a relatively simple procedure, which consists of measuring the largest part of the right calf with a non-elastic flexible plastic tape, with the participant standing, with legs relaxed and approximately 20 cm away, with the measurement being carried out in a flat and horizontal place[30].

So, SARC-F + CC comprises the 5 items of SARC-F and the additional item "calf circumference (CC)". The suggested CC cutoff point is ≤ 33 cm for women and ≤ 34 cm for men, denoting a decrease in muscle mass[28].

People with a CC below these cut-off values are considered as having low muscle mass – a criterion for sarcopenia- and receive an increase of 10 points in the original SARC-F score (Table 1)[21]. The SARC-F + CC score ranges from 0 to 20

points, and people with scores ≥11 are considered at risk for sarcopenia[28].

Table 1. CC and SARC-F scores.

GENDER	CC SCORE
FEMALES	> 33cm = 0 ≤ 33cm = 10
MALES	> 34cm = 0 ≤ 34cm = 10

SARC-CalF has greater sensitivity (66.7%) compared to the sensitivity of SARC-F alone, which is around 33.3 %; the area under the curve (AUC) has a higher value (SARC-CalF = 0.736 and SARC-F= 0.592) while specificity is comparable (82.9% vs 84.2%, respectively[28,31]).

Besides, SARC-F would probably not detect the earlier phase of pre-sarcopenia, where only decreased muscle mass is expected to exist, and the measurement of the CC could add this information.

Although recent studies developed other screening tools with increasing sensitivity and efficacy, that performed as well or better than standard SARC-F[32,33], sarcopenia research institutions such as the EWGSOP2, the Asian Working Group for Sarcopenia (AWGS2)[34], International Clinical Practice Guidelines for Sarcopenia (ICFSR)[35] and Society for Sarcopenia, Cachexia and Wasting Disorders[36] recommend the use of SARC-F for screening of sarcopenia as the preferred method for rapid sarcopenia screening to enable the diagnosis of sarcopenia in an asymptomatic period and prevent its serious health consequences.

SARC-F is a relatively simple assessment instrument and was closely associated with a future decrease in physical performance. [22]Furthermore, the analogy between survival and SARC-F was described in a meta-analysis of five observational studies, which mentioned that the combined hazard ratio for SARC-F questionnaire positivity and mortality was 1.87 ($p< 0.0001$)[37]. These findings indicate that the SARC-F denotes direct assessment of sarcopenia and therefore is a suitable tool for community sarcopenia screening and for scientific research, experimental observations, and large-scale community epidemiological investigations.

Diagnosis

The EWGSOP predicts sarcopenia identification through three distinct main factors, namely: muscle mass, muscle strength and physical performance. Dynamic tests assess muscle strength and physical performance. As sarcopenia is a progressive disorder associated with the skeletal muscle system, it is of great importance to assess the mobility and locomotion of the individual, which is why dynamic tests to assess muscle power, postural reactions and dynamic stability are performed. In addition to the clinical criteria, imaging direct or indirect tests can help to identify low muscle mass.

Dynamic tests

The Short Physical Performance Battery (SPPB)[38] is a group of tests that assess the daily rhythm and balance, through standing up and walking in a timed manner, and the walking time through the six-minute walk test for example.

Here we will describe the single most important tests to perform and aid in the diagnosis of sarcopenia such as Timed Up and Go (TUG), Gait Speed Test (GST), Handgrip Strength Test (HST), Chair Stand Test (CST), Stair Climb Power Test (SCP), among others that aim to establish the patient's deficiencies and instabilities for better clinical applicability.

The **Timed Up and Go** is a test in which the patient is asked to get up from a chair, walk for three meters, turn around and sit down again in the same chair, generally assessing balance deficit and instability of gait. The test scores are related to the assessment of the risk of falling. The test must be timed and analyzed using different observational parameters to estimate the individual's basic abilities. In a Brazilian study, the reference value for the test was a time ≥ 10.85 seconds predicting sarcopenia, considering 67% sensitivity and 88.7% specificity.

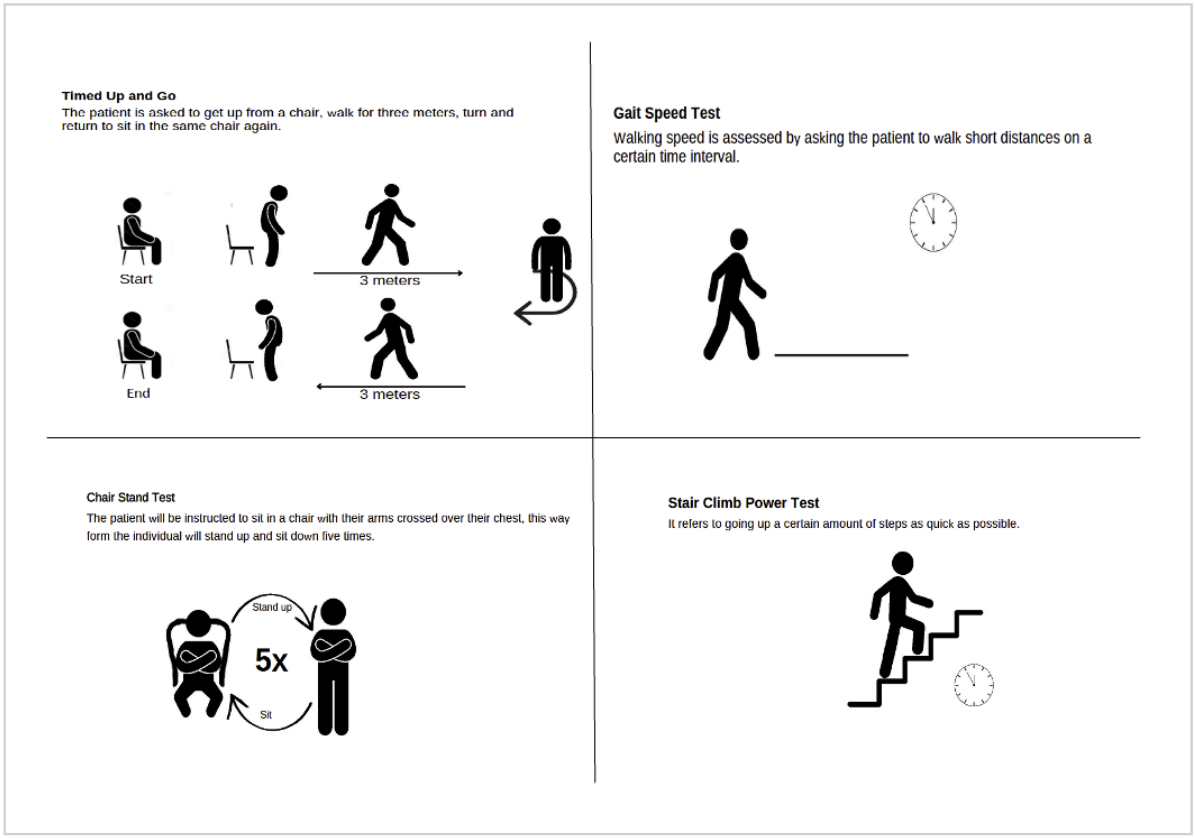
One of the main tests used is the Gait speed test, which helps quickly and safely in the diagnosis. Walking speed is assessed by asking the patient to walk short distances in a given time interval. Currently the EWGSOP recommends ≤0.8 m/s over 4 m for the definition of severe sarcopenia.

Another useful tool is the **Chair sit and stand test**[39], in which the patient will be instructed to sit in a chair with his arms crossed over the chest. In this way the individual will stand up and sit down five times during the fastest period of time he can. The test analysis will be through timed time, being ≥16.7 seconds (insufficient), from 13.7 seconds to 16.6 seconds (sufficient), from 11.2 seconds to 13.6 seconds (good) and ≤ 11.1 seconds (very good), all adjectives are rated on the patient's muscle strength performance, also recording reactions postures, balance deficit and gait instability, for a better understanding of the results.

In addition, we can also highlight the **Stair Climb Power Test**, better[40] known as the **Stair climbing power test,** used to measure muscle power, which refers to climbing flights with a certain number of steps as soon as possible, being evaluated the time used, height of steps, balance, and other factors relevant to clinical applicability. However, this test is not always applicable and functional, as it requires the use of stairs at the data collection site.

A graphic demonstration of these dynamic test is shown at Figure 2.

Figure 2 - Dynamic tests to assess sarcopenia



All components of Figure 2 were digitally drawn by Maria Eduarda Julio Lopes

We conclude that dynamic tests are fundamental and complementary for the early diagnosis of sarcopenia, efficiently helping in the development and prognosis of the disease, seeking a better quality of life for patients, as well as greater life expectancy in their lives.

Hand grip strength

Usually upon execution of the gait speed test, a **Handgrip strength test** is usually also carried out, with the help of a calibrated portable dynamometer (Figure 3) to measure the individual's muscle strength. In short, hand grip strength cut-offs were considered as <30 kg in men and <20 kg in women. The handgrip strength method is relatively simple and cost-effective. However, the results of the measurement of handgrip strength are influenced by the way in which the patient is positioned during the measurement, the dominant side of the hand, the size of the hand, the number of repeated measurements, its weight, and your height. In addition, various dynamometers can be used, such as digital, analog, hydraulic and Smedley types. This difference between measuring methods and measuring machines can induce a discrepancy between results. Despite these limitations, measurement of grip strength is a valid and reliable method to assess sarcopenia. Currently, the indicator of low grip strength is determined at <27 kg for men or <16 kg for women, according to EWGSOP data[41].

Figure 3. Two models of calibrated dynamometers for hand grip strength assessment

Image source: Obtained using the Goggle Images tool, without commercial rights of use
https://www.google.com/search?q=SAEHAN+Dinam%C3%B4metro+Hidr%C3%A1ulico+De+M%C3%A3o&kgmid=/g/11f5s3fm7w&source=.lens.button&hl=pt-BR&gl=BR
https://instrutemp.com.br/dinamometro-para-que-serve-e-como-funciona/

Bioimpedance (BIA)

The main objective of bioimpedance is to evaluate body composition, through the analysis of muscle mass, water, and fat, which may vary according to weight, age and gender. BIA does not measure muscle strength or physical performance and can identify individuals in pre-sarcopenic stages.

The analysis is done with electrodes (Figure 4), which quantify the variation of the phase angle (PhA), resulting from the increase and decrease of voltage and electric current through the body. According to recent studies, the PhA variation is related to the number of cell membranes present in the body, as well as the percentage of water and cell mass. The greater the ratio of cell membranes, the greater the PhA of the evaluated patient; patients with a high rate of muscle mass have large percentages of cell membranes, which leads to greater reactance and consequently a high PhA. Research indicates that the PhA is related to the ratio between reactance (opposition of electric current and voltage) and resistance. Different body components have different resistance to electric current during the procedure. Water conducts electrical impulses effectively, while fat is less conductive. It is through this conduction variation that it is possible to calculate the patient's percentage of muscle mass, fat, and water.

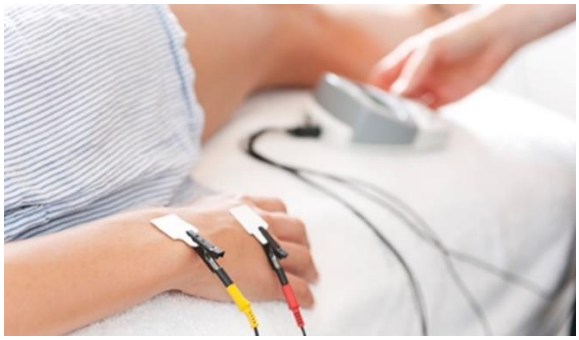
Currently, the mean phase angle variation considered within normal standards is 6. The lower the PhA rate, the higher the sarcopenia prevalence risk. Individuals with a relatively low phase angle are about 5.6 times more likely to have sarcopenia in early aging. Other studies indicate that sarcopenia becomes 2 times more prevalent in individuals who have reduced PhA throughout their lives. The PhA variation can be due to several factors, but the main ones include obesity, aging, inflammation, chronic diseases, and sedentary lifestyle.

Of course, standard rates for bioimpedance vary according to age and sex, as it is related to the amount of body muscle mass. The acceptable rate for men ranges from 6.75 to 7.40, while for women this rate is from 5.07 to 5.80.

Bioimpedance may have certain disadvantages. In cases where the patient is in extreme states of hydration, the exam can lead to a contradictory result. In addition, the test does not accurately assess muscle structure. However, in multifrequency bioimpedance there will be a compartmentalization of the water and consequently it will be possible to make a more detailed and accurate analysis of the body components, even in cases of electrolyte imbalance or dehydration. When we take this into account, we conclude that BIA is one of the

simplest, non-invasive techniques and is efficient in aiding the diagnosis of pre-sarcopenia and sarcopenia.

Figure 4. An example of the performance of a biompedance exam



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Dual-energy X-ray absorptiometry (DXA)

Dual-energy X-ray absorptiometry (DXA) is the current reference method for the assessment of osteoporosis and sarcopenia in clinical settings, primarily because it provides accurate estimates of bone, fat, and lean soft tissue (the so-called three-compartment model including BMC, FM and FFM). DXA uses low-emission X-rays to measure the attenuation of incident X-ray beams as they pass through body tissues (high attenuation for bone and low attenuation for fat). The EWGSOP recommends the use of DXA to assess lean mass as an estimate of all non-fat/non-bone tissue, fat mass and bone mineral content. Its use is suggested to calculate the appendicular lean mass index (ALMI = ALM/height2) to define sarcopenia or low muscle mass using a defined cut-off of < 5.5 kg/m2 in women and ALMI < 7.0 kg/ m2 in men.

The most relevant advantage of DXA is the definition of sarcopenia, in addition to the low exposure to radiation that is equivalent to exposure on an intercontinental flight, not requiring strict monitoring in most cases. Furthermore, DXA is cheaper compared to a standard CT scan and is easy to perform from a technical point of view. Unfortunately, DXA, even if performed accurately, has several limitations: poor accuracy in estimating trunk fat and muscle due to the inability to separate intra-abdominal organs; over/underestimation of the extent of sarcopenia or presence of obesity from the interpolated amount of fat and muscle from arms and legs and low accuracy in the presence of edema and altered hydration status, as well as the BIA. Despite these limitations, as suggested by the EWGSOP, DXA is useful in clinical practice to confirm sarcopenia when there is clinical suspicion.

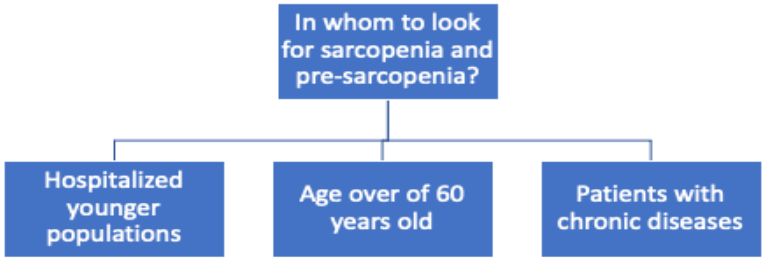
Computed tomography (CT)

Computed tomography (CT) is one of the most widely used imaging tests in a precision aspect when diagnosing sarcopenia. CT is able to show the results of clinical treatments. In addition, it is possible to evaluate in this radiological examination whether the patient is susceptible to muscle atrophy or visible visceral fat infiltration on imaging. Unfortunately, CT is not recommended for healthy sarcopenic patients, as high radiation can damage the musculature. Therefore, exposure of radioactive elements means that this examination is not indicated.

Practical approach for sarcopenia and pre-sarcopenia detection

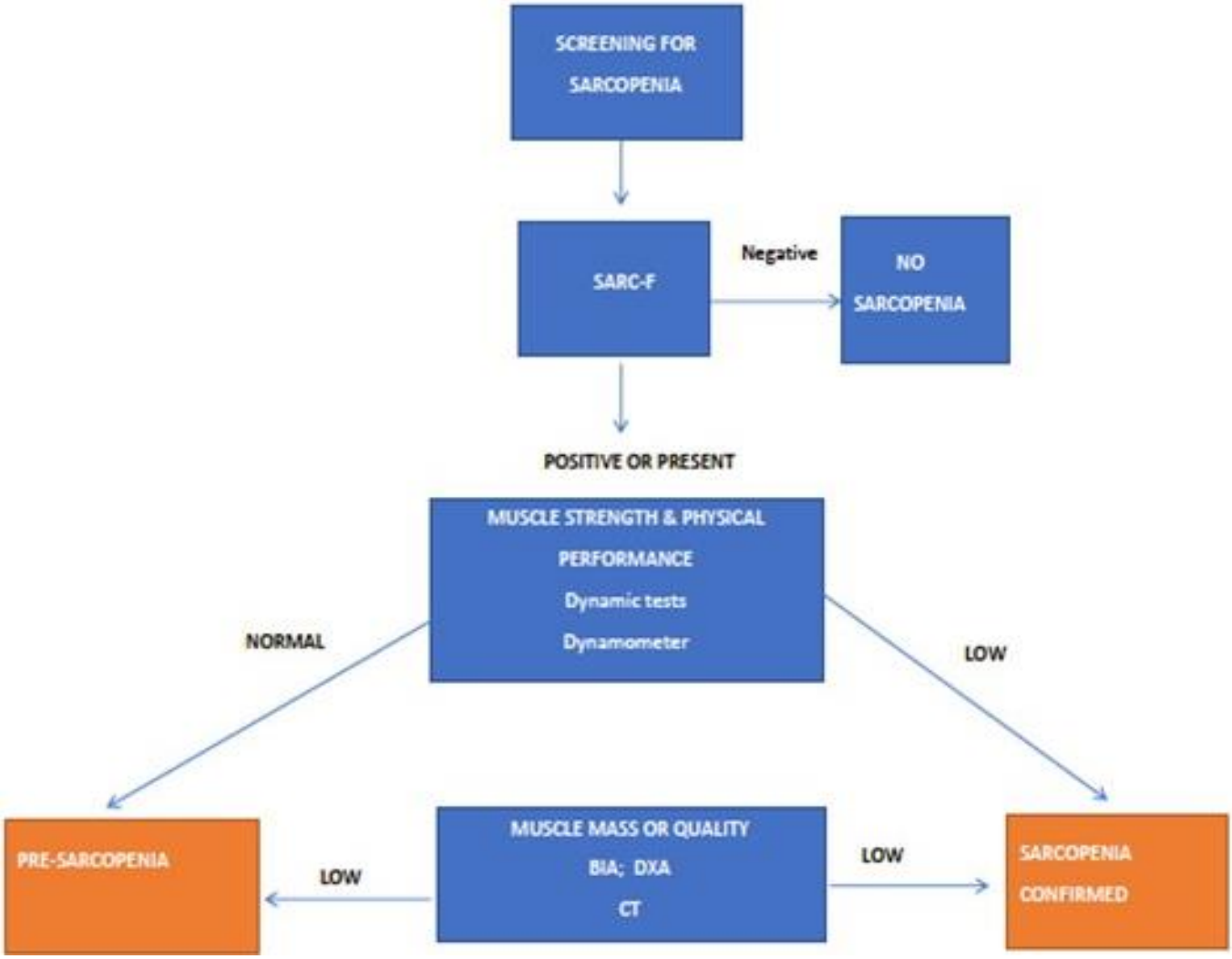
We here present a suggestion of who should be screened for sarcopenia and pre-sarcopenia (Figure 5) and which methods can be used in common clinical practice to achieve these diagnosis (Figure 6)

Figure 5- Screening fluxogram



Fluxogram developped by Laura Ribeiro Rocha.

Figure 6- Sarcopenia and pre-sarcopenia diagnosis



Fluxogram developped by Laura Ribeiro Rocha.

CONCLUSION

There has been an increase in cases of sarcopenia over the last few years. Their consequences, already mentioned, are diverse, from falls, depression, to physical dependence on family members or close people and even death. Early diagnosis can delay the process of loss of muscle mass and muscle strength or even reverse the level of sarcopenia. For these reasons, screening tests need to become routine in predisposed patients.

There are several tests that, together, will lead to an early or late diagnosis of sarcopenia, such as the SARC-F screening, dynamic tests, dynamometer, bioimpedance and DXA. The large number of existing tests for evaluating sarcopenia can analyze different aspects. According to availability and applied together, these tests can lead to an early diagnosis. It is extremely important that sarcopenia is thought of, and these tests are applied to patients with any suspected predisposition. The sooner the diagnosis occurs, the greater the chances of the sarcopenia process being reversed.

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