SARKOPENIJA: OD KLINIČKOG ASPEKTA DO TERAPIJSKIH MOGUĆNOSTI

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REVIEW ARTICLE

SARCOPENIA: FROM CLINICAL ASPECTS TO THERAPEUTIC POSSIBILITIES

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SAŽETAK

Poslednjih godina, sa produženjem životnog veka i sve većim brojem starijih ljudi, sarkopenija je prepoznata kao poseban entitet i novo područje u gerijatrijskoj medicini. Evropska radna grupa za sarkopeniju kod starijih ljudi je definisala sarkopeniju kao sindrom koji se karakteriše progresivnim i generalizovanim gubitkom skeletne mišićne mase, snage i posledično, mišićne funkcije, što sa sobom nosi povećan rizik od padova, invalidnosti, gubitka radne sposobnosti i prevremene smrtnosti. Sarkopenija kod starijih je u mnogim zemljama postala glavni fokus istraživanja zbog velikog uticaja na morbiditet, mortalitet i troškove zdravstvene zaštite. Uprkos kliničkom značaju, sarkopenija je i dalje nedovoljno prepoznata u svakodnevnoj kliničkoj praksi, delimično zbog nedostatka dostupnih dijagnostičkih testova i jedinstvenih dijagnostičkih kriterijuma, kao i jasnih smernica za lečenje. Dijagnostikovanje sarkopenije zahteva procenu mišićne mase, mišićne snage i fizičkih performansi. Lečenje sarkopenije uključuje različite nefarmakološke i farmakološke pristupe, a prvenstveno je fokusirano na vežbe otpora i snage, uz istovremenu nutritivnu potporu.

Ključne reči: sarkopenija, stari, mišićna snaga, vežbe, nutritivna potpora

ABSTRACT

In recent years, with the increase in life expectancy and the increasing number of elderly people, sarcopenia has been recognized as a separate entity and a new field in geriatric medicine. The European Working Group on Sarcopenia in Older People defined sarcopenia as a syndrome characterized by progressive and generalized loss of skeletal muscle mass, strength and consequently muscle function, which carries with it an increased risk of falls, disability, loss of work ability and premature death. Sarcopenia in the elderly is being given major research focus in many countries, due to its great impact on morbidity, mortality and health care costs. Despite its clinical importance, sarcopenia is still underrecognized in daily clinical practice, in part due to the lack of available diagnostic tests and unique diagnostic criteria, as well as the lack of clear treatment guidelines. Diagnosing sarcopenia requires assessment of muscle mass, muscle strength and physical performance. The treatment of sarcopenia includes various non-pharmacological and pharmacological approaches, and is primarily focused on resistance and strength exercises, with simultaneous nutritional support.

Key words: sarcopenia, the elderly, muscle strength, exercise, nutrition

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UVOD

Sarkopenija je sindrom koji karakteriše progresivno i generalizovano smanjenje skeletne mišićne mase i snage, koje predstavlja glavnu determinantnu povećanog rizika od pada i fraktura, smanjene sposobnosti za obavljanje svakodnevnih aktivnosti, kognitivnog propadanja, te pogoršanja kardiovaskularnih i respiratornih oboljenja, što često dovodi do invaliditeta, gubitka nezavisnosti i prerane smrti [1,2]. Evropska radna grupa za sarkopeniju kod starijih ljudi je u svojim revidiranim smernicama iz 2018. godine (ERGZS2) dodala prethodnoj definiciji pojam oslabljene mišićne funkcije i njenog određivanja, ističući da je mišićna snaga, odnosno funkcija, bolji prediktor neželjenih događaja od mišićne mase [3]. Takođe, sugeriše se korišćenje definisanog algoritma i kriterijuma za skrining, postavljanje dijagnoze i određivanje težine sarkopenije. Rano prepoznavanje i lečenje mogu prevenirati ili ublažiti neke od neželjenih ishoda sarkopenije [4].

Prevalencija sarkopenije kod starijih lica smeštenih u domovima za stare dostiže do 29%, a kod osoba smeštenih u institucijama produžene nege dostiže i do 33% [4]. Koegzistencija osteoporoze i sarkopenije se u poslednje vreme svrstava kao sindrom „osteosarkopenija". Dok se osteoporoza opisuje smanjenom koštanom masom i poremećenom mikroarhitekturom kosti, sarkopenija se karakteriše gubitkom mišićne mase, snage i funkcije. Osteosarkopenija bi mogla da obuhvati postojanje obe ove karakteristike istovremeno. Krhkost (engl. *frailty*) se može definisati kao klinički manifestno stanje povećane osetljivosti, sa slabom snagom stiska šake, smanjenom energijom pokretanja, usporenim hodom i nevoljnim gubitkom telesne mase.

FAKTORI RIZIKA ZA RAZVOJ SARKOPENIJE

Na razvoj sarkopenije utiče prisustvo određenih faktora rizika, koji su navedeni u nastavku.

1. Nedostatak vežbanja i fizičke aktivnosti smatra se jednim od vodećih faktora za razvoj sarkopenije [5].
2. Hormonski i citokinski disbalans – smanjenje koncentracije hormona rasta, testosterona, tiroidnih hormona i insulinu sličnog faktora rasta (engl. insulin-like growth factor – IGF), dovodi do gubitka mišićne mase i snage [6].
3. Neadekvatan unos hrane, smanjena sinteza i regeneracija proteina, karakteristični su za stariju populaciju sa sarkopenijom [7,8,9].
4. Remodelovanje motornih jedinica – u sarkopeniji dolazi do smanjenja broja motornih nervnih ćelija koje su odgovorne za slanje signala iz mozga u mišiće [6].
5. Hronična sistemska inflamacija, karakteristična za starenje, pojačanim oslobađanjem TNF-α (engl. tumor necrosis factor alpha), interleukina-6 (IL-6),

INTRODUCTION

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength, and it represents the main determiner of increased risk of falls and fractures, decreased ability for performing everyday activities, cognitive decline, as well as the exacerbation of cardiovascular and respiratory diseases, which commonly leads to invalidity, loss of independence, and premature death [1,2]. In its revised guidelines, from 2018, the European Working Group on Sarcopenia in Older People (EWGSOP2) added to the existing definition of sarcopenia the concept of reduced muscle function and its estimation, emphasizing that muscle strength, i.e., muscle function, is a better predictor of adverse events than muscle mass [3]. Also, the application of the defined algorithm and criteria for screening, diagnosing and determining the severity of sarcopenia is proposed within these guidelines. Early detection and treatment may prevent or alleviate some of the adverse outcomes of sarcopenia [4].

The prevalence of sarcopenia in older persons residing in nursing homes for the elderly is up to 29%, whereas the prevalence of sarcopenia in individuals residing in care facilities can reach up to 33% [4]. The coexistence of osteoporosis and sarcopenia has recently been designated as the syndrome *osteosarcopenia*. While osteoporosis is characterized by reduced bone mass and weakened bone microarchitecture, sarcopenia is characterized by loss of muscle mass, strength and function. Osteosarcopenia may encompass the existence of both of these characteristics at the same time. Frailty can be defined as a clinically manifest condition of increased sensitivity, with low grip strength, decreased energy of movement, low gait speed, and involuntary weight loss.

RISK FACTORS FOR THE DEVELOPMENT OF SARCOPENIA

The presence of certain risk factors influences the development of sarcopenia. These are listed below.

1. Lack of exercise and physical activity is believed to be one of the leading factors in the development of sarcopenia [5].
2. Hormonal and cytokine imbalance – decreased concentrations of the growth hormone, testosterone, thyroid hormones, and IGF (insulin-like growth factor), leads to the loss of muscle mass and strength, i.e., muscle wasting and weakness [6].
3. Inadequate food intake, decreased protein synthesis and regeneration, are characteristic of the elderly population with sarcopenia [7,8,9].
4. Motor unit remodeling – in sarcopenia, the number of motor neurons responsible for transmitting signals from the brain to the muscles, decreases [6].

C-reaktivnog proteina (CRP) i drugih inflamatornih citokina, dovodi do oštećenja tkiva i anaboličke rezistencije, koja je glavna determinanta sarkopenije [10,11].

KLASIFIKACIJA SARKOPENIJE

Stepenovanje sarkopenije odražava težinu i ozbiljnost zdravstvenog stanja osobe, a lekaru pomaže pri odabiru načina lečenja i postavljanju realnih ciljeva i očekivanja. Sarkopenija se deli na presarkopeniju, sarkopeniju u užem smislu i tešku sarkopeniju, odnosno na primarnu i sekundarnu sarkopeniju.

Presarkopenija podrazumeva smanjenu mišićnu masu i može se dijagnostikovati tehnikama preciznog merenja mišićne mase i poređenjem sa standardnom populacijom. Sarkopenija u užem smislu podrazumeva smanjenu mišićnu masu, uz prisustvo još jednog kriterijuma – smanjene mišićne snage. Teška sarkopenija znači da su sva tri kriterijuma prisutna (smanjena mišićna masa, smanjena snaga i smanjena funkcija mišića) [1].

Primarna sarkopenija je isključivo vezana za proces starenja, kada su svi drugi uzroci sa sigurnošću isključeni. Sekundarna sarkopenija se razvija uz barem jedan ili više jasnih uzroka koji nisu izričito povezani sa procesom starenja, a to mogu biti sedelački način života uzrokovan bolešću (onesposobljenost ili nepokretnost) ili neadekvatne svakodnevne fizičke aktivnosti [12].

DIJAGNOSTIKA SARKOPENIJE

Na sarkopeniju se najčešće posumnja kada su simptomi već prisutni. Neki od njih su osećaj mišićne slabosti, usporenosti, teškoće pri obavljanju svakodnevnih aktivnosti, učestali padovi i subjektivni osećaj gubitka mišićne mase [3]. ERGZS2 predlaže algoritam pod nazivom *Pronaći-Proceniti-Potvrditi-Težina* (engl. *Find-Assess-Confirm-Severity – FACS*) za postavljanje dijagnoze sarkopenije. Prvi korak je skrining sarkopenije, najčešće korišćenjem upitnika *Snaga, pomoć prilikom hodanja, ustajanje sa stolice, penjanje uz stepenice, padovi* (engl. *Strength, assistance with walking, rising from a chair, climbing stairs, and falls – SARC-F*). Ukoliko se pojavi sumnja na sarkopeniju, vrši se procena mišićne snage (npr. ručnom dinamometrijom), a nakon toga, ukoliko je indikovano, mogu se uraditi testovi za procenu kvantiteta i kvaliteta mišića (osteodenziometrija, analiza bioelektrične impedanse, kompjuterizovana tomografija, magnetna rezonanca). U poslednjem koraku potrebno je uraditi testove fizičke performanse i na taj način potvrditi definitivnu dijagnozu i odrediti težinu sarkopenije (Slika 1) [13].

5. Chronic systemic inflammation, which is a characteristic of ageing, through increased production of the tumor necrosis factor alpha, interleukin-6 (IL-6), C-reactive protein (CRP), and other inflammatory cytokines, leads to tissue damage and anabolic resistance, which is the main determiner of sarcopenia [10,11].

CLASSIFICATION OF SARCOPENIA

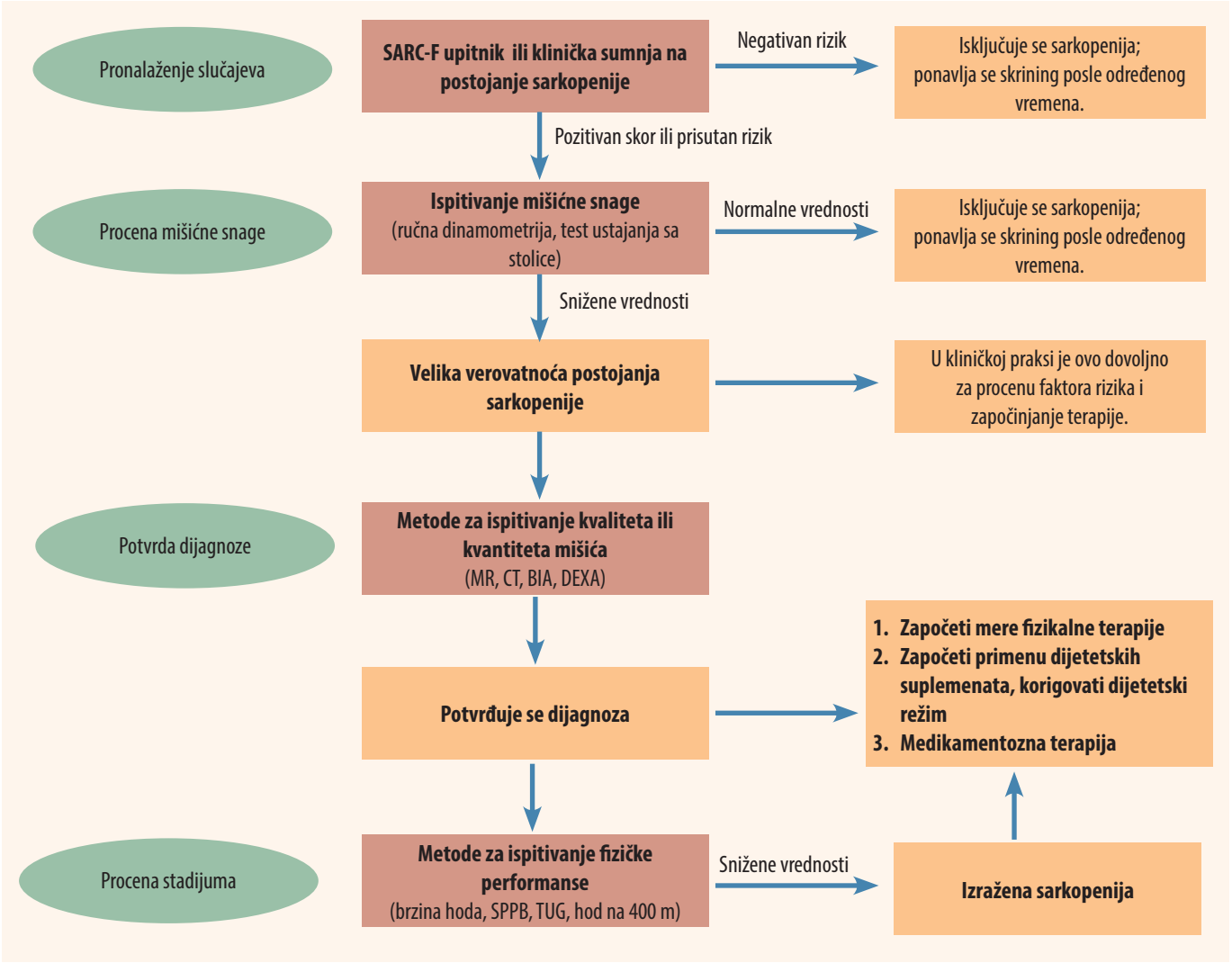
Grading sarcopenia reflects the severity and gravity of the health status of an individual, and it assists the physician in selecting the mode of treatment and in defining realistic goals and expectations. Sarcopenia is classified as presarcopenia, sarcopenia in the narrow sense, and severe sarcopenia, i.e., primary and secondary sarcopenia.

Presarcopenia involves reduced muscle mass and may be diagnosed with muscle mass measurement techniques and through comparison with the standard population. Sarcopenia in the narrow sense involves reduced muscle mass, with the presence of one more criterion – decrease in muscle strength. Severe sarcopenia entails that all three criteria are present (reduced muscle mass, reduced strength, and reduced muscle function) [1].

Primary sarcopenia is exclusively associated to the ageing process, when all other causes are excluded with certainty. Secondary sarcopenia develops with at least one or more clear causes which are not exclusively connected with the ageing process, which may be sedentary lifestyle caused by disease (disability or immobility) or inadequate daily physical activity [12].

SARCOPENIA DIAGNOSTICS

Sarcopenia is most commonly suspected when symptoms are already present. Some of them are the following: feeling of muscle weakness, slackening, difficulty in performing everyday activities, frequent falls, and the subjective feeling of muscle wasting [3]. The EWGSOP2 proposes the Find-Assess-Confirm-Severity (FACS) algorithm for establishing the diagnosis of sarcopenia. The first step is screening for sarcopenia, most commonly with the Strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) questionnaire. If sarcopenia is suspected, assessment of muscle strength is performed (for example, with hand-held dynamometry), upon which, if indicated, tests for the assessment of muscle quantity and quality (osteodensitometry, bioelectrical impedance analysis, computed tomography, magnetic resonance imaging) may be carried out. As a final step, a physical performance assessment test should be carried out, for the purpose of confirming the definitive diagnosis and determining the severity of sarcopenia (Figure 1) [13].



SARC-F upitnik (engl. *Strength, assistance with walking, rising from a chair, climbing stairs, and falls*); MR - magnetna rezonanca; *CT* – kompjuterizovana tomografija (engl. *computed tomography*); BIA – analiza bioelektrične impedanse (engl. *bioelectrical impedance analysis*); *DEXA* – dvoenergetska rendgenska apsorpciometrija iks zraka (engl. *dual-energy X-ray absorptiometry*)

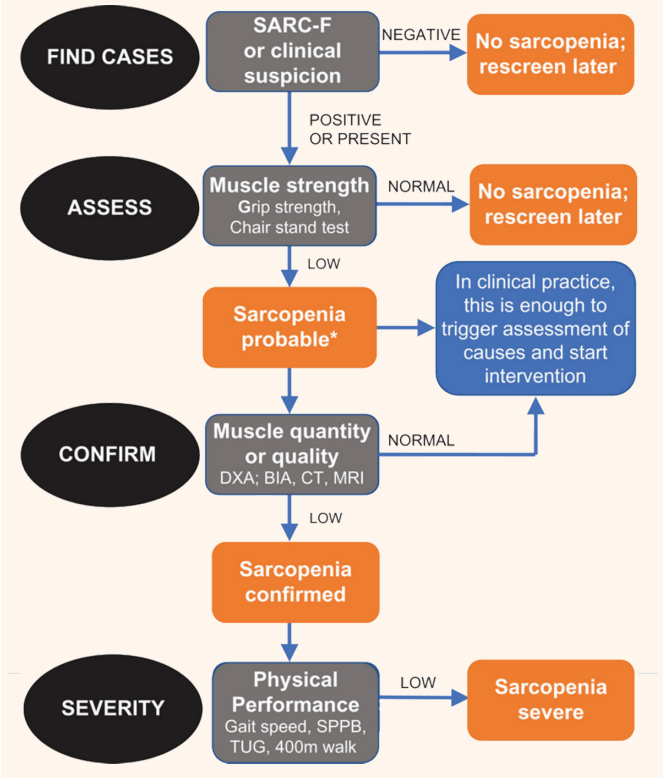
Grafikon 1. Algoritam skrininga i dijagnostike sarkopenije baziran na preporukama Evropske radne grupe za sarkopeniju kod strarijih osoba (engl. *European Working Group on Sarcopenia in Older People, EWGSOP2; Find-Assess-Confirm-Severity – FACS*)

SKRINING SARKOPENIJE

Potrebno je uraditi skrining na sarkopeniju, naročito kod bolesnika starijih od 65 godina. U kliničkoj praksi to znači da, kada pacijent prijavljuje neke od simptoma i znakova sarkopenije (npr. osećaj slabosti, usporen hod, teškoće pri ustajanju sa stolice, gubitak mišića/težine), treba uraditi skrining na sarkopeniju. U cilju procene rizika od sarkopenije koristi se nekoliko testova, a najčešće korišćeni test je *SARC-F* upitnik. *SARC-F* upitnik sastoji se od pet pitanja u vezi sa podizanjem i nošenjem tereta, poteškoćama pri hodanju, ustajanju sa stolice, penjanju uz stepenice, kao i u vezi sa učestalošću padova. Svaki odgovor se boduje od nula do maksimalno dva boda, tako da broj bodova na upitniku može biti od 0 do maksimalnih 10 poena. Smatra se da rizik od sarkopenije postoji kada je broj bodova veći od četiri [14].

SCREENING FOR SARCOPENIA

It is necessary to screen for sarcopenia, especially in patients over the age of 65 years. In clinical practice, this means that, when the patient reports some of the symptoms or signs of sarcopenia, (e.g., weakness, low gait speed, difficulty in rising from a chair, muscle wasting, weight loss), screening for sarcopenia should be performed. For the purpose of sarcopenia risk assessment, several tests are used, the most commonly applied being the SARC-F questionnaire. The SARC-F questionnaire is composed of five questions related to lifting and carrying weight, difficulties walking, rising from a chair, climbing stairs, as well as the frequency of falls. Each answer is scored from 0 to a maximum of 10 points. It is believed that the risk of sarcopenia is present when the score is higher than four points [14].



SARC-F questionnaire – Strength, assistance with walking, rising from a chair, climbing stairs, and falls; MRI – magnetic resonance imaging; CT – computed tomography; BIA – bioelectrical impedance analysis; DEXA – dual-energy X-ray absorptiometry

Figure 1. Algorithm for screening and diagnosing sarcopenia based on the recommendations of the European Working Group on Sarcopenia in Older People (EWGSOP2); Find-Assess-Confirm-Severity – FACS)

DIJAGNOZA SARKOPENIJE

Nakon skrininga, potrebno je uraditi procenu mišićne mase, snage i mišićne performanse. U kliničkom smislu, značajno je i praćenje dinamike ovih parametara, ponavljanjem merenja nakon određenog perioda. Za koju dijagnostičku metodu ćemo se odlučiti, zavisi od brojnih faktora, poput validnosti, pristupačnosti, cene, tehničke opremljenosti, stanja pacijenta, kao i svrhe merenja (kliničke ili istraživačke svrhe) [13,19].

Metode za procenu mišićne mase

Mišićna masa se može indirektno proceniti različitim tehnikama i izražava se kao ukupna telesna skeletna mišićna masa (TSM), kao apendikularna skeletna mišićna masa (ASM) ili kao površina poprečnog preseka mišića određenih mišićnih grupa. Magnetna rezonanca (MR) i kompjuterizovana tomografija (engl. *computed tomography – CT*) smatraju se zlatnim standardima za neinvazivnu procenu mase mišića, ali je njihova upotreba, zbog manje dostupnosti i cene, uglavnom ograničena na specifične kliničke studije [15,16].

Antropometrijska merenja su relativno jednostavne metode za procenu pojedinih komponenti telesne

SARCOPENIA DIAGNOSIS

Upon screening, it is necessary to assess muscle mass, strength, and muscle performance. Clinically speaking, it is important to follow-up on the dynamics of these parameters by repeating measurements after certain periods of time. Which diagnostic method is to be chosen depends on numerous factors, such as validity, availability, price, level of technical equipment, the patient's status, as well as the objective of the measurement (clinical or research purposes) [13,19].

Methods for assessing muscle mass

Muscle mass may be indirectly assessed with different techniques and is defined as total skeletal muscle mass (TSM), as appendicular skeletal muscle mass (ASM), or as the surface area of the cross section of muscles belonging to certain muscle groups. Magnetic resonance imaging (MRI) and computed tomography (CT) are considered to be the golden standard for noninvasive muscle mass assessment, however, their use, due to limited availability and price, is mainly limited to specific clinical studies [15,16].

Anthropometric measurements are relatively simple methods for assessing individual components of body composition, whereby measurements of human body dimensions (height, weight, skinfold thickness, body circumferences and diameters in certain reference points of particular regions of the body) and the use of appropriate equations, facilitate a simple method for obtaining data on body density, as well as the size of fat and lean body mass [16].

Computed tomography (CT) is a method which can be used to measure the quantity of abdominal visceral fat and to assess skeletal muscle mass, with particular focus on anatomical details, which is why it has a role in diagnosing sarcopenia [13].

Magnetic resonance imaging (MRI) is the most precise, albeit the least accessible method for assessing body composition, which is why it is most commonly used for measuring muscle mass in clinical studies. With the use of appropriate software, MRI provides precise data on the segment structure (fat, muscle, bone) of the studied body part [17].

Ultrasound (US) can also be used for determining body composition, i.e., for measuring the thickness of fatty and muscle tissue in patients. Ultrasonography can precisely measure the thickness of muscle and bone tissue, as efficiently as measuring the thickness of the subcutaneous and visceral fatty tissue. The procedure of ultrasonographic diagnostics is noninvasive and simple, however, its interpretation requires expertise and experience [18].

strukture, gde se merenjem dimenzija ljudskog tela (telesna visina, telesna masa, debljina kožnih nabora, telesni obimi i dijametri u određenim regionima tela na referentnim tačkama) i korišćenjem adekvatnih jednačina, na jednostavan način dobijaju podaci o telesnoj gustini, veličini masne i bezmasne mase tela [16].

Kompjuterizovana tomografija (*CT*) je metoda kojom se može izmeriti količina abdominalne visceralne masti i koja se može koristi za procenu skeletne mišićne mase, sa posebnim osvrtom na anatomske detalje, te je zbog toga našla svoje mesto u dijagnostikovanju sarkopenije [13].

Magnetna rezonanca (MR) predstavlja najpreciznij u, ali i najmanje dostupnu metodu za procenu telesnog sastava, te se najčešće koristi za merenje mišićne mase u kliničkim istraživanja. Korišćenjem adekvatnog softvera, MR daje precizne podatke o segmentarnoj strukturi (masti, mišići, kosti) ispitivanog dela tela [17].

Ultrazvučna (UZ) dijagnostika se takođe može koristiti za određivanje telesnog sastava, odnosno merenje debljine masnog i mišićnog tkiva kod ljudi. Ultrasonografijom je moguće precizno izmeriti debljinu mišićnog i koštanog tkiva, podjednako efikasno kao i debljinu potkožnog i visceralnog masnog tkiva. Procedura ultrasonografske dijagnostike je neinvazivna i jednostavna, ali njena interpretacija iziskuje stručnost i iskustvo [18].

Poznato je da se dvoenergetska rendgenska apsorpciometrija iks zraka (engl. *dual-energy X-ray absorptiometry – DEXA*) klinički primenjuje kao zlatni standard za postavljanje dijagnoze osteopenije i osteoporoze, ali *DEXA* aparati takođe omogućavaju procenu telesnog sastava, u čitavom telu ili pojedinim delovima tela, mereći tri glavne komponente: sadržaj minerala u kostima, bezmasnu masu tela i masnu masu tela. Kroz procenu parametara čiste mase bez kostiju, kao što je apendikularna čista masa prilagođena za indeks telesne mase (engl. *body mass index – BMI*) ili visinu, moguće je kvalifikovati one pacijente sa fiziološkim gubitkom mišićne mase u odnosu na one sa patološkim gubitkom. Zbog svoje jednostavnosti, dostupnosti, niske cene i niske izloženosti zračenju, *DEXA* je prihvaćena kao neinvazivna metoda za procenu mišićne mase u svim starosnim dobima [19].

Analiza bioelektrične impedanse (engl. *bioelectrical impedance analysis – BIA*) je jednostavan, neinvazivan i relativno jeftin metod za procenu telesnog sastava, emitovanjem naizmenične struje veoma slabog intenziteta, ispod praga percepcije, i određivanjem otpora tkiva pri prolasku struje kroz telo. Noviji uređaji pružaju tačnost merenja uporedivu sa zlatnim standardima za procenu telesnog sastava. Ova metoda se može koristiti i kod vrlo gojaznih osoba, kao i nepokretnih pa-

It is a known fact that dual-energy X-ray absorptiometry (DEXA) is clinically applied as the gold standard for establishing the diagnosis of osteopenia and osteoporosis. However, DEXA machines can also be used to assess body composition, at the level of the entire body or its individual parts, measuring three main components: mineral content of the bones, fat body mass, and lean body mass. By assessing parameters of sheer body mass without bones, such as appendicular sheer mass adjusted for body mass index (BMI) or height, it is possible to qualify patients with physiological muscle mass loss in relation to patients with a pathological loss. Because of its simplicity, availability, low cost, and low exposure to radiation, DEXA has been accepted as a noninvasive method for assessing muscle mass in all age groups [19].

Bioelectrical impedance analysis (BIA) is a simple, noninvasive, and relatively cheap method for estimating body composition, which is achieved by emitting an alternating electrical current of very low intensity, below the threshold of perception, and determining the resistance of the tissue when the current passes through the body. Newer devices provide an accuracy of measurement comparable with the gold standards for assessing body composition. This method can be used in very obese persons, as well as in immobile patients, while it is not recommended in persons with pacemakers, due to possible interference with its functioning [20].

Methods for measuring muscle strength

A hand-held dynamometer, which measures grip strength, is used for measuring muscle strength. Grip strength strongly correlates with the strength of the muscles of the lower extremities. A grip strength of less than 27 kg, for men, and less than 16 kg, for women, indicates a weakened muscle strength. Low grip strength is a strong indicator of poorer outcome, prolonged hospitalization, reduced quality of life, and premature death [21]. Due to the simplicity of the test, it is recommended that this test should be routinely administered in hospitalized patients as well as in everyday clinical practice. The chair stand test is used for assessing the strength of the proximal musculature of the legs and it measures the amount of time necessary for a patient to stand up five times in a row from the seated position without the use of the arms as support. This test requires strength and endurance. If more than 15 seconds are needed for a person to stand upright five times in a row from the seated position, this also indicates reduced muscle strength [13].

Methods for measuring physical performance

Physical performance is defined as objectively measured function of the entire body related to locomotion. This

cijenata, dok se ne preporučuje osobama sa pejsmejkerom, zbog potencijalnog izazivanja nepravilnosti u njegovom radu [20].

Metode za merenje mišićne snage

Za merenje mišićne snage koristi se ručni dinamometar, kojim se meri snaga stiska šake. Stisak šake snažno korelira sa snagom mišića donjih ekstremiteta. Vrednost stiska šake manja od 27 kg, za muškarce, odnosno manja od 16 kg, za žene, ukazuje na smanjenu snagu mišića. Mala snaga stiska šake je snažan prediktor lošijeg ishoda, produžene hospitalizacije, smanjenog kvaliteta života i prevremene smrtnosti [21]. Zbog svoje jednostavnosti izvođenja, stisak šake se preporučuje za rutinsku primenu u bolničkim uslovima i u svakodnevnoj kliničkoj praksi. Test ustajanja sa stolice (engl. *chair stand test*) se koristi za procenu snage proksimalne muskulature nogu i meri količinu vremena potrebnu da pacijent ustane pet puta iz sedećeg položaja bez upotrebe ruku. Ovaj test zahteva i snagu i izdržljivost. Ako je potrebno duže od 15 sekundi za pet ustajanja sa stolice, to takođe ukazuje na smanjenu snagu mišića [13].

Metode za merenje fizičke performanse

Fizička performansa se definiše kao objektivno izmerena funkcija celog tela koja se odnosi na lokomociju. Ovaj koncept ne uključuje samo mišiće, već i centralni i periferni nervni sistem, uključujući i ravnotežu. Brzina hoda se smatra brzim, bezbednim i visoko pouzdanim testom za sarkopeniju i ima široku primenu u praksi. Uobičajeni test brzine hoda izvodi se na razdaljini od četiri metra, pri čemu se brzina meri pomoću štoperice, a brzina manja od 0,8 m/s ukazuje na tešku sarkopeniju. Ovaj test se preporučuje za evaluaciju fizičke performanse u praksi [13].

Često korišćena metoda je i Kratak test fizičke performanse (engl. *Short physical performance battery - SPPB*) kojim se procenjuje ravnoteža, brzina, hod, snaga i izdržljivost pojedinca. Maksimalni rezultat je 12 poena, a rezultat ≤ 8 poena ukazuje na lošu fizičku funkciju [13,22].

TERAPIJA U SARKOPENIJI

Pravovremeno prepoznavanje i lečenje su od ključnog značaja u poboljšanju ishoda kod pacijenata sa sarkopenijom. Potencijalne strategije usmerene na povećanje mišićne mase i snage su kalorijska i proteinska nadoknada, fizička aktivnost, hormonska terapija i terapija specifično usmerena na mehanizme uzročnika sarkopenije [23].

Nutritivna potpora i fizička aktivnost su dve najvažnije intervencije koje je najbolje sprovoditi istovremeno [24]. Smernice ERGZS2, iz 2018. godine, preporučuju fizičku aktivnost kao prvi korak u lečenju sarkopenije [25]. Vežbe sa otporom su naročito korisne kod starih

concept includes, not only muscles, but the central and peripheral system as well, including balance. Gait speed is believed to be a quick, safe, and highly reliable test for sarcopenia, and it is widely used in everyday practice. The common gait speed test is performed for a distance of four meters, whereby the gait speed is measured with a stopwatch, while a speed of less than 0.8 m/s indicates severe sarcopenia This test is recommended for evaluating physical performance in clinical practice [13].

A frequently applied method is the short physical performance battery (SPPB) test, which is used to assess balance, speed, gait, strength, and endurance of an individual. The maximum score is 12 points, while the score of ≤ 8 points indicates poor physical function [13,22].

SARCOPENIA TREATMENT

Timely identification and treatment are key in improving outcomes in patients with sarcopenia. Potential strategies directed at increasing muscle mass and strength are calory and protein supplementation, physical activity, hormone therapy, and therapy specifically targeting the mechanisms causing sarcopenia [23].

Nutritional support and physical activity are the two most important interventions which are best carried out simultaneously [24]. The EWGSOP2 guidelines, from 2018, recommend physical activity as the first step in treating sarcopenia [25]. Resistance exercises are especially useful in the elderly [26,27]. This type of training improves muscle mass, strength, and function, it stimulates neurological adaptation (intermuscular and intramuscular coordination), and also improves bone density and metabolic health [28]. Resistance training has a positive effect on the neuromuscular system, it increases the concentration of hormones and the speed of protein synthesis. Resistance and strength training have proven very successful in the prevention and treatment of sarcopenia. Strength exercises can increase physical mass, while endurance exercises can improve functional capacity [29]. Although there are numerous exercise programs used in everyday practice, there is a need for setting specific guidelines for patients with sarcopenia [13].

Sarcopenia requires a special dietary regimen, which involves the appropriate intake of proteins, vitamin D, antioxidants, and branched-chain amino acids [30,31]. The recommended daily intake of proteins is 1 – 1.5 g/kg, while the optimal daily energy intake must not be below 35 kcal/kg, in order to preserve the necessary oxygen balance and reduce the proteolysis of skeletal muscles. Plant-based protein sources are better than animal-based proteins sources, as they contain proteins rich with branched-chain amino acids

lica [26,27]. Ova vrsta treninga poboljšava mišićnu masu, snagu i funkciju, pospešuje neurološku adaptaciju (međumišićnu i unutarmišićnu koordinaciju) i unapređuje gustinu kostiju i metaboličko zdravlje [28]. Trening otpora pozitivno utiče na neuromišićni sistem, povećava koncentraciju hormona i brzinu sinteze proteina. Vežbe otpora i vežbe snage mišića su se pokazale veoma uspešnim u prevenciji i lečenju sarkopenije. Vežbe snage mogu povećati fizičku masu, a vežbe izdržljivosti mogu unaprediti funkcionalni kapacitet [29]. Iako postoje razne varijante programa za vežbanje u praksi, ipak postoji potreba za izradom konkretnih smernica za pacijente sa sarkopenijom [13].

Sarkopenija zahteva poseban režim ishrane, koji uključuje adekvatan unos proteina, vitamina D, antioksidanasa i aminokiselina razgranatog lanca [30,31]. Preporučen dnevni unos proteina iznosi 1 – 1,5 g/kg, a optimalan dnevni energetski unos ne sme biti manji od 35 kcal/kg, kako bi se održala adekvatna ravnoteža kiseonika i smanjila proteoliza skeletnih mišića. Proteini biljnog porekla imaju prednost nad proteinima životinjskog porekla jer su bogati aminokiselinama razgranatih lanaca [32]. Suplementacija aminokiselinama razgranatog lanca, naročito leucinom i njegovim metabolitom beta-hidroksi beta-metilbutiratom (HMB), može podstaći sintezu proteina u mišićima [33].

Nedostatak vitamina D doprinosi rastu mortaliteta, te se sugeriše suplementacija 600 – 1.000 IU vitamina D dnevno. Dnevna nadoknada vitamina D takođe doprinosi porastu snage i smanjenju krhkosti kod starijih osoba i time olakšava fizičku aktivnost i vežbanje [34,35]. Povećan oksidativni stres i poremećaj u sastavu antioksidanasa predstavlja karakteristiku starenja organizma i hroničnih bolesti, te je potrebno razmotriti i upotrebu antioksidanasa u lečenju sarkopenije [36]. Studija iz 2015. godine, pokazala je dobrobiti omega-3 polinezasićenih masnih kiselina iz ribljeg ulja za rast mišićne mase i snage [37].

Terapija anaboličkim hormonima, testosteronom i hormonima rasta ne preporučuje se u terapiji sarkopenije. Hormon rasta povećava sintezu mišićnih proteina i povećava mišićnu masu, ali ne dovodi do povećanja snage i funkcije mišića. Neefikasnost ovog hormona je posledica rezistencije njegovog efektora, insulinu sličnog faktora rasta (IGF-1) u mišićima koji stare [38]. Testosteron, odnosno drugi anabolički steroidi su takođe ispitivani. Ovi hormoni imaju skroman pozitivni efekat na mišićnu masu i snagu i njihova upotreba je ograničena, zbog njihovih štetnih efekata, kao što su povećani rizik od raka prostate i ukupni povećani rizik od kardiovaskularnih događaja [39].

Novi terapijski modaliteti u lečenju sarkopenije se još uvek ispituju. Selektivni modulatori androgenih receptora (*selective androgen receptor modulators* – [32]. Supplementation with branched-chain amino acids, especially leucin and its metabolite beta-hydroxy-beta-methylbutyrate (HMB), may stimulate protein synthesis in muscles [33].

Vitamin D deficiency contributes to the rise in mortality, which is why daily supplementation of 600 – 1.000 IU of vitamin D is recommended. Daily vitamin D supplementation also contributes to the increase in strength and to the reduction in frailty in the elderly, thus facilitating physical activity and exercise [34,35]. Increased oxidative stress and disturbance of antioxidant composition is a characteristic of ageing and chronic diseases, which is why it is necessary to consider the use of antioxidants in the treatment of sarcopenia [36]. A study from 2015 showed the benefits of omega-3 polyunsaturated fatty acids from fish oil, for the increase in muscle mass and strength [37].

Treatment with anabolic hormones, testosterone, and the growth hormone is not recommended in the treatment of sarcopenia. The growth hormone increases muscular protein synthesis and increases muscle mass; however, it does not lead to an increase in muscle strength and function. The inefficiency of this hormone is the consequence of the resistance of its effector, insulin-like growth factor-1 (IGF-1) in ageing muscles [38]. Testosterone or other anabolic steroids have also been tested. These hormones have a modest positive effect on muscle mass and strength and their use is limited, due to their harmful effects, such as the increased risk of prostate cancer and the overall increased risk of cardiovascular events [39].

New therapeutic modalities in the treatment of sarcopenia are still being investigated. Selective androgen receptor modulators (SARM) are particularly significant due to their selectivity in relation to tissue [40]. Other compounds being explored are myostatin, thalidomide, celecoxib, anabolic agents, such as ghrelin and its analogues, and MT-102. The above-mentioned agents are still being investigated in clinical studies and have not yet been approved for the treatment of sarcopenia [41].

CONCLUSION

As an entity, sarcopenia can be considered a geriatric syndrome. Sarcopenia in the elderly is connected to adverse health outcomes, such as falls, invalidity, inability to care for oneself, resulting in a reduced quality of life in the elderly, an increased number of hospital admissions, and premature death. Revised EWGSOP2 guidelines, from 2018, propose the application of the FACS algorithm with clearly defined criteria, for the purpose of establishing the diagnosis of sarcopenia. Combining resistance exercises with certain pharma-

SARM) su od posebnog značaja zbog svoje selektivnosti po pitanju tkiva [40]. Druga jedinjenja koja se ispituju uključuju miostatin, talidomid, celekoksib, anaboličke agense, kao što su grelin i njegovi analozi, te MT-102. Pomenuti agensi se još uvek ispituju u kliničkim studijama i nisu odobreni za lečenje sarkopenije [41].

ZAKLJUČAK

Sarkopenija se kao entitet može smatrati gerijatrijskim sindromom. Sarkopenija je kod starih povezana sa neželjenim zdravstvenim ishodima, kao što su padovi, invaliditet, nemogućnost brige o sebi, što za posledicu ima pogoršanje kvaliteta života starih, povećan broj hospitalizacija i prevremenu smrt. Revidirane smernice ERGZS2, iz 2018. godine, predlažu korišćenje *FACS* algoritma sa jasno definisanim kriterijumima, u cilju postavljanja dijagnoze sarkopenije. Kombinovanje vežbi sa otporom sa nekim farmakološkim jedinjenjima i dijetetskim suplementima može imati blagotvoran efekat na starije osobe i na taj način prevenirati i usporiti napredovanje sarkopenije. Povećanje svesti o važnosti sarkopenije je od velikog značaja za postizanje povoljnijih ishoda u lečenju i praćenju gerijatrijske populacije.

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cological compounds and dietary supplements may have a beneficial effect on the elderly, and in this way, prevent and decelerate the progression of sarcopenia. Raising awareness on the significance of sarcopenia is of great importance for achieving favorable outcomes in the treatment and follow-up of the geriatric population.

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LITERATURA / *REFERENCES*

1. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F; European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010 Jul;39(4):412-23. doi: 10.1093/ageing/afq034.
2. Senior HE, Henwood TR, Beller EM, Mitchell GK, Keogh JW. Prevalence and risk factors of sarcopenia among adults living in nursing homes. Maturitas. 2015 Dec;82(4):418-23. doi: 10.1016/j.maturitas.2015.08.006.
3. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. Lancet. 2019 Jun 29;393(10191):2636-2646. doi: 10.1016/S0140-6736(19)31138-9.
4. Beaudart C, McCloskey E, Bruyère O, Cesari M, Rolland Y, Rizzoli R, et al. Sarcopenia in daily practice: assessment and management. BMC Geriatr. 2016 Oct 5;16(1):170. doi: 10.1186/s12877-016-0349-4.
5. Faulkner JA, Larkin LM, Claflin DR, Brooks SV. Age-related changes in the structure and function of skeletal muscles. Clin Exp Pharmacol Physiol. 2007 Nov;34(11):1091-6. doi: 10.1111/j.1440-1681.2007.04752.x.
6. Ryall JG, Schertzer JD, Lynch GS. Cellular and molecular mechanisms underlying age-related skeletal muscle wasting and weakness. Biogerontology. 2008 Aug;9(4):213-28. doi: 10.1007/s10522-008-9131-0.
7. Marty E, Liu Y, Samuel A, Or O, Lane J. A review of sarcopenia: Enhancing awareness of an increasingly prevalent disease. Bone. 2017 Dec;105:276-86. doi: 10.1016/j.bone.2017.09.008.
8. Marcell TJ. Sarcopenia: causes, consequences, and preventions. J Gerontol A Biol Sci Med Sci. 2003 Oct;58(10):M911-6. doi: 10.1093/gerona/58.10.m911.
9. Haran PH, Rivas DA, Fielding RA. Role and potential mechanisms of anabolic resistance in sarcopenia. J Cachexia Sarcopenia Muscle. 2012 Sep;3(3):157-62. doi: 10.1007/s13539-012-0068-4.
10. Visser M, Pahor M, Taaffe DR, Goodpaster BH, Simonsick EM, Newman AB, et al. Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC Study. J Gerontol A Biol Sci Med Sci. 2002 May;57(5):M326-32. doi: 10.1093/gerona/57.5.m326.
11. Beyer I, Mets T, Bautmans I. Chronic low-grade inflammation and age-related sarcopenia. Curr Opin Clin Nutr Metab Care. 2012 Jan;15(1):12-22. doi: 10.1097/MCO.0b013e32834dd297.
12. Santilli V, Bernetti A, Mangone M, Paoloni M. Clinical definition of sarcopenia. Clin Cases Miner Bone Metab. 2014 Sep;11(3):177-80.
13. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al.; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jan 1;48(1):16-31. doi: 10.1093/ageing/afy169.
14. Yang M, Hu X, Xie L, Zhang L, Zhou J, Lin J, et al. Screening Sarcopenia in Community-Dwelling Older Adults: SARC-F vs SARC-F Combined With Calf Circumference (SARC-CalF). J Am Med Dir Assoc. 2018 Mar;19(3):277.e1-277.e8. doi: 10.1016/j.jamda.2017.12.016.
15. Wen X, An P, Chen WC, Lv Y, Fu Q. Comparisons of sarcopenia prevalence based on different diagnostic criteria in Chinese older adults. J Nutr Health Aging. 2015 Mar;19(3):342-7. doi: 10.1007/s12603-014-0561-x.
16. Martin AD, Spenst LF, Drinkwater DT, Clarys JP. Anthropometric estimation of muscle mass in men. Med Sci Sports Exerc. 1990 Oct;22(5):729-33. doi: 10.1249/00005768-199010000-00027.
17. Woodrow G. Body composition analysis techniques in the aged adult: indications and limitations. Curr Opin Clin Nutr Metab Care. 2009 Jan;12(1):8-14. doi: 10.1097/MCO.0b013e32831b9c5b.

18. Watanabe Y, Yamada Y, Fukumoto Y, Ishihara T, Yokoyama K, Yoshida T, et al. Echo intensity obtained from ultrasonography images reflecting muscle strength in elderly men. Clin Interv Aging. 2013;8:993-8. doi: 10.2147/CIA.S47263.
19. Albano D, Messina C, Vitale J, Sconfienza LM. Imaging of sarcopenia: old evidence and new insights. Eur Radiol. 2020 Apr;30(4):2199-2208. doi: 10.1007/s00330-019-06573-2.
20. Chien MY, Huang TY, Wu YT. Prevalence of sarcopenia estimated using a bioelectrical impedance analysis prediction equation in community-dwelling elderly people in Taiwan. J Am Geriatr Soc. 2008 Sep;56(9):1710-5. doi: 10.1111/j.1532-5415.2008.01854.x.
21. Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol (1985). 2003 Nov;95(5):1851-60. doi: 10.1152/japplphysiol.00246.2003.
22. Kwon S, Perera S, Pahor M, Katula JA, King AC, Groessl EJ, et al. What is a meaningful change in physical performance? Findings from a clinical trial in older adults (the LIFE-P study). J Nutr Health Aging. 2009 Jun;13(6):538-44. doi: 10.1007/s12603-009-0104-z.
23. Alemán-Mateo H, Carreón VR, Macías L, Astiazaran-García H, Gallegos-Aguilar AC, Enríquez JR. Nutrient-rich dairy proteins improve appendicular skeletal muscle mass and physical performance, and attenuate the loss of muscle strength in older men and women subjects: a single-blind randomized clinical trial. Clin Interv Aging. 2014 Sep 12;9:1517-25. doi: 10.2147/CIA.S67449.
24. Denison HJ, Cooper C, Sayer AA, Robinson SM. Prevention and optimal management of sarcopenia: a review of combined exercise and nutrition interventions to improve muscle outcomes in older people. Clin Interv Aging. 2015 May 11;10:859-69. doi: 10.2147/CIA.S55842.
25. Chen HT, Chung YC, Chen YJ, Ho SY, Wu HJ. Effects of Different Types of Exercise on Body Composition, Muscle Strength, and IGF-1 in the Elderly with Sarcopenic Obesity. J Am Geriatr Soc. 2017 Apr;65(4):827-832. doi: 10.1111/jgs.14722.
26. Suetta C, Magnusson SP, Rosted A, Aagaard P, Jakobsen AK, Larsen LH. Resistance training in the early postoperative phase reduces hospitalization and leads to muscle hypertrophy in elderly hip surgery patients--a controlled, randomized study. J Am Geriatr Soc. 2004 Dec;52(12):2016-22. doi: 10.1111/j.1532-5415.2004.52557.x.
27. Hassan BH, Hewitt J, Keogh JW, Bermeo S, Duque G, Henwood TR. Impact of resistance training on sarcopenia in nursing care facilities: A pilot study. Geriatr Nurs. 2016 Mar-Apr;37(2):116-21. doi: 10.1016/j.gerinurse.2015.11.001.
28. Mueller M, Breil FA, Vogt M, Steiner R, Lippuner K, Popp A, et al. Different response to eccentric and concentric training in older men and women. Eur J Appl Physiol. 2009 Sep;107(2):145-53. doi: 10.1007/s00421-009-1108-4.
29. Beckwée D, Delaere A, Aelbrecht S, Baert V, Beaudart C, Bruyere O, et al. Exercise Interventions for the Prevention and Treatment of Sarcopenia. A Systematic Umbrella Review. J Nutr Health Aging. 2019;23(6):494-502. doi: 10.1007/s12603-019-1196-8.
30. Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, Morley JE, et al. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc. 2013 Aug;14(8):542-59. doi: 10.1016/j.jamda.2013.05.021.
31. Phillips SM, Martinson W. Nutrient-rich, high-quality, protein-containing dairy foods in combination with exercise in aging persons to mitigate sarcopenia. Nutr Rev. 2019 Apr 1;77(4):216-229. doi: 10.1093/nutrit/nuy062.
32. Baum JI, Wolfe RR. The Link between Dietary Protein Intake, Skeletal Muscle Function and Health in Older Adults. Healthcare (Basel). 2015 Jul 9;3(3):529-43. doi: 10.3390/healthcare3030529.
33. Katsanos CS, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR. A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. Am J Physiol Endocrinol Metab. 2006 Aug;291(2):E381-7. doi: 10.1152/ajpendo.00488.2005.
34. Bosdou JK, Konstantinidou E, Anagnostis P, Kolibianakis EM, Goulis DG. Vitamin D and Obesity: Two Interacting Players in the Field of Infertility. Nutrients. 2019 Jun 27;11(7):1455. doi: 10.3390/nu11071455.
35. Remelli F, Vitali A, Zurlo A, Volpato S. Vitamin D Deficiency and Sarcopenia in Older Persons. Nutrients. 2019 Nov 21;11(12):2861. doi: 10.3390/nu11122861.
36. Cesari M, Penninx BW, Pahor M, Lauretani F, Corsi AM, Rhys Williams G, Guralnik JM, Ferrucci L. Inflammatory markers and physical performance in older persons: the InCHIANTI study. J Gerontol A Biol Sci Med Sci. 2004 Mar;59(3):242-8. doi: 10.1093/gerona/59.3.m242.
37. Smith GI, Atherton P, Reeds DN, Mohammed BS, Rankin D, Rennie MJ, et al. Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial. Am J Clin Nutr. 2011 Feb;93(2):402-12. doi: 10.3945/ajcn.110.005611.
38. Giannoulis MG, Martin FC, Nair KS, Umpleby AM, Sonksen P. Hormone replacement therapy and physical function in healthy older men. Time to talk hormones? Endocr Rev. 2012 Jun;33(3):314-77. doi: 10.1210/er.2012-1002.
39. Xu L, Freeman G, Cowling BJ, Schooling CM. Testosterone therapy and cardiovascular events among men: a systematic review and meta-analysis of placebo-controlled randomized trials. BMC Med. 2013 Apr 18;11:108. doi: 10.1186/1741-7015-11-108.
40. Rooks D, Roubenoff R. Development of Pharmacotherapies for the Treatment of Sarcopenia. J Frailty Aging. 2019;8(3):120-130. doi: 10.14283/jfa.2019.11.
41. Stewart Coats AJ, Srinivasan V, Surendran J, Chiramana H, Vangipuram SR, Bhatt NN, et al.; on behalf of the ACT-ONE Trial Investigators. The ACT-ONE trial, a multicentre, randomised, double-blind, placebo-controlled, dose-finding study of the anabolic/catabolic transforming agent, MT-102 in subjects with cachexia related to stage III and IV non-small cell lung cancer and colorectal cancer: study design. J Cachexia Sarcopenia Muscle. 2011 Dec;2(4):201-207. doi: 10.1007/s13539-011-0046-2.