Sarkopenija kod osoba oboljelih od demencije

/ Sarcopenia in Persons Suffering from Dementia

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Sarkopenija je slabo istražena, a sve intrigantnija tema u psihijatriji, a osobito u psihogerijatriji. Cilj našeg rada bio je pregledati literaturu o sarkopeniji kod osoba oboljelih od demencije. Literatura je pretraživana korištenjem baza PubMed i Google Scholar. Demencija i sarkopenija dijele određene etiološke procese i rizične faktore. Kod oboljelih od demencije postoji povećani rizik za razvoj sarkopenije. Kao alat probira za sarkopeniju preporuča se SARC-F, a za postavljanje dijagnoze bioelektrična impedancija i dinamometar. U prevenciji i liječenju svoju ulogu imaju vježbe, prehrana bogata proteinima i proteinski dodatci. O mogućim biomarkerima sarkopenije potrebna su dodatna istraživanja. Valjalo bi provesti dodatna istraživanja i o najboljim alatima probira, kao i o dijagnostičkim kriterijima i sredstvima. Metode prevencije i liječenja također zahtijevaju dodatna istraživanja. Istraživanja svih ovih aspekata sarkopenije trebala bi obratiti više pažnje populaciji oboljelih od demencije.

/ Sarcopenia is a poorly researched, but increasingly intriguing topic in psychiatry, especially in psychogeriatrics. The aim of our study was to review the literature on sarcopenia in persons suffering from dementia. The literature was searched using the PubMed and Google Scholar databases. Dementia and sarcopenia share certain etiological processes and risk factors. People suffering from dementia have an increased risk of developing sarcopenia. SARC-F is recommended as a screening tool for sarcopenia, and bioelectrical impedance and dynamometer are recommended for diagnosis. Exercise, protein-rich diet and protein supplements play a role in prevention and treatment. Additional research is needed with regard to possible biomarkers of sarcopenia. Additional research should also be conducted regarding the best screening tools, as well as the diagnostic criteria and means used. Prevention and treatment methods require additional research as well. Research into all these aspects of sarcopenia should focus more on the population of individuals suffering from dementia.

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UVOD

Demencija je kronična, progresivna bolest mozga koja pogađa pamćenje, razmišljanje, emocije, ponašanje, motivaciju i narušava svakodnevno funkcioniranje. Procjenjuje se da u svijetu boluje više od 55 milijuna ljudi od demencije. Svake godine se evidentira otprilike 10 milijuna novooboljelih (1). Smatra se da će prema procjenama udio osoba oboljelih od demencije ostati stabilan za razdoblje od 2019. do 2050. godine, no zbog rasta i starenja populacije broj oboljelih će vjerojatno doseći 152,8 (130,8-175,9) milijuna (2).

Demencija i sarkopenija dijele rizične faktore. Također, sarkopenija je faktor rizika za brže kognitivno propadanje, blagi kognitivni poremećaj, razvoj demencije, a vrijedi i obrnuto. Sarkopenija je gubitak mišićne mase i snage te time i funkcije. Dio je prirodnog procesa starenja no češća je kod osoba oboljelih od demencije (3-5). U populaciji zdravih osoba iznad 60 godina, i kod žena i kod muškaraca, prevalencija sarkopenije je 10-16 %. Kod osoba oboljelih od demencije prevalencija se kreće od 20 % do 65 %. Procjene toliko variraju zbog problema definiranja dijagnostičkih kriterija sarkopenije i različitih populacija (npr. ambulantni pacijenti *vs*. bolnički pacijenti), ali nije uočena razlika u prevalenciji s obzirom na tip demencije (6-10). Sarkopenija je značajna jer povećava rizik od pada, prijeloma, smanjene mobilnosti, invalidnosti, disfagije, upale pluća, delirija i smrti, na duži i kraći rok, kod inače zdravih starijih osoba, a osobito kod osoba oboljelih od demencije (5,11,12). Sarkopenija smanjuje samostalnost, funkcionalnost i kvalitetu života, povećava i rizik od hospitalizacije, broj hospitalizacija, otežava posthospitalno liječenje i oporavak, povećava troškove liječenja tijekom i nakon hospitalizacije. Prema procjenama Goatesa i sur. iz 2019. troškovi hospitalizacija osoba sa sarkopenijom u Sjedinjenim Američkim Državama iznosili su 40,4 milijardi američkih dolara. Trošak hospitalizacije i posthospitalnog

INTRODUCTION

Dementia is a chronic, progressive brain disease that affects memory, thinking, emotions, behavior, motivation, and disrupts daily functioning. It is estimated that more than 55 million people suffer from dementia worldwide. Approximately 10 million new cases of dementia are recorded every year (1). The prevalence of persons suffering from dementia is expected to remain stable in the period from 2019 to 2050, however, due to the growing and aging population, the number of affected individuals is likely to reach 152.8 (130.8-175.9) million (2).

Dementia and sarcopenia share risk factors. Additionally, sarcopenia represents a risk factor for faster cognitive decline, mild cognitive impairment, development of dementia, and vice versa. Sarcopenia involves the loss of muscle mass and strength, thereby impacting function. It is part of the natural aging process, but is more common in persons suffering from dementia (3-5). In the population of healthy individuals over 60 years of age, both in women and in men, the prevalence of sarcopenia is between 10% and 16%. In individuals suffering from dementia, the prevalence ranges from 20% to 65%. Estimates vary due to issues in defining the diagnostic criteria for sarcopenia and the inclusion of different populations (for example, outpatients vs. hospitalized patients), but no difference in prevalence has been observed based on the type of dementia (6-10). Sarcopenia is significant because it increases the risk of falls, fractures, reduced mobility, disability, dysphagia, pneumonia, delirium and death, in the long and short term, in otherwise healthy older individuals, and especially in those suffering from dementia (5, 11, 12). Sarcopenia reduces independence, functionality and quality of life. It also increases the risk of hospitalization, the number of hospitalizations, complicates post-hospital treatment and recovery, and increases the costs of treatment during and after hospitalization. According to estimates provided by Goates et al. in 2019, the costs of hospitalization for individuals with sarcopenia in the United States amounted to 40.4 billion US dollars. The cost of hospitalization and post-hospital treatment in a period of one year

liječenja tijekom godine dana za osobe sa sarkopenijom veći je 35 % do 60 % u odnosu na osobe bez sarkopenije, a varira ovisno o dobi (13-15).

Zajedničkim pretraživanjem pojmova demencija i sarkopenija („dementia" and „sarcopenia") u PubMed-u dobije se 366 rezultata. U razdoblju od 2019. godine do danas pronalazimo 272 rezultata (16). Očito je riječ o novom i zanimljivom području u kojemu postoji još mnogo mjesta za napredak u znanstvenom i kliničkom smislu. Značajan je i utjecaj sarkopenije na cjelokupno zdravlje i kvalitetu života pojedinca, kao i na troškove liječenja. S obzirom na navedeno, cilj našeg istraživanja je pregled literature na temu povezanosti sarkopenije i demencije te metoda probira, dijagnostike, prevencije i liječenja sarkopenije kod osoba oboljelih od demencije.

METODE

Literaturu smo pretraživali korištenjem baza *PubMed* i *Google Scholar*. Koristili smo pojmove: *„dementia", „dementia epidemiology", „ dementia WHO", „sarcopenia", „sarcopenia and dementia", „sarcopenia etiology", „sarcopenia and dementia and etiology", „sarcopenia risk factors", „dementia risk factors", „sarcopenia and dementia and risk factors", „sarcopenia guidelines", „sarcopenia diagnostic criteria", „diagnosis of sarcopenia", „SARC-F", „sarcopenia treatment", „sarcopenia therapy", „sarcopenia prevention", „sarcopenia exercise", „dementia exercise", „sarcopenic obesity"*. Literaturu su neovisno pretraživala dva istraživača.

PREGLED LITERATURE

Etiologija

Sarkopenija i demencija dijele rizične faktore i neke etiološke procese pa je stoga sarkopenija česta kod osoba oboljelih od demencije (4).

for individuals with sarcopenia is 35% to 60% higher than for those without sarcopenia, and it varies depending on age (13-15).

By conducting a combined search for the terms "dementia" and "sarcopenia" in PubMed, we obtained 366 results. In the period from 2019 to present day, 272 results were obtained (16). Clearly, this is a novel and interesting field with ample room for advancement in both scientific and clinical aspects. Furthermore, the impact of sarcopenia on the overall health and quality of life of an individual, including the treatment costs, is significant. In view of the above, the objective of our research was to review the literature addressing the association between sarcopenia and dementia, as well as the methods for screening, diagnosis, prevention, and treatment of sarcopenia in individuals suffering from dementia.

METHODS

We searched the literature using the PubMed and Google Scholar databases. Our search terms included the following: "dementia," "dementia epidemiology," "dementia WHO," "sarcopenia," "sarcopenia and dementia," "sarcopenia etiology," "sarcopenia and dementia and etiology," "sarcopenia risk factors," "dementia risk factors," "sarcopenia and dementia and risk factors," "sarcopenia guidelines," "sarcopenia diagnostic criteria," "diagnosis of sarcopenia," "SARC-F," "sarcopenia treatment," "sarcopenia therapy," "sarcopenia prevention," "sarcopenia exercise," "dementia exercise," "sarcopenic obesity." The literature was independently searched by two researchers.

LITERATURE REVIEW

Etiology

Sarcopenia and dementia share risk factors and some etiological processes, therefore, sarcopenia is common in individuals suffering from dementia (4).

Demencija i sarkopenija dijele upalnu etiologiju, tj. u oba procesa uključeni su medijatori upale. Ulogu ima i oksidativni stres. Sustavna upala, koja prati stariju životnu dob, dodatno je izražena kod osoba oboljelih od demencije. Uz Alzheimerovu bolest se osobito veže interleukin 6. Sustavna upala se povezuje s gubitkom mišićne mase i snage. Smatra se da potiče kataboličke procese što dovodi do razvoja sarkopenije. Proteini amilod beta i tau djeluju na glijalne stanice tako što potiču proizvodnju medijatora upale, a to dovodi do gubitka sinapsi. Gubitak nemasne tjelesne mase povezuje se s atrofijom mozga (4,10). I povišena razina homocisteina ima ulogu u razvoju demencije. Vezuje se uz oksidativni stres i oštećenje endotela, uz to je i neurotoksičan, potiče akumulaciju proteina amiloid beta i povezan je s atrofijom mozga, osobito kore i hipokampusa. Povezuje se uz smanjenu mišićnu snagu, vjerojatno zbog smanjenja funkcije mitohondrija (17,18). Sa starenjem dolazi do disbioze crijevne mikroflore i slabljenja mukozne membrane crijeva. Veća permeabilnost crijeva pogoduje upali i oksidativnom stresu. Pokazalo se da osobe oboljele od Alzheimerove bolesti imaju povećane vrijednosti zonulina, biomarkera propusnosti crijeva. Njegove razine rastu s progresijom Alzheimerove bolesti, ali i s težinom sarkopenije. Dokazana je i korelacija između razine C terminalnog fragmenta agrina 22 (CAF22), produkta raspada agrina, i težine sarkopenije, tj. gubitka mišićne mase i snage. U sarkopeniji dolazi do propadanja neuromišićnih veza što uzrokuje otpuštanje agrina. Tako će osobe s umjerenom Alzheimerovom bolesti imati veće vrijednosti zonulina i CAF22, kao i teži oblik sarkopenije, negoli osobe s blagim oblikom bolesti (19). Poznata je i uloga angiotenzin-konvertirajućeg enzima 1 (ACE1) u upali i oksidativnom stresu, a sve više se istražuje njegovo mjesto u razvoju demencije i sarkopenije (20). Snižene vrijednosti vitamina B12 i vitamina D povezuju se i s demencijom i sa sarkopenijom. Snižene vrijednosti vitamina B12 posredno dovode do po-

Dementia and sarcopenia share an inflammatory etiology, meaning that both processes involve inflammatory mediators. Oxidative stress also plays a role in this aspect. Systemic inflammation, which accompanies older age, is additionally pronounced in individuals suffering from dementia. Alzheimer's disease, in particular, is associated with interleukin-6. Systemic inflammation is associated with the loss of muscle mass and strength, and is believed to stimulate catabolic processes thus leading to the development of sarcopenia. Amyloid-beta and tau proteins affect glial cells by promoting the production of inflammatory mediators, resulting in the loss of synapses. The loss of lean body mass is associated with brain atrophy (4, 10). Additionally, elevated levels of homocysteine contribute to the development of dementia. They are associated with oxidative stress and endothelial damage, in addition to being neurotoxic, promoting the accumulation of amyloid-beta protein and being linked to brain atrophy, particularly of the cortex and hippocampus. They are also associated with reduced muscle strength, likely due to decreased mitochondrial function (17, 18). Dysbiosis of the gut microbiota and weakening of the gut mucous membrane occur with ageing. Increased gut permeability favors inflammation and oxidative stress. Studies have shown that individuals suffering from Alzheimer's disease have elevated levels of zonulin, a biomarker of gut permeability. Zonulin levels increase with the progression of Alzheimer's disease, as well as with the severity of sarcopenia. Furthermore, a correlation has been proved between the levels of C-terminal agrin fragment-22 (CAF22), a breakdown product of agrin, and the severity of sarcopenia, i.e. loss of muscle mass and strength. Sarcopenia causes a breakdown of neuromuscular junctions, causing the release of agrin. Therefore, individuals suffering from moderate Alzheimer's disease will have higher levels of zonulin and CAF22, as well as a more severe form of sarcopenia, compared to those suffering from a mild form of the disease (19). The role of angiotensin-converting enzyme 1 (ACE1) in inflammation and oxidative stress is well-known, and more and more research is being conducted with regard to its involvement in the

višenih vrijednosti homocisteina što pogoduje razvoju sarkopenije što je već spomenuto. Niske razine vitamina D smanjuju anaerobni kapacitet i dovode do atrofije mišića (21-25).

Hipertenzija, dijabetes i hiperlipidemija su faktori rizika za razvoj demencije, ali i za razvoj sarkopenije (26-33). Malnutricija je česta kod starijih osoba, a osobito je prisutna kod osoba oboljelih od demencije. Najčešće je smanjen unos proteina što posebno pogoduje razvoju sarkopenije. Sjedilački način života i smanjena fizička aktivnost također povećavaju rizik za razvoj sarkopenije (10). Neuropsihijatrijski simptomi poput promjene apetita i depresivnosti mogu pogodovati smanjenom unosu hrane, pa i proteina, kao i smanjenom kretanju, što sve dovodi do razvoja sarkopenije. Paranoidnost, pa i psihotičnost općenito, kod osoba oboljelih od demencije mogu dovesti do anoreksije, a time i sarkopenije (10,34-36).

Metode probira i dijagnosticiranja sarkopenije

Europska radna skupina za sarkopeniju kod starijih osoba (EWGSOP2) 2018. je revidirala preporuke iz 2010. godine. Usuglašeno je da se rizik za sarkopeniju procjenjuje na temelju smanjene mišićne snage. Dijagnoza sarkopenije postavlja se potvrđivanjem smanjene kvalitete ili kvantitete mišića. Lošije fizičke sposobnosti upućuju na tešku sarkopeniju. Kao test probira preporuča se upitnik *Strength, assistance with walking, rising from a chair, climbing stairs, and falls* (SARC-F) (37). To je test u kojem pacijent daje procjenu vlastite snage, pomoći pri hodanju, ustajanja sa stolca, penjanja uz stube, učestalosti padova. Četiri ili više prikupljenih bodova upućuje na povećani rizik za sarkopeniju (tablica 1) (38,39).

U slučaju pozitivnog rezultata, potrebno je provjeriti mišićnu snagu. To se može napraviti pomoću testiranja snage stiska šake dinamometrom. Za muškarce je granična vrijednost ispod

development of dementia and sarcopenia (20). Reduced levels of vitamin B12 and vitamin D are also associated with both dementia and sarcopenia. Reduced levels of vitamin B12 indirectly lead to elevated homocysteine levels, promoting the development of sarcopenia, as previously discussed. Low levels of vitamin D reduce anaerobic capacity and lead to muscle atrophy (21-25).

Hypertension, diabetes, and hyperlipidemia all represent risk factors for the development of dementia, as well as for the development of sarcopenia (26-33). Malnutrition is common in older individuals, particularly among those suffering from dementia. The most frequent issue is a reduced intake of protein, which significantly contributes to the development of sarcopenia. Sedentary lifestyle and reduced physical activity also increase the risk of developing sarcopenia (10). Neuropsychiatric symptoms such as changes in appetite and depression can contribute to reduced food intake, thus affecting protein intake, as well as decreased mobility, all of which lead to the development of sarcopenia. Paranoid tendencies and psychosis in general can lead to anorexia and, consequently, sarcopenia in persons suffering from dementia (10, 34-36).

Screening and diagnosis methods for sarcopenia

The European Working Group on Sarcopenia in Older People (EWGSOP2) revised its recommendations in 2018, updating the guidelines from 2010. It was agreed that the risk of sarcopenia should be assessed based on reduced muscle strength. The diagnosis of sarcopenia is established by confirming reduced muscle quality or quantity. Poorer physical abilities indicate severe sarcopenia. The strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) questionnaire is recommended as a screening test for sarcopenia (37). This test requires the patient to provide a self-assessment of their own strength, assistance needed with walking, rising from a chair, climbing stairs, and the frequency of falls. A score of four or more points suggests an increased risk of sarcopenia (Table 1.) (38, 39).

TABLICA 1. SARC-F: alat za procjenu rizika za sarkopeniju (36)
TABLE 1. SARC-F: sarcopenia risk assessment tool (36)

Sastavnica / Component	Pitanje / Question	Bodovanje / Scoring	Bodovi / Points
Snaga / Strength	Imaš li poteškoća s podizanjem i nošenjem 4,5 kg tereta? / How much difficulty do you have in lifting and carrying 4.5 kg?	Nemam / None = 0 Ponekad / Some = 1 Često ili uvijek / A lot or unable = 2	
Pomoć pri hodanju / Assistance in walking	Imaš li poteškoća pri hodanju sobom? / How much difficulty do you have walking across a room?	Nemam / None = 0 Ponekad / Some = 1 Često ili uvijek / A lot, use aids, or unable = 2	
Ustajanje sa stolca / Rise from a chair	Imaš li poteškoća pri premještanju sa stolca ili kreveta? / How much difficulty do you have transferring from a chair or bed?	Nemam / None = 0 Ponekad / Some = 1 Često ili uvijek / A lot or unable without help = 2	
Penjanje po stubama / Climb stairs	Imaš li poteškoća pri penjanju uz 10 stuba? / How much difficulty do you have climbing a flight of 10 stairs?	Nemam / None = 0 Ponekad / Some = 1 Često ili uvijek / A lot or unable = 2	
Padovi / Falls	Koliko puta si pao u posljednjih godinu dana? / How many times have you fallen in the past year?	Niti jednom / None = 0 1 – 3 pada / 1 – 3 falls = 1 4 ili više padova / 4 or more falls = 2	
Ukupno bodova / Total score:	Manje od 4 boda / Less than 4 points = nema rizika za sarkopeniju / no risk of sarcopenia 4 ili više bodova / 4 or more points = povećan rizik za sarkopeniju / increased risk of sarcopenia		

27 kg, dok je za žene manje od 16 kg. Druga mogućnost je test ustajanja sa stolca u kojemu se mjeri vrijeme potrebno za pet ustajanja, pri čemu se ne smiju koristiti ruke. Ako to vrijeme iznosi više od 15 sekundi, osoba vjerojatno ima sarkopeniju. Da bi se potvrdila dijagnoza sarkopenije, tj. utvrdila kvantiteta ili kvaliteta mišića mogu se koristiti denzitometrija, bio-impedancija, kompjutorska tomografija (CT) ili magnetska rezonancija (MR). U praksi se najčešće apendikularna skeletna mišićna masa (udovi, rameni obruč i zdjelica) utvrđuje analizom bioelektrične impedancije. Za muškarce, vrijednost manja od 20 kg upućuje na sarkopeniju, dok je kod žena ta vrijednost 15 kg. S obzirom da mišićna masa korelira s veličinom tijela, ove se vrijednosti mogu podijeliti s kvadratom visine. Za muškarce vrijednost ispod 7 kg/m^2 potvrđuje sarkopeniju, dok kod žena sarkopeniju potvrđuje vrijednost ispod 5,5 kg/m^2 (37).

In case of a positive result, it is necessary to assess muscle strength. This can be done using the handgrip strength test, for which a dynamometer is used. The threshold value for men is below 27 kg, while for women it is less than 16 kg. Another option is the chair stand test, where the time required to complete five chair stands without using hands is measured. If this time exceeds 15 seconds, the individual likely has sarcopenia. Techniques such as densitometry, bioimpedance, computed tomography (CT) or magnetic resonance imaging (MRI) can be used in order to confirm the diagnosis of sarcopenia, i.e. to determine the quantity or quality of muscles. In practice, appendicular skeletal muscle mass (limbs, shoulder girdle, and pelvis) is most commonly determined using bioelectrical impedance analysis. For men, a value below 20 kg indicates sarcopenia, while for women this value is 15 kg. Since muscle mass correlates with body size, these values can be divided by the square of height. For men, a value below

Da bi se utvrdila težina sarkopenije koriste se: test brzine hoda, set kratkih testova fizičke sposobnosti, test „ustani i idi", test 400 metara hoda. Test brzine hoda mjeri brzinu potrebnu da osoba normalnim hodom pređe četiri metra ravne površine. Brzina od 0,8 m/s ili niža upućuje na tešku sarkopeniju. EWGSOP2 preporuča upravo test brzine hoda. Set testova uključuje test brzine hoda, test ravnoteže i test ustajanja sa stolca. Osam bodova ili više upućuje na tešku sarkopeniju. U testu „ustani i idi" osoba mora ustati sa stolca, prošetati tri metra, okrenuti se, vratiti i sjesti na stolac. Ako je za to potrebno 20 sekundi ili više možemo reći da osoba ima tešku sarkopeniju. Tijekom testa 400 metara hoda osoba mora prošetati 20 krugova od 20 metara, svaki najbrže moguće, pri čemu može dva puta stati i odmoriti se tijekom testiranja. Ako osoba ne može to izvršiti ili joj je potrebno šest minuta ili više, ima teški oblik sarkopenije. Testovi „ustani i idi" te 400 metara hoda imaju prediktivnu vrijednost za procjenu smrtnosti (37).

Postoje i drugi testovi koji se mogu koristiti za ispitivanje sarkopenije. S obzirom da SARC-F ovisi o procjeni pacijenta, za probir se može koristiti i Ishii test. On u obzir uzima dob, snagu stiska šake i opseg potkoljenice (37). Erdogan i suradnici smatraju da Ishii test može potencijalno biti dijagnostički test za sarkopeniju (40). Postoji i SarSA-Mod, alat za probir koji uključuje dob, težinu i opseg potkoljenice (41). Kod starijih osoba, ako druge dijagnostičke metode nisu na raspolaganju, može donekle poslužiti opseg potkoljenice. Opseg potkoljenice manji od 31 cm ima prediktivnu vrijednost za očekivano preživljenje i pokretljivost (37). Preporuča se mjeriti opseg potkoljenice u stojećem položaju. Preporuke za graničnu vrijednost, tj. opseg ispod kojega postoji povećani rizik za sarkopeniju, variraju od 31 cm za muškarce i 30 cm za žene do 34 cm za muškarce i 33 cm za žene. SARC-CalF je kombinacija SARC-F i opsega potkoljenice. Istraživanja mu daju prednost

7 kg/m^2 confirms sarcopenia, while for women a value below 5.5 kg/m^2 confirms sarcopenia (37).

Various tests are employed in order assess the severity of sarcopenia: the gait speed test, a set of short physical performance battery tests, the "Timed Up and Go" test, the 400-meter walk test. The gait speed test measures the time it takes for an individual to walk four meters on a flat surface at a normal pace. A speed of 0.8 m/s or lower indicates severe sarcopenia, and EWGSOP2 specifically recommends this test. The set of tests includes the gait speed test, the balance test, and the chair stand test. A score of eight points or higher suggests severe sarcopenia. In the "Timed Up and Go" test, an individual must stand up from a chair, walk three meters, turn around, return, and sit back down on the chair. If this action takes 20 seconds or more, it indicates severe sarcopenia. During the 400-meter walk test, an individual must walk 20 laps of 20 meters each, as quickly as possible, with the option to stop and rest twice during the test. If they cannot complete this task or if it takes six minutes or more, it is an indicator of severe sarcopenia. Both the "Timed Up and Go" test and the 400-meter walk test have a predictive value for assessing mortality (37).

There are other tests that can be used to evaluate sarcopenia as well. Given that SARC-F relies on patient assessment, the Ishii test can also be used for screening. This test takes into account the age, handgrip strength and calf circumference (37). Erdogan et. al believe that the Ishii test could potentially be a diagnostic test for sarcopenia (40). There is also the SarSA-Mod, a screening tool that includes age, weight and calf circumference (41). In older individuals, when other diagnostic methods are not available, calf circumference may be somewhat indicative. A calf circumference of less than 31 cm has a predictive value for expected survival and mobility (37). It is recommended to measure calf circumference in a standing position. Recommended threshold values, i.e. the circumference below which there is an increased risk of sarcopenia, vary from 31 cm for men and 30 cm for women to 34 cm for men and 33 cm for women. SARC-CalF is a combination of SARC-F and calf

u odnosu na SARC-F jer se pokazalo da dio pacijenata sa sarkopenijom neće biti identificiran ako se koristi samo SARC-F (42-44). Za test snage stiska šake također postoje dvojbe. Van Ancum i suradnici su pokazali da će se prema kriterijima EWGSOP2 dio ispitanika previdjeti. Oni bi inače bili zahvaćeni prijašnjim graničnim vrijednostima testa snage stiska šake koji su 30 kg za muškarce i 20 kg za žene, nasprot sadašnjih 27 kg i 16 kg (45). Kao jedan od mogućih testova spominje se i CT trećeg lumbalnog kralješka. Pokazalo se da mišićna masa u tom području korelira s mišićnom masom cijeloga tijela. Za to može poslužiti i MR. Središnji mišići bedra pokazuju još bolju korelaciju s mišićima cijeloga tijela. Postoje dvojbe oko vrijednosti CT i MR psoasa. Ultrazvuk je dobar za procjenu debljine i kvalitete mišića. Ultrazvučna procjena debljine mišića *gastrocnemius, rectus femoris* i *rectus abdominis* spominje se kao moguća metoda probira na sarkopeniju (46). U istraživanjima se u prvom redu koristi test razrjeđivanja kreatina (37). Odnedavno se navodi sarkopenijski indeks. To je omjer kreatinina i cistatina C pomnožen sa 100. Ako je vrijednost za muškarca manja od 62, a za ženu od 55, tada postoji visoki rizik za sarkopeniju (47). Spekulira se o uporabljivosti zonulina i CAF22 kao biomarkera za sarkopeniju (19).

Metode prevencije i liječenja sarkopenije

Prevencija i liječenje sarkopenije kod osoba oboljelih od demencije temelje se ponajprije na adekvatnoj prehrani i tjelovježbi. Većina istraživanja o toj tematici napravljena je kod zdravih starijih osoba ili kod osoba koje nisu bile dementne. O prevenciji sarkopenije potrebno je razmišljati kada postoji rizik za malnutriciju, kada je ograničena sposobnost kretanja ili ako pacijent već duže vrijeme boravi u krevetu te ako ima određene bolesti koje pogoduju razvoju sarkopenije. Preporuka je da se hospitaliziranim pacijentima u dobi od 65 godina ili više

circumference. Conducted studies favor this test over SARC-F alone because it has been observed that some patients with sarcopenia may not be identified if only SARC-F is used (42-44). Uncertainties also exist with regard to the handgrip strength test. Van Ancum et. al have proved that according to EWGSOP2 criteria, some participants would be overlooked. They would otherwise have been covered within the previous cutoff values for the handgrip strength test, which were 30 kg for men and 20 kg for women, as opposed to the current 27 kg and 16 kg (45). One of the potential tests mentioned is also the CT of the third lumbar vertebra. It has been shown that muscle mass in this area correlates with the muscle mass of the whole body. MRI can also be used for this purpose. The central muscles of the thigh show an even better correlation with the muscles of the entire body. There are debates about the values of CT and MRI of the psoas. Ultrasound is effective for assessing muscle thickness and quality. Ultrasound assessment of the thickness of the *gastrocnemius*, *rectus femoris*, and *rectus abdominis* muscles is mentioned as a possible screening method for sarcopenia (46). The test primarily used in research is the creatine dilution test (37). The sarcopenic index has been mentioned lately as well. It represents the ratio of creatinine to cystatin C multiplied by 100. If the value is lower than 62 for a man and 55 for a woman, there is a high risk of sarcopenia (47). There is also speculation about the usability of zonulin and CAF22 as biomarkers for sarcopenia (19).

Prevention and treatment methods for sarcopenia

The prevention and treatment of sarcopenia in individuals suffering from dementia primarily rely on adequate nutrition and physical exercise. Most studies on this topic have been conducted in healthy older individuals or those without dementia. Prevention of sarcopenia should be considered when there is a risk of malnutrition, in cases of limited mobility, or if the patient has been bedridden for an extended period, along with specific conditions that predispose to the

provjeri rizik za sarkopeniju. Isto vrijedi i za mlađe osobe koje imaju komorbiditete koji bi mogli dovesti do sarkopenije. Smjernice Stručne radne skupine Australskog i novozelandskog društva za istraživanje sarkopenije i slabosti (ANZSSFR) daju preporuku i za dijagnosticiranje sarkopenije, a ne samo za utvrđivanje postojanja povećanog rizika (48). S obzirom na sve navedeno, jasno je da je kod osoba oboljelih od demencije korisno raditi probir na sarkopeniju. Već smo naveli da je SARC-F koristan alat za tu namjenu. S obzirom da rezultat SARC-F četiri ili više upućuje na povećani rizik za sarkopeniju, može se razmišljati o uvođenju preventivnih mjera. Potrebno je testirati i pretile osobe jer postoji sarkopenijska pretilost. Takve osobe se u praksi mogu slučajno zanemariti u procesu probira na sarkopeniju (49).

Za prevenciju je bitna prehrana bogata proteinima, a može se razmisliti i o proteinskim dodatcima prehrani koji su svakako dio preporuka u sklopu liječenja sarkopenije. Pacijentima je važno i ugodno okruženje, a često postoji i potreba za asistencijom tijekom hranjenja. Europsko društvo za kliničku prehranu i metabolizam (ESPEN) preporuča unos barem 30 kcal/kg tjelesne mase do 38 kcal/kg za pothranjene starije pacijente. Oralni suplementi bi trebali sadržavati 400 kcal i 30 g proteina; to su dnevne potrebe (48,50). Meta-analiza iz 2021. g. dovodi u pitanje korist proteinskih dodataka prehrani kod starijih osoba sa sarkopenijom (51). Ukupan preporučeni unos proteina trebao bi iznositi 1.2-1.5 g/kg tjelesne mase na dan do 2 g/kg u slučaju težih bolesti i pretilosti. To bi trebalo spriječiti ili minimizirati gubitak mišićnog tkiva. Spekulira se o ulozi leucina, beta-hidroksi beta-metilbutirata, vitamina D, kreatina i omega-3 masne kiseline, no rezultati istraživanja nisu jasni (48). Postoje indicije da bi unos vitamina B12 mogao biti osobito koristan zbog usporavanja atrofije mozga i progresa demencije, ali i zbog prevencije sarkopenije (21-24). Nadoknada vitamina D svakako se preporuča

development of sarcopenia. It is recommended to evaluate the risk of sarcopenia in hospitalized patients aged 65 years or older. The same applies to younger individuals with comorbidities that could lead to sarcopenia. The guidelines from the Expert Working Group of the Australian and New Zealand Society for Sarcopenia and Frailty Research (ANZSSFR) provide recommendations not only for determining the increased risk of sarcopenia, but also for its diagnosis (48). Considering all of the above, it is evident that screening for sarcopenia is beneficial in individuals suffering from dementia. As mentioned earlier, SARC-F is a useful tool for this purpose. Given that a SARC-F score of 4 or higher indicates an increased risk of sarcopenia, preventive measures can be considered. It is also essential to test obese individuals due to the fact that sarcopenic obesity exists as well. Such individuals may be inadvertently overlooked in the screening process for sarcopenia (49).

A diet rich in proteins is crucial for prevention, and consideration can be given to protein supplements, which are certainly included in the recommendations for the treatment of sarcopenia. Patients require a comfortable environment, and there is often a need for assistance during feeding. The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends an intake of at least 30 kcal/kg of body weight up to 38 kcal/kg for malnourished older patients. Oral supplements should contain 400 kcal and 30 g of protein in order to meet the daily needs (48, 50). However, a meta-analysis conducted in 2021 questions the benefit of protein supplements in older individuals with sarcopenia (51). The overall recommended protein intake should amount to 1.2-1.5 g/kg of body weight per day, up to 2 g/kg in the case of severe illnesses and obesity. This should prevent or minimize muscle tissue loss. There is speculation about the role of leucine, beta-hydroxy beta-methylbutyrate, vitamin D, creatine and omega-3 fatty acids, however research results are unclear (48). There are indications that vitamin B12 intake could be particularly beneficial for slowing brain atrophy and dementia progression, as well as preventing sarcopenia (21-24). Vitamin D supplementation is

kada je njegova razina ispod 30 mcg/L (37). Pozitivno djelovanje mediteranske prehrane na razvoj sarkopenije je upitno. Izglednije je da ima više preventivni učinak nego terapijski (52,53).

Adekvatne vježbe važne su u prevenciji i liječenju sarkopenije. Mogu se kombinirati različite vježbe, ovisno o mogućnostima pacijenta. Mogu uključivati treninge brzine, ravnoteže, vježbe s otporom. Podatci pokazuju da se pozitivan efekt može postići i vježbama od 20 minuta tijekom pet dana u tjednu. Redovito šetanje i vježba ustajanja sa stolca jedan do tri puta na dan, po 20 minuta, također mogu biti korisni (48). Osobito su se dobrima pokazale vježbe s otporom i to s blagim otporom koji iznosi 20-30 % od maksimalnog broja ponavljanja (54). Korisne su i vježbe poput stajanja na jednoj nozi, prebacivanja težine s jedne noge na drugu, vježbe iskoraka, hodanje uz male prepreke ili po liniji u polutandemu. Navedene vježbe su sigurne za osobe oboljele od demencije (55). Iako postoje istraživanja o vježbama koje su korisne za prevenciju pada i sigurne su za osobe oboljele od demencije, o vježbama koje su dobre za prevenciju sarkopenije kod starijih osoba, još uvijek ne postoje istraživanja o utjecaju vježbi na sarkopeniju kod osoba oboljelih od demencije.

Pretpostavlja se da je najbolje kombinirati vježbe i nutritivnu potporu (48). Još uvijek ne postoji farmakoterapija za sarkopeniju. Istražuju se nadomjestak testosterona, nadomjestak hormona rasta, protutijela na miostatin, antagonist aktivinskog receptora, modulatori androgenskog receptora, nesteroidni protuupalni lijekovi. Za sada ništa od navedenog nije ušlo u kliničku praksu (48,56). Kao terapijska mogućnost spominje se i neuromuskularna električna stimulacija, no potrebna su dodatna istraživanja (57). Spekulira se o koristi ACE inhibitora u liječenju demencije i sarkopenije (20). Istražuju se različiti ekstrakti morske i kopnene flore, poput ekstrakta zelenog čaja tretiranog tanazom,

certainly recommended when its levels are below 30 mcg/L (37). Positive effects of the Mediterranean diet on the development of sarcopenia are questionable. It seems more likely that its effect is preventive rather than therapeutic (52, 53).

Adequate exercise is important in the prevention and treatment of sarcopenia. Different types of exercise can be combined depending on the patient's capabilities. They can include speed training, balance exercises and resistance exercises. Data indicate that a positive effect can be achieved by 20 minutes of exercise five days a week. Regular walking and chair stand exercises one to three times a day for 20 minutes can also be beneficial (48). Resistance exercises, especially with mild resistance ranging from 20-30% of the maximum number of repetitions, have proved to be particularly effective (54). Exercises such as standing on one leg, shifting weight from one leg to the other, lunges, walking over small obstacles or walking in a semi-tandem stance are useful as well. These exercises are considered safe for individuals with dementia (55). Although there are studies addressing exercises beneficial for fall prevention that are also considered safe for individuals suffering from dementia, as well as those addressing exercises that are good for preventing sarcopenia in the elderly, studies specifically addressing the impact of exercises on sarcopenia in persons suffering from dementia are still lacking.

It is presumed that the optimal approach is to combine exercises and nutritional support (48). There is still no pharmacotherapy specifically designed for the treatment of sarcopenia. Investigative efforts encompass testosterone and growth hormone replacements, myostatin antibodies, activin receptor antagonists and androgen receptor modulators, along with nonsteroidal anti-inflammatory drugs. None of these have been integrated into clinical practice so far (48, 56). Neuromuscular electrical stimulation has been proposed as a therapeutic option, however additional research on the topic is required (57). There has also been speculation about the potential therapeutic efficacy of ACE inhibitors in the treatment of dementia and sarcopenia (20). Ongoing research involves

zatim različiti probiotici, no istraživanja su tek u povojima (58).

ZAKLJUČAK

Sarkopenija na različite načine utječe na kvalitetu života i mortalitet. Postoji upitnik o utjecaju sarkopenije na kvalitetu života (SarQoL) preveden na brojne svjetske jezike, pa i na hrvatski jezik (59-61). S obzirom na globalni rast očekivanog životnog vijeka, rast udjela populacije osoba starijih od 65 godina, a time i osoba oboljelih od demencije, sarkopenija predstavlja neizbježan izazov s kojim se valja suočiti. Kao sredstvo probira na sarkopeniju ističe se SARC-F, osobito za osobe oboljele od demencije. Kao dijagnostičke metode najčešće se koriste dinamometar i analiza bioelektrične impedancije. Adekvatna tjelovježba i pojačani unos proteina klasičnom prehranom ili dodatcima temelj su prevencije i liječenja sarkopenije. S obzirom na sve do sada navedeno, jasno je da su potrebna dodatna istraživanja o metodama probira i dijagnosticiranja sarkopenije, osobito u području biomarkera za sarkopeniju i o sarkopeniji kod oboljelih od demencije. I dalje traju rasprave o kriterijima za postavljanje dijagnoze sarkopenije. Postoje dvojbe i o najboljem alatu probira te koji su alati adekvatni za koju populaciju pacijenata. Metode prevencije, a još više terapijske metode, nedovoljno su istražene, osobito na populaciji osoba oboljelih od demencije. Unatoč tome potrebno je osvijestiti problem sarkopenije, njegovu raširenost kod osoba oboljelih od demencije te važnost prevencije i liječenja sa svim sredstvima koja su nam trenutno dostupna.

diverse extracts derived from marine and terrestrial flora, including green tea extracts treated with tannase and various probiotics, however, research in these domains is still nascent (58).

CONCLUSION

Sarcopenia has a multifaceted impact on both quality of life and mortality. A Sarcopenia and Quality of Life questionnaire (SarQoL) is also in use, and it is available in various languages, including Croatian (59-61). In light of the global increase in life expectancy, increase in the proportion of the population aged 65 years and above, and consequently an increase in the share of individuals suffering from dementia, sarcopenia emerges as an inevitable challenge necessitating careful consideration. The SARC-F tool stands out as a screening tool for sarcopenia, particularly for individuals suffering from dementia. The most commonly applied diagnostic methods include dynamometry and bioelectrical impedance analysis. Adequate physical exercise and increased protein intake, achievable through conventional nutritional sources or supplements, represent the basis for sarcopenia prevention and treatment. In view of all of the above, it is clear that further research is required regarding the screening and diagnosis methods for sarcopenia, particularly with regard to its biomarkers, and the manifestation of sarcopenia in patients suffering from dementia. Ongoing discourse persists concerning the criteria required for diagnosing sarcopenia. There are also uncertainties regarding the optimal screening tools and the applicability of different screening tools to patient subgroups. There has been insufficient research addressing the prevention methods and, more significantly, therapeutic interventions, especially among the individuals suffering from dementia. Despite these challenges, it is important to elevate awareness with regard to sarcopenia, its prevalence within the population of individuals suffering from dementia, and the significance of prevention and treatment strategies utilizing all the tools we currently have at our disposal.

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