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REVIEW ARTICLE

Sarcopenia disease in Iran: an overview

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Abstract

Background Sarcopenia is a geriatric disease with adverse clinical outcomes, high rate of mortality and a major challenge to healthy elderly. This study aimed to undertake a survey to identify gaps and highlight strengths in sarcopenia research in order to progress research in this area for the next years in Iran.

Methods This study included all studies published from the beginning until the first of 2019 in national and international journals by Iranian authors conducted in the field of sarcopenia. The databases including MEDLINE (via PubMed), Web of Science and SCOPUS were used as the sources of information. All relevant available academic studies, including review articles, original articles, case reports, conference abstracts, and letters were included in the analysis.

Findings A total of 48 articles obtained and then categorized into six groups. These groups were; about Pathophysiology, Epidemiology of sarcopenia, Screening of sarcopenia, Nutrition, Physical activity and Association of Sarcopenia and Other Diseases that briefly findings of each study had been described. These findings showed that the prevalence of sarcopenia was 16.5% to 32.5%, using different definitions. A study developed and validated a screening model for identifying people with sarcopenia. Lifestyle changes such as diet can be appropriate strategies for the prevention of sarcopenia and also, physical activity is considered to be one of the few effective strategies to improve sarcopenia and prevent its outcomes, especially if in combination with appropriate nutritional supplementation. Sarcopenia is associated with adverse outcomes and other serious areas such as metabolic disorders, cancers, cardiovascular diseases, nephrology, gastroenterology, psychiatry, other geriatric diseases (such as osteoporosis, etc) and death. Some studies about these areas have been done in Iran.

Conclusions By this study, we found that studies on sarcopenia, the gaps of sarcopenia research in Iran, and highlighted the research priorities for future works. The outcome of the present research is to ultimately improve the health, quality of life and well-being of sarcopenic people.

Keywords Sarcopenia · Research · Iran

Introduction

Sarcopenia, as the age-related loss of muscle mass characterized by the poor muscle function (strength or performance), has been highlighted as a health concern in recent years. Studies have demonstrated that the decline of skeletal muscle mass could start from the age of 30–40 years. Sarcopenia is a common health issue in the elderly population and has an association with adverse health outcomes, such as falls, fracture, metabolic disorders, disability, loss of independence and mortality. Therefore, this disease has high personal, social and economic burdens and optimal care for sarcopenic people is essential.

Given the importance of this condition, in 2016, an ICD-10 code was assigned for sarcopenia.

The existence of code for this disease, progress toward a single definition and diagnosis of the importance of sarcopenia

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in other disease and its complications have led to the increased awareness of physicians and researchers to this disease [1].

These findings call for an imperative need to broaden research strategies for understanding the causes and characteristics of sarcopenia and, therefore, develop effective prevention strategies and therapies. In a recent decade, a plethora of research has focused on limited aspects of Sarcopenia while many major areas still pend to further research. Therefore, a critical goal of the present research is to discover ways entailing lasting health benefits for individuals with or at risk of sarcopenia and improve the social burden of this distressing disease [2, 3].

This review aims to provide recent progress in sarcopenia research in Iran and to identify gaps and highlight strengths in order to develop future researches for the next years (Table 1).

Methods

In connection with the aims of the present review, we conducted a throughout search to yield an overview of sarcopenia research in Iran. Therefore, the authors considered sarcopenia research in its broadest sense including, where possible, all aspects of this disease, from molecules, cells, and tissues, to whole animal studies, and clinical sciences and care. In the present review, we included all studies from the beginning until the first of 2019 published in national and international journals by Iranian authors conducted on the subject of sarcopenia. The sources of information were MEDLINE (via PubMed), Web of Science and SCOPUS databases. The keywords used for the search were "sarcopenia*" and "Iran*" as the author's affiliations.

After an assignment, duplicate results were removed by authors through reviewing the document title as well as the journal volume and issue. All review articles, original articles, case reports, conference abstracts, and letters relevant to our research purpose were included in the analysis.

Finally, 48 documents remained and in the next step, all obtained articles from databases were merged and categorized according to the articles' titles to six groups. These grouping are:

- Epidemiology of Sarcopenia ($n = 6$)
- Pathophysiology ($n = 4$)
- Screening of Sarcopenia($n = 2$)
- Nutrition ($n = 12$)
- Physical activity($n = 9$)
- Association of Sarcopenia and Other Diseases($n = 15$)

Epidemiology of sarcopenia

In two decades, several definitions of sarcopenia are proposed in the world. Early definitions included only muscle mass, however, researches in Europe and Asia have used several parameters to develop the consensus sets of definitions and diagnostics criteria for sarcopenia. In 2010, a practical clinical definition was proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) [2]. Similar approaches were considered by the International Working Group on Sarcopenia (IWGS) and Asian Working Group for Sarcopenia (AWGS) [3, 4]. According to these consensual definitions, sarcopenia is defined as the progressive and generalized loss of skeletal muscle mass combined with poor muscle function. However, several major differences exist between definitions, including the method of assessment of components, different measurement tools, cutoff points and definitions which may lead to different statistics with regard to the prevalence of sarcopenia. To get rid of such problems, some working groups recommend the use of normative (healthy young adult) rather than predictive reference populations.

For this reason, in 2018, a study was conducted to determine cut-off points of low muscle mass which led to reference values in Iran and other Middle East countries. A total of 691 subjects aged ≥18 years participated in this population-based study in Bushehr, Iran. Two standard deviations below the mean skeletal muscle index (SMI) of reference groups were as cut-off values of low muscle mass that were 7.0 Kg/m in men and 5.4 Kg/m among women [5].

Another study, as a part of the Prospective Urban Rural Epidemiology (PURE) study, identified reference ranges for handgrip strength (HGS) derived from healthy adults from all income strata aged 35–70 years living in 21 countries. The findings showed that median HGS differs across the geographic regions and different ethnic groups. Iran is a middle-income country and the median HGS was 21 [18–24] kg and 35 [31–40] Kg among women and men, respectively [6].

Few studies have been conducted so far to assess the prevalence of sarcopenia in Iran. In 2011, a cross-sectional population-based study named "The **Sar**copenia and its determinants among **Ir**anian elderly (**SARIR**) study was designed to determine the prevalence of sarcopenia in 300 subjects aged ≥55 years living in Tehran [7]. The prevalence values of presarcopenia, sarcopenia, and severe sarcopenia were 52.7%, 20.7%, and 6%, in men and 25.3%, 15.3%, and 5.3% in women, respectively. [8].

A cross-sectional study was performed among adults aged ≥60 years in Tehran health centers. The results of this study suggested that the prevalence of sarcopenia was 16.5% and 32.5%, respectively using different definitions of AWGOS and EWGOS. Males had 21.3% sarcopenic cases compared to 8.9% in females [9].

In another study, a systematic review and meta-analysis was conducted by authors to find the overall prevalence of sarcopenia in both genders in different regions of the world. In this study, the population-based studies between January 2009 and December 2016 exploring the prevalence of sarcopenia in healthy individuals aged ≥60 years using the

Table 1 Characteristics of documents based on field of study

Title	Published year	Field of study	Type of document
Appendicular Skeletal Muscle Mass Reference Values and the Peak Muscle Mass to Identify Sarcopenia among Iranian Healthy Population [5]	2018	Epidemiology	Original Article
Reference ranges of handgrip strength from 125,462 healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study [6].	2016	Epidemiology	Original Article
Sarcopenia and its determinants among Iranian elderly (SARIR): Study protocol [7].	2012	Epidemiology	Protocol
Sarcopenia and its associated factors in Iranian older individuals: Results of SARIR study [8]	2016	Epidemiology	Original Article
Prevalence of Sarcopenia and Its Association with Socioeconomic Status among the Elderly in Tehran [9]	2016	Epidemiology	Original Article
Prevalence of sarcopenia in the world: a systematic review and meta-analysis of general population studies [10]	2017	Epidemiology	Systematic review
Identification of candidate genes and proteins in aging skeletal muscle (sarcopenia) using gene expression and structural analysis [11].	2018	Pathophysiology	Review
Ursolic acid: A versatile triterpenoid compound in regulating the aging. Physiology and Pharmacology [12].	2017	Pathophysiology	Review Article
Isolation and optimization of mice skeletal muscle satellite cells using preplating method and culture media substitution [13].	2016	Pathophysiology	Original Article
Circulating cell-free nucleic acids as potential biomarkers for sarcopenia: a step toward personalized medicine [14]	2017	Pathophysiology	Commentary
Bushehr Elderly Health (BEH) programme: study protocol and design of musculoskeletal system and cognitive function (stage II) [15].	2017	Sarcopenia screening	Protocol
Development and validation of sarcopenia screening for older people: The Bushehr Elderly Health program [16]	2018	Sarcopenia screening	Abstract
Nutrition and physical activity in the prevention and treatment of sarcopenia: systematic review [17].	2017	Nutrition	Systematic review
Nutrition and sarcopenia: A review of the evidence of nutritional influences. Critical reviews in food science and nutrition [18]	2017	Nutrition	Review
Nutritional supplementation for activities of daily living and functional ability of older people in residential facilities: A systematic review [19].	2018	Nutrition	Systematic review
Diet and its relationship to sarcopenia in community dwelling Iranian elderly: A cross sectional study [20] .	2015	Nutrition	Original Article
Relationship between major dietary patterns and sarcopenia among menopausal women [21].	2017	Nutrition	Original Article
Does Magnesium Supplementation Improve Body Composition and Muscle Strength in Middle-Aged Overweight Women? A Double-Blind, Placebo-Controlled, Randomized Clinical Trial [22].	2013	Nutrition	Original Article
Epicatechin Supplementation and Resistance Training-Induced Improvement of Muscle Strength and Circulatory Levels of Plasma Follistatin and Myostatin in Sarcopenic Older Adults [23].	2018	Nutrition	Original Article
Ursolic acid ameliorates aging-metabolic phenotype through promoting of skeletal muscle rejuvenation [24].	2015	Nutrition	Hypotheses
Socioeconomic inequality of sarcopenia in Iran: The Bushehr Elderly Health program [25]	2018	Nutrition	Abstract
Prevalence of food industry and its association with muscle mass, hand grip strength and gait speed among elderly in Tehran [26]	2016	Nutrition	Original Article
Association between nutritional status and sarcopenia in a community dwelling older population: The Bushehr Elderly Health (BEH) Program [27].	2018	Nutrition	Abstract
Vitamin D and Sarcopenia [28].	2017	Nutrition	Mini Review
Biochemical Pathways of Sarcopenia and Their Modulation by Physical exercise: A Narrative Review [29]	2017	Physical activity	Narrative Review
	2017	Physical activity	Original Article

Table 1 (continued)

Title	Published year	Field of study	Type of document
Effect of 8-Week Resistance Training on Hypertrophy, Strength, & Myostatin Concentration in Old and Young Men [30].	2013	Physical activity	Original Article
Relationship between plasma myostatin with muscular volume and muscular maximal strength and it's response to acute resistance exercise in the elderly [31]	2018	Physical activity	Original Article
The Effect of 8-Week Resistance Training and Leucine Supplementation on Protein Synthesis Among Elderly Men With Sarcopenia [32].	2016	Physical activity	Abstract
Cyclic yoga for the prevention of age- related sarcopenia [33]	2017	Physical activity	Original Article
Exercises of Lumbar Stabilizer Muscles, Resistance Training, and Soy Food Consumption: A Comparative Study Between Old and Young Women [34].	2018	Physical activity	Original Article
Mild aerobic training with blood flow restriction increases the hypertrophy index and MuSK in both slow and fast muscles of old rats: Role of PGC-1 alpha [35].	2017	Physical activity	Original Article
Long-term Low-Intensity Endurance Exercise along with Blood-Flow Restriction Improves Muscle Mass and Neuromuscular Junction Compartments in Old Rats [36]	2018	Physical activity	Original Article
The Effect of Fun Physical Activities on Sarcopenia Progression among Elderly Residents in Nursing Homes: a Randomized Controlled Trial [37].	2018	Association of Sarcopenia and Other Diseases	Abstract
Association of sarcopenia and its parameters with type 2 diabetes: The Bushehr Elderly Health Program [38].	2018	Association of Sarcopenia and Other Diseases	Abstract
Association between metabolic syndrome and muscle health, quality and quantity of bone: The Bushehr Elderly Health Program [39].	2017	Association of Sarcopenia and Other Diseases	letter
Prognostic Value of Computed Tomography: Measured Parameters of Body Composition in Primary Operable Gastrointestinal Cancers: Methodologic Issues [40]	2018	Association of Sarcopenia and Other Diseases	Abstract
Association of cognitive impairment and sarcopenia in older people: The Bushehr Elderly Health Program [41]	2018	Association of Sarcopenia and Other Diseases	Abstract
Association of osteosarcopenia and cognitive impairment in a community dwelling older population: The Bushehr Elderly Health (BEH) program [42].	2011	Association of Sarcopenia and Other Diseases	Review
Sarcopenia and diabetes: Pathogenesis and consequences [43].	2014	Association of Sarcopenia and Other Diseases	Original Article
Body composition in adults with newly diagnosed type 2 diabetes: Effects of metformin [44].	2018	Association of Sarcopenia and Other Diseases	Original Article
Prevalence of dynapenic obesity and sarcopenic obesity and their associations with cardiovascular disease risk factors in peritoneal dialysis patients [45].	2018	Association of Sarcopenia and Other Diseases	Original Article
Prevalence of Sarcopenia and Dynapenia and Their Determinants in Iranian Peritoneal Dialysis Patients [46].	2018	Association of Sarcopenia and Other Diseases	Abstract
Association of osteosarcopenia with cardiometabolic factors in older people: The Bushehr Elderly Health Program [47]	2018	Association of Sarcopenia and Other Diseases	Abstract
Association of sarcopenia components and bone parameters with risk of falling in older people: The Bushehr Elderly Health Program [48].	2017	Association of Sarcopenia and Other Diseases	Original Article
Muscle wasting in young patients with dilated cardiomyopathy [49].	2018	Association of Sarcopenia and Other Diseases	Original Article
Introducing the 'Drucebo' effect in statin therapy: a systematic review of studies comparing reported rates of statin-associated muscle symptoms, under blinded and open-label conditions [50].	2018	Association of Sarcopenia and Other Diseases	Review
Prosarcopenic Effects of Statins May Limit Their Effectiveness in Patients with Heart Failure [51].	2017	Association of Sarcopenia and Other Diseases	Review
Curcumin: An effective adjunct in patients with statin-associated muscle symptoms? [52]			

EWGSOP, the International Working Group on Sarcopenia (IWGS) and AWGS definitions were selected. The overall estimate of prevalence was 10% in both genders. The prevalence was higher among not- Asian than Asian individuals in both genders especially, when the BIA was used to measure muscle mass [10].

Pathophysiology of sarcopenia

These studies focus on in-vitro or in-vivo studies such as animal experiment, genetic and cell studies. Several types of molecular mechanisms are involved in the onset and progression of sarcopenia including mitochondrial dysfunction, insulin resistance, inflammatory states and loss of α- motor, and biological changes. A vivid understanding of molecular pathology would provide greater insight into the aging process of muscle mass and could be of great help to early diagnosis, prevention, and intervention of sarcopenia.

Recently, a study was conducted to discover the underlying genes, proteins, and pathways associated with sarcopenia in both males and females. Differentially expressed genes (DEGs) between old and young skeletal muscles was recognized with integrated analysis of microarray datasets and then Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were then conducted to uncover the functions of the DEGs. Moreover, a protein-protein interaction (PPI) network was constructed based on the DEGs. Ribosome biogenesis genes and genes involved in lipid storage are probable players in aging muscles in men and women, respectively. Neurotrophic Receptor Tyrosine Kinase 1 (NTRK1), Cullin 3 (CUL3) and P53 have been identified as significant hub proteins in both genders [11].

In another study, authors identified ursolic acid (UA), a versatile triterpenoid compound, to play a role in regulating aging and age-related diseases. UA decreases aging through the overexpression of anti-aging biomarkers such as sirtuin (SIRT) 1, SIRT6 and peroxisome proliferator-activated receptor-gamma coactivator 1-alpha/beta (PGC-1α/β), Klotho and orexin-A in organs. Some studies have revealed that UA decreased cellular energy charges (ATP and ADP) leads to the induction of mitochondrial biogenesis through SIRT1 and PGC-1α/β overexpression. UA promotes new fiber type generation through satellite cell proliferation and also, augments myoglobin level in skeletal muscle with increasing both PGC-1α and β in the elderly. It becomes apparent that UA might be considered as a potential candidate for the treatment of pathological conditions associated with muscular atrophy and dysfunction, such as sarcopenia [12].

Considering the fact that satellite cells are the main regenerative cell type in muscles, a study found a modified digestion and pre-plating method for the isolation of slow or weak adherent cells for the enrichment of satellite cells. These findings showed that more elaborate assays such as western-blot analysis are needed to be done on Pax7 and some surface markers like CD34. In addition, the pre-plating technique is introduced as a useful procedure for the isolation of satellite cells and it is a way for seeking several therapeutic methods for skeletal muscle-related disorders such as sarcopenia [13].

The findings of another study demonstrated that circulating cell-free nucleic acids (ccfNA) as a novel biomarker have been explored in various body fluids. Elevated cf-DNA levels are identified to play a role in various cancers, metastasis, and recurrence of tumors and other conditions such as cardiovascular diseases, sepsis, and trauma. Also, higher levels of cf-DNAs are associated with systematic inflammation. Considering that sarcopenia is associated with increased inflammation, apoptosis and necrosis mediate skeletal muscle fiber loss in age-related mitochondrial enzymatic abnormalities; it becomes apparent that cell-free nucleic acids may be suggested as a potential biomarker to access the proper therapeutic policy of sarcopenia in personalized medicine and also, to decide the early stage of disease [14].

Sarcopenia screening

Early detection of high-risk individuals susceptible to sarcopenia forms the basis for the primary prevention of sarcopenia progression and reduces its severe outcomes. By using the setting of population screening, the EWGSOP and AWGS have developed diagnostic algorithms. However, the screening of all cases according to these algorithms with DXA, CT and/or MRI incur huge costs and time and seem to be impractical approaches for clinical practice. Recently, some innovative screening tools have been developed to identify old people at higher risk for sarcopenia; however, most of these assessment tools / neither have undergone external validation nor been tested with other ethnic populations [2, 3].

The researchers included a total of 2211 adults aged ≥60 years, participating in stage II of **B**ushehr **E**lderly **H**ealth (**BEH**) program [15]. They randomized the study samples into development and validation sets of models. Firstly, in order to develop a screening model, they selected candidate variables based on previous studies, cost-effectiveness, feasibility and availability of variables to be measured, and the results of bivariate analysis. After the parameter selection procedure, the simple models named **SarSA-Mod** (Sarcopenia Scoring Assessment Models) were developed with high sensitivity and specificity in both genders. The model performance underwent a test in the validation set with 80% accuracy. In this study, SARC-F questionnaire (a five-domain questionnaire) and SarSA-Mod were compared together. SarSA-Mod could identify 80.6% of people with sarcopenia, but the SARC-F questionnaire classified only 16.8% of individuals as screening targets.

This study is the first in its own to develop and validate a sarcopenia screening model for older people in Iran. Since SarSA-Mod is easy to calculate with simple variables, it seems to be a useful screening model for sarcopenia in a primary care setting. [16].

Nutrition

Today, there is a consensus on the essential role of nutrition and physical activity in the prevention and management of sarcopenia. A growing body of literature highlights the importance of proper nutrition, especially protein intake, and physical activity to attenuate age-related effects disabling the proper function of muscle strength and skeletal muscle mass.

So far, some studies are conducted to put light on the mechanisms involved in sarcopenia such as nutrition, taking supplements, and dietary pattern among Iranian sarcopenic people.

In 2017, The IOF-ESCEO Sarcopenia Working Group published a systematic review of the effect of combined exercise and nutrition intervention on muscle mass and muscle function.

The results of 37 RCTs revealed that physical exercise has a positive impact on muscle mass and muscle function in subjects aged ≥65 years. However, any interactive effect of dietary supplementation appears to be limited [17].

The prevention and delay of sarcopenic complications require understanding lifestyle factors and the potential benefits of early interventions. Optimizing diet and nutrition status during life may be an important strategy for preventing sarcopenia and enhancing physical ability in older age [18].

One systematic review conducted in 2017 provided favorable evidence on nutritional supplementation for activities of daily living and functional ability of older individuals in residential facilities. The findings of this review showed that nutritional intervention is effective in improving handgrip strength among old people [19].

Lifestyle modifications such as diet change are appropriate strategies for the prevention of sarcopenia. In 2015, a study demonstrated that elderly individuals (at least 55 years old) in the highest tertile of the Mediterranean dietary pattern had a lower odds ratio for sarcopenia than those in the lowest tertile [OR = 0.42(0.18–0.97)]. In contrast, adherence to the Western dietary pattern and the mixed dietary pattern were not identified to be associated with sarcopenia [20].

Another study among menopausal women provided similar results and suggested that the Mediterranean dietary pattern has a favorable role in the prevention of sarcopenia [21].

Magnesium plays essential roles in muscle function such as electrolyte balance, energy production, transmembrane transport, and muscle contraction and relaxation. However, the daily intake of 250 mg magnesium oxide for 8 weeks does not contribute to greater beneficial effects in handgrip strength and knee extension strength in elderly individuals. To observe any significant improvements in muscle strength, an optimal level of magnesium in muscle is needed, which needs to be further elucidated [22].

Epicatechin, as part of the chemical family of flavonoids, is a supplement with positive effects on muscle, which is found in dark chocolate and green tea. A supervised 8-week randomized controlled trial was conducted on 62 sarcopenic males aimed at investigating the effects of resistance training and Epicatechin supplementation on muscle strength, follistatin and myostatin in sarcopenic older adults. It seems that resistance training along with Epicatechin intake have influential effects on improving muscle growth factors and thence they prevent the sarcopenia progression [23].

Some studies have demonstrated that single molecules such as UA with anabolic effects on skeletal muscles can attenuate aging and prevent age-related diseases such as sarcopenia. UA decreases cellular energy charges (ATP and ADP) and elucidates skeletal muscle rejuvenation as well as satellite cells proliferation and neo-myogenesis. Thence, UA can be considered as a potential candidate for the treatment of pathological conditions associated with muscular atrophy and dysfunction as in the case of sarcopenia [24].

On the other hand, food insecurity and socioeconomic inequality [25] are important factors to sustain muscle mass and function. Old individuals living in a food-insecure status have shown lower mean standard deviation of muscle mass strength and physical performance. Therefore, effective interventions by health sectors need to be done and attention should be given to elderly people so as to improve the quality of life and to avoid the prevalence of food insecurity and other related factors in older people [26].

In stage II of the BEH cohort, sarcopenic people consumed less dietary intakes of total calories, protein, and carbohydrates ($P < 0.001$). Also, a strong inverse association was shown between sarcopenia and minerals such as Calcium, Iron, Magnesium, Phosphorus, Potassium, Zinc, and vitamins (A, E, C, Biotin, B2, B3 and B6). The analysis of the odds ratios for sarcopenia according to daily nutrients intake tertile showed that the risk for sarcopenia decreased as daily minerals and vitamins intake increased from the first to the third tertile, even after correction for confounding variables. Participants in the higher tertiles of daily protein intake, carbohydrate, and total calories revealed a significant reduced risk of sarcopenia**.** These findings suggest a strong inverse association between daily nutrients intake and sarcopenia in older Iranian adults [27].

In addition, vitamin D level is one environmental agent associated with age-related muscle loss. Vitamin D insufficiency is linked with muscle weakness and atrophy of type II fibers and sarcopenia. Considering the vital role of vitamin D for the normal function of different organs, particularly in the elderly, there is a rationality for the supplementation of vitamin D during the aging in order to improve the muscle mass and performance, public's health status and quality of life [28].

Physical activity

To date, Physical activity is perceived to be one of the few effective strategies to improve sarcopenia entailing preventing

outcomes, especially if in combination with appropriate nutritional supplementation.

Physical exercise is typically distinguished in endurance training (ET) and resistance training (RT) in which multiple cellular and molecular processes are involved in both exercise regimens. It seems that physical exercise affects the pathways involved in sarcopenia such as the IGF-1/ Akt/mTOR axis, FoxOs, NF-κB, MAPKs, mitochondrial quality control processes, and apoptosis [29].

A study assessed the effect of 8-week resistance training on muscle mass, strength, and myostatin concentration in old and young men in Ahvaz, Iran. Myostatin is an effective and negative factor to maintain and set the growth of muscle mass. The findings suggested that resistance training is linked with a reduction in myostatin level and an increase in the muscle mass and cross-sectional area [30].

Similar to these findings, another study on12 healthy old male showed that acute RT can decrease the plasma myostatin. This may reduce the prevalence of sarcopenia in the elderly [31]. Also, muscle protein synthesis and muscle strength raised after resistance training with consumption of leucine supplement in elderly men suffering from sarcopenia [32].

Cyclic yoga is introduced as a new exercise that implies positive effects on muscle strength and flexibility on elderly individuals. A study on 46 postmenopausal females demonstrated that regular long- term cyclic yoga (60 min, one time/ week for >5 years) had a positive impact on muscle strength and body fitness [33].

Another study investigated the impact of lumbar stabilizer muscles exercise among elderly female compared to the young ones in response to RT and soy milk supplementation for 10 weeks. Combination exercise-nutrition intervention resulted in muscle improvement, performance, and capabilities of elderly females and reduced the difference between them and young females [34].

In the case of endurance training, Iranian investigators demonstrated that ten weeks of mild aerobic exercise combined with limb blood-flow restriction (BFR) in old rats led to beneficial effects on muscle mass and nicotinic acetylcholine receptors (nAChRs) at the neuromuscular junction [35, 36].

However, due to the specific physical and mental traits of elderly individuals such as fatigue, chronic pain, and a variety of diseases, they may be unable to take full advantage of regular exercise. Therefore, motivation and effective participation of older adults in fun exercise is likely to have positive effects on muscle mass. A randomized controlled trial study revealed that the mean score of the sarcopenia criterion (balance, distance walked, muscle strength) significantly increased in the fun physical exercise group than in the routine exercises group [37].

Association of sarcopenia and other diseases

Sarcopenia is a geriatric disease with significant importance since it is associated with adverse outcomes and other serious conditions such as metabolic disorders [diabetes [38], metabolic syndrome [39], obesity, etc], cancers [40], cardiovascular diseases, nephrology, gastroenterology, psychiatry [41, 42], other geriatric diseases (such as osteoporosis, etc) and death. Some studies have been conducted in Iran shading light on these areas.

Due to the association between sarcopenia and oxidative stress and insulin resistance state, it seems that the pathophysiology of this health condition would be similar to diabetes [43]. On the other hand, metformin as the most commonly used medication in the treatment of diabetes acts by reducing insulin resistance and subsequent hyperinsulinemia. Also, metformin modifies body composition by reducing total fat content and increasing muscle mass. An observational study including 51 newly diagnosed patients with type 2 diabetes demonstrated that 1000 mg metformin two times a day for 6 months can result in better metformin body composition and insulin sensitivity [44].

One study investigated the prevalence of dynapenic (low muscle strength) obesity and sarcopenic obesity and their associations with CVD risk factors in peritoneal dialysis (PD) patients in peritoneal dialysis centers in Tehran, Iran. Due to high protein wasting in PD patients, the prevalence of dynapenic obesity and sarcopenic obesity was low (11.4% and 3.8%, respectively).

Serum hs-CRP and serum soluble intercellular adhesion molecule type 1 (sICAM-1), and lipid profile were significantly higher in PD patients with dynapenic obesity. Kidney failure, bio-incompatibility of PD solutions, chronic inflammation, and increased synthesis of inflammatory cytokines due to the accumulation of various compounds are common complications in PD patients. Additionally, obesity itself leads to an inflammatory state and the simultaneous presence of dynapenia and obesity in dynapenic obese patients, is the main reason for higher serum concentrations in comparison with dynapenic non-obese and non-dynapenic non-obese patients. Moreover, the absorption of glucose from PD solutions and high serum glucose concentration in PD patients leads to higher hepatic synthesis of triglycerides, cholesterol, and LDL-C [45, 46].

The pathophysiology of sarcopenia and osteoporosis shows overlapping interactions and features. Due to these interactions between muscle and bone, individuals suffering from both, sarcopenia and osteopenia/ osteoporosis, were categorized as osteosarcopenic (OS) subjects.

A study in 2018 investigated the association between OS and cardiometabolic risk factors among a population of Iranian elderly adults. Of 2192 Iranian adults aged ≥60 years, participating in the stage II of BEH program, OS was

diagnosed in 340 females and 246 males. The results showed that BMI was strongly associated with OS, so that one unit increase in BMI can reduce the odds of osteosarcopenia by 29% in men and 44% in women. Physical activity had a significant negative association in men but not in women; however, the related point effect was in the same direction. High-fat mass showed the strongest association in both sexes since it can increase the odds of OS by 2.27 folds in men and 5.8 folds in women. The odds of OS associated with diabetes was conferred a 46% increase in women and 43% in men, although this association was not significant among males [47].

Falling is a major health threat in older people owning a prevalence of approximately 30% so that two-thirds of deaths from unintentional injuries are attributed to falls. Sarcopenia is perceived as an important risk factor for falling because of its significant association with poor endurance, physical inactivity, slow gait speed and decreased mobility [48].

Several studies conducted on disease-specific populations, demonstrated that sarcopenia is associated with poor outcomes subsequent to the treatment of other diseases. However, it is not clear whether sarcopenia has been added to these diseases or already existed.

Although muscle loss or sarcopenia is an age-related health issue appearing in elderly times g, subjects suffering chronic diseases such as heart failure, chronic renal failure, and chronic lung disease are more prone to be affected by the disease.

One study concluded that muscle wasting is relatively prevalent in younger patients suffering heart failure particularly in those with lower left ventricular ejection fraction (LVEF) and a higher rate of hospitalization. The inflammatory process secondary to heart failure contributes to an imbalance between anabolism and catabolism and play a role in breaking down proteins and muscle mass loss [49].

The emergence of drug-related symptoms while treating with the given drug, which are not associated with the medicine but with knowledge of these possible adverse effects. Despite the safe an effective role of statins in the prevention of cardiovascular diseases, they have been detected to be associated with some adverse effects such as muscle-related symptoms.

Some of the mechanistic basis of statin-mediated muscle such as decrease of IGF-1, stimulation of the ubiquitin-proteasome system, apoptosis and muscle atrophy are linked with mechanisms of sarcopenia [50, 51]. In the same direction, Curcumin can lessen muscle-related symptoms by blocking the nuclear factor inflammatory pathway, attenuation of muscular atrophy, enhancement of muscle fiber regeneration and antioxidant effects. In addition, Curcumin can enhance the levels of cyclic adenosine monophosphate, which results in an increase in the number of mitochondrial DNA duplicates in skeletal muscle cells. Considering the safety of curcumin proven in clinical practice, it is recommended to use it as a therapy for the treatment of statin-associated muscle symptoms [52].

Summary

In summary, this review has highlighted recent advances in sarcopenia research particularly various aspects of epidemiology, nutrition, physical activity and association of sarcopenia and other diseases. Generally, it has been demonstrated that the presence of sarcopenia can predict adverse outcomes in older adults, but it's not clear that what role each component can play and whether these associations are independent of potential confounders. Finally, in a variety of disease-specific populations, sarcopenia has also been demonstrated to predict disease progression or functional status. However, in most of these studies, the measures of strength or gait speed are not included, so sarcopenia has remained largely unevaluated in these populations as a multicomponent disease. The field of sarcopenia continues to hold considerable promise, and work continues to resolve outstanding concerns in this field.

Compliance with ethical standards

Conflict of interest The authors declared that they have no conflict of interest.

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