

Do we know about dynapenia?

 **Ridvan Sivritepe**,¹  **Ozge Kiran Siyer**,²  **Serhat Mert Tiril**,³  **Sema Ucak Basat**³

¹Department of Internal Medicine, Istanbul Medipol University Faculty of Medicine, Istanbul, Turkiye

²Department of Endocrinology, University of Health Sciences, Haydarpaşa Numune Training and Research Hospital, Istanbul, Turkiye

³Department of Internal Medicine, University of Health Sciences, Umraniye Training and Research Hospital, Istanbul, Turkiye

ABSTRACT

Dynapenia is a condition characterized by decreased muscle strength and function in older adults that is not due to a specific underlying disease or medical condition. Dynapenia is common among older adults and has significant health effects, including functional impairment, disability, increased risk of falls, hospitalization, and death. Oxidative stress, mitochondrial dysfunction and chronic inflammation are involved in the etiopathophysiology of dynapenia. Diagnosis of dynapenia is based on the evaluation of muscle strength and function using methods such as hand grip strength, timed up and go test and short physical performance battery. Management of dynapenia involves a multifaceted approach that includes exercise, nutrition, pharmacological interventions, management of underlying medical conditions, and fall prevention strategies. With appropriate interventions, older adults with dynapenia can improve muscle strength and function, reduce the risk of falls and disability, and maintain their independence and quality of life.

Keywords: Dynapenia; geriatrics; muscle strength.

Cite this article as: Sivritepe R, Kiran Siyer O, Tiril SM, Ucak Basat S. Do we know about dynapenia? North Clin Istanbul 2024;11(6):593–599.

Dynapenia is a medical term used to describe age-related loss of muscle strength or function that is not caused by a specific disease or medical condition. It is a common condition in the geriatric population [1]. Dynapenia can occur due to various factors such as decreased physical activity, hormonal changes, decreased protein synthesis and inflammation. It can lead to functional decline, decreased mobility, increased risk of falling, and loss of independence [1]. Treatment of dynapenia includes exercise and appropriate nutritional interventions [2]. Resistance exercises have been shown to be effective in improving muscle strength and function. A balanced and healthy diet, adequate protein intake, complex carbohydrates and monounsaturated fatty acids consumption are important to maintain muscle mass and function [2]. In this review, we will provide a comprehensive overview of dynapenia, including its definition, prevalence, etiology, mechanism, prevention, and treatment methods.

DEFINITION OF DYNAPENIA

Dynapenia is a progressive medical condition characterized by age-related decline in muscle strength and function in the absence of underlying neurological or muscular disease or medical condition [1]. The term dynapenia was first used by Clark and Manini in 2008 to describe age-related decreases in muscle strength [2]. This condition, which is common in the geriatric population, can lead to functional decline, decreased mobility, increased risk of falls, and loss of independence [1].

EPIDEMIOLOGY OF DYNAPENIA

Dynapenia is a gradually developing progressive condition that is common in older adults [2]. Prevalence estimates vary depending on the definition used and



Received: November 20, 2023

Revised: January 11, 2024

Accepted: January 17, 2024

Online: November 22, 2024

Correspondence: Ridvan SIVRITEPE, MD. Istanbul Medipol Universitesi Tip Fakultesi, İc Hastalıkları Anabilim Dalı, İstanbul, Türkiye.
Tel: +90 216 682 80 00 - 4101 e-mail: dr.ridvansivritepe@gmail.com

Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

the population examined. However, it is generally accepted that the prevalence of dynapenia increases with age and is more common in women than in men [1]. It typically begins in the 4th decade of life and accelerates after age 65. It is estimated to affect approximately 50% of people over the age of 65 and up to 80% of people over the age of 80 [1, 3, 4]. Dynapenia has significant health effects, including decreased physical performance and an increased risk of disability, falls, hospitalization and death [5]. Additionally, dynapenia has been associated with several chronic conditions, including type 2 diabetes mellitus, cardiovascular disease, and chronic obstructive pulmonary disease [6, 7]. Dynapenia has also been shown to be an independent predictor of mortality [8]. Studies report that older adults with low muscle strength or poor muscle function are at higher risk of death than those with higher muscle strength or better muscle function [8, 9]. Given the significant effects of dynapenia on health and healthcare expenditures, efforts to prevent or treat this condition are important [5].

DIAGNOSIS OF DYNAPENIA

There is no consensus on specific diagnostic criteria for dynapenia. Diagnosing dynapenia in general requires a comprehensive evaluation of muscle strength and function, considering the many factors that may contribute to muscle weakness in older adults [1].

The following methods can be used to diagnose dynapenia.

Hand Grip Strength

Hand grip strength is a simple and reliable measure of overall muscle strength that can be easily performed in clinical settings [10]. Decreased hand grip strength is the most prominent feature of dynapenia [1]. There are several different methods that can be used to measure muscle strength, including hand dynamometer, isokinetic dynamometer, and hand grip dynamometer [11]. Muscle strength cut-off values used to define dynapenia vary depending on the population studied and the measurement method used. However, the generally accepted cut-off for hand grip strength in men is <30 kg and in women <20 kg [12]. In addition to hand grip strength, other measures of muscle strength and power, such as knee extension strength and power, can also be used to evaluate dynapenia [1].

Highlight key points

- Dynapenia is a condition ignored by physicians.
- Muscle strength and performance must be evaluated in the diagnosis of dynapenia.
- Management of dynapenia involves a multifaceted approach that includes exercise, nutritional and pharmacological interventions, as well as management of underlying medical conditions.

Timed Up and Go Test

The timed up and go test is a measure of functional mobility and balance that evaluates the time it takes for an individual to get up from a chair, walk a short distance, turn, walk back, and sit down again [13]. Slower times on this test are associated with poorer muscle function and increased risk of falls [14].

Short Physical Performance Battery [SPPB]

The SPPB is a series of tests that evaluate lower extremity function, including standing balance, walking speed, and repeated chair postures [15]. Low scores on the SPPB are associated with poorer muscle function and increased risk of disability and death [16].

Muscle Biopsy

In rare cases, muscle biopsy may be used to evaluate muscle fiber size and composition and identify underlying structural or metabolic abnormalities [2].

Dual-Energy X-Ray Absorptiometry [DXA]

DXA can be used to evaluate muscle mass, an important component of muscle strength and function [17]. However, DXA alone cannot differentiate between sarcopenia and dynapenia.

MECHANISMS OF DYNAPENIA

Dynapenia is a multifactorial process affected by both internal and external factors [18]. Although the exact pathophysiology underlying dynapenia has not been clearly elucidated, we can summarize the multiple underlying conditions as follows.

Neuromuscular Changes

Neuromuscular changes are one of the primary mechanisms of dynapenia [19]. With aging, there is a decrease in the number of skeletal muscle motor units, which leads

to a decrease in muscle mass and strength. In addition, aging is associated with a decrease in muscle fiber size, type II fiber atrophy, and an increase in intermuscular fat and connective tissue [20]. These changes contribute to decreased muscle quality, which can lead to decreased muscle power production. Additionally, changes in the nervous system, especially the neuromuscular junction, which is the connection between nerve and muscle, can also lead to the development of dynapenia [19].

Hormonal Changes

Hormonal changes are also an important mechanism of dynapenia [21]. During the aging process, a decrease in anabolic hormones such as testosterone, growth hormone and insulin-like growth factor-1 occurs [22]. These hormones play a critical role in muscle protein synthesis and repair, and their decrease can contribute to a decrease in muscle mass and strength [21].

Inflammation

Low-grade chronic inflammation is common in older adults and may contribute to the development of dynapenia [23].

Oxidative Stress and Mitochondrial Dysfunction

Oxidative stress and mitochondrial dysfunction are two mechanisms involved in the development of dynapenia [24]. Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species [ROS] and the body's ability to detoxify and repair the resulting damage [25]. ROS can damage cellular components such as proteins, lipids, and DNA, leading to impaired muscle function and increased risk of muscle atrophy. Oxidative stress can also contribute to inflammation and activation of signaling pathways that promote muscle wasting [24]. Mitochondrial dysfunction can lead to decreased ATP production and increased ROS production, which can contribute to oxidative stress, leading to impaired muscle contraction and increased muscle fatigue [24, 25].

Physical Inactivity

Decreasing physical activity with aging is an important external factor contributing to dynapenia [1]. It is well known that physical activity plays a critical role in maintaining muscle mass, strength, and function. Lack of physical activity can lead to muscle disuse and atrophy, which can contribute to decreased muscle strength and power [1, 26].

Medicines

Many medications commonly used in the treatment of chronic diseases can cause dynapenia [27]. Statins, sulfonyleureas, glinides, glucocorticoids, myorelaxants, some antidepressants, antipsychotics and sedatives can cause dynapenia [27–29]. Additionally, opioid group analgesics may also cause this side effect [29].

Nutritional Factors

Nutrition is also an important external factor contributing to dynapenia [30]. Adequate intake of nutrients such as protein, vitamin D and omega-3 fatty acids is important for maintaining muscle mass and function [30–32]. However, with aging, a decrease in appetite and impaired nutrient absorption can also lead to malnutrition, which can lead to the development of dynapenia [30].

In general, all these factors lead to muscle atrophy, disruption of muscle protein synthesis and changes in muscle metabolism, leading to the development of dynapenia. However, more research is needed to clearly understand the underlying mechanisms.

MANAGEMENT OF DYNAPENIA

Management of dynapenia involves a multifaceted approach that includes exercise, nutritional and pharmacological interventions, as well as management of underlying medical conditions [1]. Clinical research on the treatment of dynapenia continues. We can summarize the treatment interventions for dynapenia as follows.

Exercise

Exercise is the most effective way to improve muscle strength and function in older adults with dynapenia [2]. Recent studies have investigated the optimal type, intensity, and duration of exercise interventions for dynapenia. High-intensity interval training and aerobic exercises can be done, but it is suggested that traditional resistance training alone may be more effective in treating dynapenia [33]. Resistance exercise has been shown to increase muscle strength, improve physical function, and reduce the risk of falls in older adults with dynapenia [34]. It is recommended that older adults do resistance exercise that focuses on large muscle groups at least two to three times a week [34]. As resistance exercises, patients with dynapenia may be advised to do squats, lunge movements, chest presses and biceps curls [35]. In addition to resistance exercises, aerobic

exercises such as walking, cycling or swimming can also be done [36]. However, exercise programs should be individualized according to the person's fitness level and functional limitations and should be supervised by a trained professional.

Nutrition

Nutrition is also important in treatment, as adequate protein intake is necessary for the maintenance and repair of muscle tissue [1]. Older adults with dynapenia should be included in a protein-rich diet to support muscle protein synthesis [2]. A balanced diet that includes fruits, vegetables, whole grains, and lean protein sources is important for older adults with dynapenia. Older adults should aim to consume 1.0 to 1.2 grams of protein per kilogram of body weight per day. Good sources of protein include lean meat, fish, poultry, eggs and dairy products [37]. Research is ongoing on the role of certain nutrients, such as omega-3 fatty acids, creatine, and leucine, in muscle health and dynapenia [31]. Emerging evidence suggests that these nutrients may play a role in muscle protein synthesis and muscle function. In addition, since vitamin D is important for muscle function and calcium is necessary for maintaining bone health, these patients should be sure to consume adequate amounts of vitamin D and calcium [38]. Older adults should aim to consume at least 1,000 to 1,200 milligrams of calcium per day and get adequate sunlight exposure or take a vitamin D supplement to ensure adequate vitamin D levels [38].

Pharmacological Interventions

Several medications have been studied for their potential to improve muscle strength and function in older adults with dynapenia, including anabolic steroids, growth hormone, and testosterone [31, 39–41]. However, the use of these medications is controversial, and their effectiveness and safety in older adults are still unclear. Some of the pharmacological interventions being investigated for dynapenia include the following.

Anabolic Steroids

Anabolic steroids are synthetic hormones that stimulate muscle protein synthesis, increasing muscle mass and strength. However, these drugs can have significant side effects, such as liver damage, cardiovascular disease, and mood disorders [39].

Growth Hormone

Growth hormone is a hormone that supports the growth and renewal of cells and tissues, including muscles. However, its use is associated with significant side effects such as insulin resistance, joint pain and increased risk of cancer [40].

Testosterone

Testosterone is a hormone that plays a role in muscle growth and maintenance of muscle mass. Testosterone replacement therapy has been shown to increase muscle mass and strength in older men with low testosterone levels. However, testosterone use has significant side effects such as prostate cancer, sleep apnea and cardiovascular disease [41].

Vitamin D

Vitamin D deficiency has been associated with dynapenia in older adults. Vitamin D supplementation has been shown to improve muscle strength and function, but its effectiveness is still unclear [31].

In general, caution should be exercised in pharmacological interventions for dynapenia. The risks and benefits of these interventions should be carefully evaluated, and non-pharmacological interventions such as exercise and nutrition should be prioritized.

Management of Underlying Medical Conditions

Chronic diseases that contribute to dynapenia, such as chronic obstructive pulmonary disease, heart failure or osteoarthritis, should be treated effectively and the negative effects of these diseases on muscle strength and function should be minimized [42]. Additionally, it is important to consider psychosocial factors that may contribute to dynapenia in older adults. Depression, social isolation, and other mental health problems can contribute to the development of dynapenia by leading to decreased physical activity and muscle function. Addressing these factors through counseling or other interventions may be important for improving muscle function and overall health in older adults [43].

Fall Prevention

Older adults with dynapenia are at increased risk of falling, which can lead to serious consequences. Therefore, fall prevention strategies such as changing the home environment, improving balance and mobility, and reducing medications that increase the risk of falling should be implemented [1, 2].

WHAT AWAITS US IN THE FUTURE IN THE TREATMENT OF DYNAPENIA?

The future of dynapenia treatment is promising, as ongoing research reveals new insights into the mechanisms of dynapenia and identifies potential therapeutic targets. Some of the potential future advances in the treatment of dynapenia include.

Precision Medicine

Precision medicine involves tailoring treatment to an individual's genetic and molecular profile [44]. As our understanding of the genetic and molecular factors that contribute to dynapenia improves, precision medicine may enable more targeted and personalized treatments.

New Therapeutic Targets

Many new drug targets have been investigated for the treatment of dynapenia in recent years. There are ongoing studies such as activators of the AMPK protein, which regulates energy metabolism and mitochondrial function; inhibitors of the ATF4 protein, which plays a role in the regulation of muscle protein synthesis; and modulation of the intestinal microbiome [45].

Stem Cell Therapy

Stem cells have the potential to regenerate damaged or diseased tissues, including muscles. The use of stem cell therapy in the treatment of dynapenia continues to be investigated. However, more studies are needed to determine the safety and effectiveness of this treatment [46].

Gene Therapy

Gene therapy involves delivering therapeutic genes to target tissues to correct genetic defects or improve cellular function. Researchers are investigating the use of gene therapy to treat dynapenia, such as administering myostatin inhibitors or muscle-specific transcription factors to increase muscle growth and function [47].

Biomarkers

Research is still ongoing to develop biomarkers that can accurately diagnose dynapenia and predict the risk of adverse outcomes such as falls, hospitalization, and death [48].

Telemedicine

The COVID-19 pandemic has accelerated the use of telemedicine and remote monitoring in healthcare, including dynapenia management. To improve muscle strength and function in dynapenic patients the feasibility and effectiveness of telemedicine-based interventions are being investigated [49].

Artificial Intelligence

Artificial intelligence has the potential to improve the diagnosis and management of dynapenia by analyzing data from large numbers of patients and identifying pre-dynapenia clinical conditions and markers of the disease. AI-based tools can also help healthcare providers develop personalized exercise and nutrition plans for older adults with dynapenia [50].

Conclusion

Dynapenia is a common condition among older adults, characterized by decreased muscle strength without significant loss of muscle mass. The underlying mechanism of dynapenia is not fully understood but is believed to be related to changes in neuromuscular junction and muscle fiber composition. It is a rapidly developing field with research on diagnosing, treating, and improving the outcomes of dynapenia. The future of dynapenia treatment is promising as ongoing research reveals new information regarding this condition and identifies potential therapeutic targets. Advances in precision medicine, stem cell therapy, gene therapy, new drug targets, and artificial intelligence may lead to more effective and personalized treatments for dynapenia in the future.

Although dynapenia is common among older adults, it is not an inevitable part of aging. With proper management, older adults can maintain muscle strength and function into later years and maintain their independence and quality of life.

Authorship Contributions: Concept – RS; Design – RS, SMT; Supervision – RS, SUB; Fundings – RS, OKS; Materials – RS, OKS; Data collection and/or processing – RS; Analysis and/or interpretation – RS, SMT; Literature review – RS, OKS; Writing – RS, SMT; Critical review – RS, SUB.

Conflict of Interest: No conflict of interest was declared by the authors.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

REFERENCES

- Clark BC, Manini TM. What is dynapenia? *Nutrition* 2012;28:495–503. [CrossRef]
- Clark BC, Manini TM. Sarcopenia \neq dynapenia. *J Gerontol A Biol Sci Med Sci* 2008;63:829–34. [CrossRef]
- As'habi A, Najafi I, Tabibi H, Hedayati M. Prevalence of sarcopenia and dynapenia and their determinants in Iranian peritoneal dialysis patients. *Iran J Kidney Dis* 2018;12:53–60.
- Rodríguez-García WD, García-Castañeda L, Vaquero-Barbosa N, Mendoza-Núñez VM, Orea-Tejeda A, Perkisas S, et al. Prevalence of dynapenia and presarcopenia related to aging in adult community-dwelling Mexicans using two different cut-off points. *Eur Geriatr Med* 2018;9:219–25. [CrossRef]
- Clark BC, Manini TM. Functional consequences of sarcopenia and dynapenia in the elderly. *Curr Opin Clin Nutr Metab Care* 2010;13:271–6. [CrossRef]
- Choi YA, Lee JS, Kim YH. Association between physical activity and dynapenia in older adults with COPD: a nationwide survey. *Sci Rep* 2022;12:7480. [CrossRef]
- Leahy S, Cassarino M, O'Connell MD, Glynn L, Galvin R. Dynapenic obesity and its association with health outcomes in older adult populations: protocol for a systematic review. *BMJ Open* 2019;9:e027728. [CrossRef]
- Rossi AP, Fantin F, Caliarì C, Zoico E, Mazzali G, Zanardo M, et al. Dynapenic abdominal obesity as predictor of mortality and disability worsening in older adults: a 10-year prospective study. *Clin Nutr* 2016;35:199–204. [CrossRef]
- Silva RR, Galvão LL, Meneguci J, Santos DAT, Virtuoso Júnior JS, Tribess S. Dynapenia in all-cause mortality and its relationship with sedentary behavior in community-dwelling older adults. *Sports Med Health Sci* 2022;4:253–9. [CrossRef]
- Bohannon RW. Grip strength: an indispensable biomarker for older adults. *Clin Interv Aging* 2019;14:1681–91. [CrossRef]
- Benfica PDA, Aguiar LT, Brito SAF, Bernardino LHN, Teixeira-Salmela LF, Faria CDCM. Reference values for muscle strength: a systematic review with a descriptive meta-analysis. *Braz J Phys Ther* 2018;22:355–69. Erratum in: *Braz J Phys Ther* 2019;23:549. [CrossRef]
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al; 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;39:412–23. [CrossRef]
- Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991;39:142–8. [CrossRef]
- Sanders DB, Guptill JT, Aleš KL, Hobson-Webb LD, Jacobus DP, Mahmood R, et al. Reliability of the triple-timed up-and-go test. *Muscle Nerve* 2018;57:136–9. [CrossRef]
- Treacy D, Hassett L. The short physical performance battery. *J Physiother* 2018;64:61. [CrossRef]
- Lauretani F, Ticinesi A, Gionti L, Prati B, Nouvenne A, Tana C, et al. Short-Physical Performance Battery (SPPB) score is associated with falls in older outpatients. *Aging Clin Exp Res* 2019;31:1435–42. [CrossRef]
- DeVita MV, Stall SH. Dual-energy X-ray absorptiometry: a review. *J Ren Nutr* 1999;9:178–81. [CrossRef]
- Tieland M, Trouwborst I, Clark BC. Skeletal muscle performance and ageing. *J Cachexia Sarcopenia Muscle* 2018;9:3–19. [CrossRef]
- Clark BC. Neuromuscular changes with aging and sarcopenia. *J Frailty Aging* 2019;8:7–9.
- Nilwik R, Snijders T, Leenders M, Groen BB, van Kranenburg J, Verdijk LB, et al. The decline in skeletal muscle mass with aging is mainly attributed to a reduction in type II muscle fiber size. *Exp Gerontol* 2013;48:492–8. [CrossRef]
- Gungor O, Ulu S, Hasbal NB, Anker SD, Kalantar-Zadeh K. Effects of hormonal changes on sarcopenia in chronic kidney disease: where are we now and what can we do? *J Cachexia Sarcopenia Muscle* 2021;12:1380–92. [CrossRef]
- Gupta P, Kumar S. Sarcopenia and endocrine ageing: are they related? *Cureus* 2022;14:e28787. [CrossRef]
- Ribeiro JC, Duarte JG, Gomes GAO, Costa-Guarisco LP, de Jesus ITM, Nascimento CMC, et al. Associations between inflammatory markers and muscle strength in older adults according to the presence or absence of obesity. *Exp Gerontol* 2021;151:111409. [CrossRef]
- Diaz-Morales N, Rovira-Llopió S, Escribano-Lopez I, Bañuls C, Lopez-Domenech S, Falcón R, et al. Role of oxidative stress and mitochondrial dysfunction in skeletal muscle in type 2 diabetic patients. *Curr Pharm Des* 2016;22:2650–6. [CrossRef]
- Chainy GBN, Sahoo DK. Hormones and oxidative stress: an overview. *Free Radic Res* 2020;54:1–26. [CrossRef]
- Rezuş E, Burlui A, Cardoneanu A, Rezuş C, Codreanu C, Pârvu M, et al. Inactivity and skeletal muscle metabolism: a vicious cycle in old age. *Int J Mol Sci* 2022;21:592. [CrossRef]
- Campins L, Camps M, Riera A, Pleguezuelo E, Yebenes JC, Serra-Prat M. Oral drugs related with muscle wasting and sarcopenia. A review. *Pharmacology* 2017;99:1–8. [CrossRef]
- Gupta A, Gupta Y. Glucocorticoid-induced myopathy: pathophysiology, diagnosis, and treatment. *Indian J Endocrinol Metab* 2013;17:913–6. [CrossRef]
- Sandvik MK, Watne LO, Brugård A, Wang-Hansen MS, Kersten H. Association between psychotropic drug use and handgrip strength in older hospitalized patients. *Eur Geriatr Med* 2021;12:1213–20. [CrossRef]
- Treuil M, Mahmutovic M, Di Patrizio P, Nguyen-Thi PL, Quilliot D. Assessment of dynapenia and undernutrition in primary care, a systematic screening study in community medicine. *Clin Nutr ESPEN* 2023;57:561–8. [CrossRef]
- Sivritepe R. The relationship between dynapenia and vitamin D level in geriatric women with type 2 diabetes mellitus. *North Clin Istanbul* 2022;9:64–73. [CrossRef]
- Tessier AJ, Chevalier S. An update on protein, leucine, omega-3 fatty acids, and vitamin D in the prevention and treatment of sarcopenia and functional decline. *Nutrients* 2018;10:1099. [CrossRef]
- de Mello RGB, Dalla Corte RR, Gioscia J, Moriguchi EH. Effects of physical exercise programs on sarcopenia management, dynapenia, and physical performance in the elderly: a systematic review of randomized clinical trials. *J Aging Res* 2019;2019:1959486. [CrossRef]
- Law TD, Clark LA, Clark BC. Resistance exercise to prevent and manage sarcopenia and dynapenia. *Annu Rev Gerontol Geriatr* 2016;36:205–28. [CrossRef]
- Vincent KR, Braith RW, Feldman RA, Magyari PM, Cutler RB, Persin SA, et al. Resistance exercise and physical performance in adults aged 60 to 83. *J Am Geriatr Soc* 2002;50:1100–7. [CrossRef]
- Crowley E, Harrison AJ, Lyons M. The impact of resistance training on swimming performance: a systematic review. *Sports Med* 2017;47:2285–307. [CrossRef]
- Deutz NE, Bauer JM, Barazzoni R, Biolo G, Boirie Y, Bosy-Westphal A, et al. Protein intake and exercise for optimal muscle function with

- aging: recommendations from the ESPEN Expert Group. *Clin Nutr* 2014;33:929–36. [\[CrossRef\]](#)
38. Halfon M, Phan O, Teta D. Vitamin D: a review on its effects on muscle strength, the risk of fall, and frailty. *Biomed Res Int* 2015;2015:953241. [\[CrossRef\]](#)
 39. Ganesan K, Rahman S, Zito PM. Anabolic steroids. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2023.
 40. Olarescu NC, Gunawardane K, Hansen TK, Møller N, Jørgensen JOL. Normal physiology of growth hormone in adults. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, eds. *Endotext*. South Dartmouth, MA: MDText.com, Inc.; 2000.
 41. Barbonetti A, D'Andrea S, Francavilla S. Testosterone replacement therapy. *Andrology* 2020;8:1551–66. [\[CrossRef\]](#)
 42. Komatsu TR, Borim FS, Neri AL, Corona LP. Association of dynapenia, obesity and chronic diseases with all-cause mortality of community-dwelling older adults: a path analysis. *Geriatr Gerontol Int* 2019;19:108–12. [\[CrossRef\]](#)
 43. Venant V, Pouget M, Lahaye C, Gentes E, Pereira B, Lambert C, et al. Depression severity as a risk factor of sarcopenic obesity in morbidly obese patients. *J Nutr Health Aging* 2019;23:761–7. [\[CrossRef\]](#)
 44. König IR, Fuchs O, Hansen G, von Mutius E, Kopp MV. What is precision medicine? *Eur Respir J* 2017;50:1700391. [\[CrossRef\]](#)
 45. Kjøbsted R, Hingst JR, Fentz J, Foretz M, Sanz MN, Pehmøller C, et al. AMPK in skeletal muscle function and metabolism. *FASEB J* 2018;32:1741–77. [\[CrossRef\]](#)
 46. Wong RSY, Cheong SK. Therapeutic potential of mesenchymal stem cells and their derivatives in sarcopenia. *Malays J Pathol* 2022;44:429–42.
 47. Maricelli JW, Bishaw YM, Wang B, Du M, Rodgers BD. Systemic SMAD7 gene therapy increases striated muscle mass and enhances exercise capacity in a dose-dependent manner. *Hum Gene Ther* 2018;29:390–9. [\[CrossRef\]](#)
 48. Kamper RS, Schultz M, Hansen SK, Andersen H, Ekman A, Nygaard H, et al. Biomarkers for length of hospital stay, changes in muscle mass, strength and physical function in older medical patients: protocol for the Copenhagen PROTECT study—a prospective cohort study. *BMJ Open* 2020;10:e042786. [\[CrossRef\]](#)
 49. An J, Ryu HK, Lyu SJ, Yi HJ, Lee BH. Effects of preoperative telerehabilitation on muscle strength, range of motion, and functional outcomes in candidates for total knee arthroplasty: a single-blind randomized controlled trial. *Int J Environ Res Public Health* 2021;18:6071. [\[CrossRef\]](#)
 50. Wei M, Meng D, Guo H, He S, Tian Z, Wang Z, et al. Hybrid exercise program for sarcopenia in older adults: the effectiveness of explainable artificial intelligence-based clinical assistance in assessing skeletal muscle area. *Int J Environ Res Public Health* 2022;19:9952. [\[CrossRef\]](#)