*Agata Kusz-Rynkun, Iga Żarnowska

Sarcopenia and osteoporosis – cofactors of increased risk of falls and bone fractures

Sarkopenia i osteoporoza – czynniki zwiększonego ryzyka upadków i złamań kostnych

Department of Geriatrics, Internal Medicine and Metabolic Bone Diseases, Centre of Postgraduate Medical Education, Warsaw
Head of Department: Associate Professor Marek Tałałaj, MD, PhD

Keywords

falls, bone fractures, sarcopenia, osteoporosis, elderly age

Słowa kluczowe

upadki, złamania, sarkopenia, osteoporoza, podeszły wiek

Summary

With aging, there is an increase in incidence of falls and, in consequence, of bone fractures. Fractures in elderly persons may cause not only pain and temporal immobilization but also permanent mobility deficiency, functional deterioration and increased mortality. Following hip fracture approximately half of the people who had managed to move independently prior to the injury do not regain their full mobility and 1/3 remain dependent of environment with the high risk of institutionalization. Reduced mass and strength of bone in osteoporosis and skeletal muscles in sarcopenia play a main role in the age-related incidence of fragility fractures. Both sarcopenia and osteoporosis have recently been noted for their relationship with locomotive syndrome and are increasingly frequent among older people. Although the reduction of muscle tissue can be partially explained by reduced physical activity with age, sarcopenia also involves metabolic abnormalities. Muscle strength plays an important role in reducing the risk of falling and thus the risk of fractures.

Streszczenie

Wraz ze starzeniem się wzrasta ryzyko upadków, a w konsekwencji także ryzyko złamań kości. Skutkiem złamań u starszych osób może być nie tylko ból, ale także okresowe lub stałe unieruchomienie, pogorszenie funkcjonalne oraz wzrost śmiertelności. Po złamaniu biodra około połowa osób, które poruszały się samodzielnie przed urazem, nie wraca do pełnej sprawności, a 1/3 z nich pozostaje uzależniona od pomocy otoczenia lub wymaga instytucjonalizacji. Redukcja masy i wytrzymałości kości w osteoporozie oraz masy i siły mięśniowej w sarkopenii odgrywają główną rolę w złamaniach niskoenergetycznych związanych z wiekiem. W ostatnich latach zwraca się uwagę na związek osteoporozy i sarkopenii z zespołem lokomocyjnym wśród starszych pacjentów. Chociaż redukcję masy mięśniowej u seniorów można częściowo tłumaczyć zmniejszeniem aktywności fizycznej, to należy pamiętać, że w przebiegu sarkopenii obserwowane są także zaburzenia metaboliczne. Należy podkreślić, że siła mięśniowa odgrywa ważną rolę w redukcji ryzyka upadków i w konsekwencji ryzyka złamań kości.

Conflict of interest
Konflikt interesów

None
Brak konfliktu interesów

Address/adres:

*Agata Kusz-Rynkun
Department of Geriatrics,
Internal Medicine and Metabolic Bone Diseases
Centre of Postgraduate Medical Education
ul. Czerniakowska 231, 00-416 Warszawa
tel. +48 (22) 584-11-47
kl.geriatrii@szpital-orlowskiego.pl

INTRODUCTION

Ageing results in the progressive and parallel loss of bone tissue (osteopenia) and skeletal muscle (sarcopenia) with profound consequences for quality of life. Age-associated sarcopenia results in reduced endurance, poor balance, and reduced mobility that predispose elderly individuals to falls, which frequently result in skeletal fractures because of concomitant osteoporosis. A better understanding of the mechanisms underlying the parallel involution of these tissues is critical to developing new and more effective means to prevent both osteoporosis and sarcopenia in our growing older population (1).

RISK OF FALLS AND BONE FRACTURES

With aging, an increased incidence of falls and, in consequence, of bone fractures is observed. It is caused by two main determinants. The first is the weakness of bones which are unable to resist mechanical loading due to loss of tissue contained within the periosteal envelope and deterioration of the cortical and trabecular bone microstructure – specified in the

definition of osteoporosis (2, 3). The second is reduced muscle mass and strength (i.e. sarcopenia) that result in postural instability, increased risk of falling, and higher incidence of fractures. Fracture risk is additionally intensified by hip subcutaneous fat pad thinness which increases mechanical impact exerted on already fragile bone structure (3).

Falls among elderly people are known as one of the great geriatric problems that have major individual and social consequences. According to United States Department of Health and Human Services falls of elderly are the main reason of injuries and the second main reason of death caused by unintended injuries in this age group (4). Falls are undesirable consequences of sarcopenia and the frailty syndrome that includes sarcopenia together with reduced muscle strength, lower physical activity and functional limitations. Approximately 5-6% of falls result in bone fractures followed by dysfunction, forcible immobilization, and complications such as infections, thromboembolism, exacerbating of chronic diseases especially of cardiovascular and pulmonary systems, decubitus, ulcers and disturbances of urinary system (5).

The elements connecting the higher risk of falling and skeletal fractures in elderly are contained in the term “sarcoosteoporosis”. The fractures caused by falls are low-energy fractures. The results of the Study of Osteoporotic Fractures that included over 9,000 white women aged 65 years or more, that have been observed for 4 years, confirmed positive correlation between the frequency of falls and the occurrence of fractures. Among women who experienced at least one fall the nonvertebral fractures as well as fractures of the proximal femur and distal forearm occurred nearly twice as often compared to women who did not fall during the observation (6).

Fractures in elderly persons cause not only pain and temporal immobilization but may also result in permanent mobility deficiency, functional deterioration and increased mortality. That refers primarily to the fractures of proximal femur, spine and distal forearm. It was estimated that following hip fracture approximately half of the people who had managed to move independently prior to the injury do not regain their full mobility and 1/3 remain dependent of environment with the high risk of institutionalization (5).

SARCOPENIA

Many studies have focused on sarcopenia since Irwin Rosenberg first identified the condition in 1989 but a precise definition, measurement methods and index of sarcopenia have yet to be established (7, 8). In recent studies, sarcopenia is defined as a systemic continuous decrease in skeletal muscle strength and mass so that the diagnosis of sarcopenia has to be confirmed by measurements of muscle mass and assessment of functional muscle strength (3).

Sarcopenia is diagnosed in 30% of individuals aged 60 years or older and in more than 50% of those aged at least 80 years (9). It is caused by imbalance between protein synthesis and degradation. Increased, with age, fatty infiltration of skeletal muscles (myosteatosis) reduces muscle strength and increases the propensity to falls as well as the risk of fractures (3, 10).

Sarcopenia is considered to be one of the major factors responsible for functional limitations and motor dependency in elderly persons (11). This relationship was originally thought to be explained by an increased risk of falling in sarcopenic patients (12). Since a definition of sarcopenia encompasses muscle size, strength and physical performance, the relationships between each of these parameters and bone size, density and strength were investigated to interrogate this hypothesis further in participants from the Hertfordshire Cohort Study (HCS). In years 2004-2005, 437 men and 447 women from the geographical area of East Hertfordshire were invited for a follow up study. Of these, 322 men (65%) and 320 women (68%) agreed to participate. A detailed questionnaire was administered to obtain information on lifestyle, medical history, cigarette smoking and alcohol consumption. Details regarding physical activity, dietary calcium intake, socioeconomic status and, in women, years since menopause and use of estrogen replacement therapy had already been obtained from a questionnaire which was administered by trained nurses when the participants were initially recruited into the HCS (1998-2003). Physical activity was calculated as a standardized score ranging from 0 to 100 derived from frequency of gardening, housework, climbing stairs and carrying loads in a typical week. Higher scores indicated greater levels of activity. Dietary calcium intake was assessed using a food frequency questionnaire. Socioeconomic status was determined using own current or most recent occupation of the participant in men and single women, and of the husband in ever-married women based on the OPCS Standard Occupational Classification scheme for occupation and social class. The Hertfordshire Cohort Study has shown that muscle size is strongly associated with bone size and bone strength in both men and women and that these relationships remain robust after rigorous adjustment (12).

It was shown that muscle mass decreased by 3-8% per decade just after the age of 30 years, and after the age of 60 years the rate of muscle loss has only accelerated (13). The loss of muscle mass and strength was found to be the result of progressive atrophy, loss of muscle fibers, reduced motor neuron input and impaired function of the contractile apparatus within each fiber. Reduction in quality of muscle units and motor neuron number was reported to contribute to the significant progressive decline in physical capacity with aging (14).

Although the reduction of muscle tissue can be partially explained by reduced physical activity in elderly persons, sarcopenia also involves metabolic abnormalities, including reduced insulin sensitivity, fat and connective tissue infiltration, impaired resistance

against oxidative stress, reduced hormone levels, and decreased mitochondrial activity that further confound muscle function (9, 10, 15, 16).

Genetic, developmental, endocrine and lifestyle factors, such as physical activity, exert significant effects on both muscles and bones. Several mechanisms were also determined to play a role in the age-related decrease in muscle mass and strength, including altered hormonal status, inflammatory processes, reduced physical activity and malnutrition, most often resulting from low dietary intake of energy and protein (3, 9).

The gender difference in the relationship between bone and muscle are explained by gender specific effects of sex hormones. In men, changes to bone and muscle are controlled by the levels of testosterone and IGF-1. Age related reduction in serum testosterone and IGF-1 concentrations may lead to a decrease in both mass and strength of muscles and bones. In women the absolute level and rate of decline of serum testosterone concentration are much lower and muscle mass can be relatively preserved. On the other hand mechanical strain and estrogens were found to share a common pathway involving activation of estrogen receptor α (ERα). A decline in ERα number with menopause results in reduced ability of mechanical loading to induce an osteogenic response of bone tissue. Resetting of mechanostat due to estrogen deficiency may explain the uncoupling of muscle mass and bone mineral density (BMD) in postmenopausal women, while in older men correlations between muscle mass and BMD tend to be preserved. Numerous studies confirm, however, that low muscle mass is accompanied by low BMD values (8, 17-19).

The results of the Sarcopenia and Hip Fracture study, that included 23 women, observed for 12 months, revealed that sarcopenia was a frequent phenomenon and occurred in 65% of elderly women at mean age of 83 years. It was also found that Bland-Altman plots demonstrated an underestimation by the lean body weight equation compared to fat free mass determined with dual energy x-ray absorptiometry. The degree of bias may not be clinically important although further studies of larger heterogeneous cohorts are needed to investigate and potentially improve the accuracy of this predictive equation in larger clinical cohorts (20).

The load to the skeleton exerted by muscles and fat tissue was shown to increase the number and activity of osteoblasts and stimulate new bone formation (21). In both fat and muscle tissues androgens are aromatized to estrogens that play significant protective role in postmenopausal women (22). The association between greater muscle mass and greater BMD is likely to be determined by multiple factors including common nutrition, life style and genes influencing body size (23, 24). On the other hand changes in body composition observed in elderly persons include the accumulation of fat in the bone marrow as well as between and within muscle fibers. The entity referred to as "sarcopenic obesity" was found to accompany muscle loss in obese elderly people and has been associated with functional disability (16).

The mechanostat hypothesis suggests that bones adapt to mechanical loads generated by voluntary mechanical usage, including that of muscle contraction, implying the direct role of muscles in bone structure and strength (25). Aging is often complicated by long-term periods of bed rest or inactivity due to injury, such as a hip fracture, which can result in profound losses of both bone and muscle in parallel (26). Even in healthy older patients, 10 days of bed rest can produce loss of muscle strength of over 13% along with loss of aerobic capacity (27). Bed rest may also have deleterious effects on postural support that could predispose to joint damages and/or falls (28).

The risk of fragility fractures increases exponentially with aging. Reduced mass and strength of bones in osteoporotic patients and of skeletal muscles in individuals with sarcopenia play a key role in the high, age-related incidence of fragility fractures (3). Diminished mass and strength of skeletal muscles is also considered as one of the most important factors implicated in the progression of disability with aging (3, 27, 29).

Both osteoporosis and sarcopenia have common causal factors, such as low levels of vitamin D, testosterone, estrogen, and insulin, as well as reduced calorie intake and malnutrition (8). The nutrients that have the greatest physiological impact on the competence of skeletal and muscular systems are calcium, vitamin D, inorganic phosphate, and proteins (3). Prolonged vitamin D insufficiency in the elderly is associated with reductions in both bone mineral density and type 2 muscle fibers resulting in skeletal fragility and reduced muscle strength leading to increased risk of falls and fractures (3).

ROLE OF DIET

A diet can be rich in energy but nutrient poor. This type of consumption can result in nutrient deficits even in obese persons, as observed among children and elderly people in developed countries, such as the United States (3, 30, 31). Numerous clinical studies reported the relations between dairy product consumption and bone variables including BMD, serum concentration or urine excretion of bone turnover markers, and incidence of fractures in adult subjects (3, 32). It was reported that insufficiency in the 4 nutrients: calcium, phosphate, vitamin D, and proteins can contribute to a reduction in both mass and strength of bone and skeletal muscles (9). The decrease in protein intake was shown to result in a decline in the circulating level of insulin-like growth factor 1 (IGF-1) – a significant bone anabolic factor (3, 33). A large prospective study, including persons at risk of experiencing hip fracture, showed that increased protein intake resulted in the reduction in the rate of osteoporotic fractures, that may be ascribed, at least in part, to a beneficial effect on neuromuscular functions reducing the risk and consequences of falling (3).

Selective deficiency in protein intake was documented to have severe consequences on bone integrity, with reduced bone formation and increased bone resorption leading to increased skeletal fragility. Inadequate protein intake was found to affect the neuromuscular system, impairing coordination of movements and reducing muscle mass and strength. Protein-derived essential amino acids, that are important component of bone matrix and muscle fibers were shown to stimulate the production of IGF-1. Low protein intake was found to be associated with low serum IGF-1 concentration, osteoporosis and sarcopenia. The serum level of IGF-1 was shown to decrease with aging and to be associated with an increased risk of osteoporotic fractures (3).

Muscle weakness, especially of proximal muscles of lower extremities, is considered a clinical feature of severe vitamin D deficiency. It is manifested with difficulty in walking, standing up from a chair, and/or climbing stairs (16). Several studies reported an association between low vitamin D status and reduced muscle performance and postural instability. The reduction in fragility fractures observed with vitamin D supplementation in the elderly can be ascribed not only to its preventive effect on bone loss but also to the reduction in the risk of falling (3). Recent interventional studies showed beneficial effects of vitamin D fortified dairy products on bone remodeling and/or bone mineral density in postmenopausal women and in the elderly (34).

ROLE OF PHISICAL ACTIVITY

Sarcopenia can be counteracted by adequate interventions, particularly by the combination of adequate nutritional intake and exercise training. Improved intake of proteins can prevent or at least reduce the progression of muscle loss (35).

The regular resistance exercises together with habitual ingestion of adequate amounts of dietary protein in older people are able to slow down the progression of the age-related loss of skeletal muscle mass and function as well as improve their balance and physical functioning capabilities (3).

Physical activity, particularly weight-bearing exercise, can provide the mechanical stimuli important for the maintenance and improvement of bone health, whereas physical inactivity is implicated in bone loss. Both aerobic and resistance training exercise can provide weight-bearing stimulus to bone but resistance training may have a more profound site specific effect than aerobic exercise. High-intensity resistance training, in contrast to pharmacological and nutritional approaches, exerts additional benefit in elderly people influencing multiple risk factors for osteoporosis, such as strength and balance (36). Long-term exercise has been associated with a higher skeletal mass in elderly people. A randomized study in postmenopausal women, aged 45-65 years has shown a small but significant beneficial effect of fast walking (3 × 30 min/week) and physical training (twice weekly) continued over 1 year on total hip BMD (37).

CONCLUSIONS

There is an increased incidence of falls and bone fractures observed with aging. Falls among elderly are one of the great geriatric problems that have major individual and social consequences. Reduced mass and strength of bones in osteoporotic patients and of skeletal muscles in individuals with sarcopenia play a key role in the high, age-related incidence of fragility fractures with profound consequences for quality of life. Diminished mass and strength of skeletal muscles is considered as one of the most important factors implicated in the progression of disability with aging. At present, it seems reasonable to recommend avoidance of a sedentary lifestyle and participation in the moderate exercise program for individuals seeking to prevent or treat osteoporosis. Significant part of the expected benefit should be the result of increased muscle strength, coordination, and flexibility (38).

BIBLIOGRAPHY

1. DiGirolamo DJ, Kiel DP, Karyn A: Bone and skeletal muscle: Neighbors with close ties. J Bone Miner Res 2013; 28(7): 1509-1518.
2. Bischoff-Ferrari HA, Dietrich T, Orav EJ et al.: Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged ≥ 60 years. Am J Clin Nutrit 2004; 80(3): 752-758.
3. Sanders KM, Scott D, Ebeling PR: Vitamin D deficiency and its role in muscle--bone interactions in the elderly. Curr Osteoporos Rep 2014; 12: 74-81.
4. Skalska A, Fedyk-Łukasik M: Upadki jako przyczyna złamań i zwiększonej śmiertelności. [W:] Czerwiński E (red.): Osteoporoza – problem interdyscyplinarny. PZWL, Warszawa 2015: 173-183.
5. Stevens JA, Corso PS, Finkelstein EA et al.: The costs of fatal and nonfatal falls among older adults. Inj Prev 2006 Oct; 12(5): 290-295.
6. Schwartz AV, Nevitt MC, Brown BW Jr, Kelsey JL: Increased falling as a risk factor for fracture among older women. Am J Epidemiol 2005; 161: 180-185.
7. Rosenberg IH: Epidemiologic and methodologic problems in determining nutritional status of older persons. Am J Clin Nutr 1989; 50: 1231-1233.
8. Kim S, Won CW, Kim BS et al.: The association between the low muscle mass and osteoporosis in elderly Korean people. J Korean Med Sci 2014; 29: 995-1000.
9. Van den Berghe G, Van Roosbroeck D, Vanhove P et al.: Bone turnover in prolonged critical illness: effect of vitamin D. J Clin Endocrinol Metab 2003; 88(10): 4623-4632.
10. Phillips T, Leeuwenburgh C: Muscle fiber specific apoptosis and TNF-alpha signaling in sarcopenia are attenuated by life-long calorie restriction. FASEB J 2005; 19(6): 668-670.
11. Tarantino U, Baldi J, Celi M et al.: Osteoporosis and sarcopenia: the connections. Aging Clin Exp Res 2013; 25: 93-97.
12. Edwards MH, Gregson CL, Patel HP et al.: Muscle size, strength and physical performance and their associations with bone structure in the Hertfordshire Cohort Study. Bone Miner Res 2013; 28(11): 2295-2304.
13. Binkley N: Is vitamin D the fountain of youth? Endocr Pract 2009; 15(6): 590-596.
14. Visser M, Pahor M, Taaffe DR et al.: Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC study. J Gerontol 2002; 57(5): 326-332.
15. Scott W, Stevens J, Binder-Macleod SA: Human skeletal muscle fiber type classifications. Phys Ther 2001; 81(11): 1810-1816.
16. Bonjour J-P, Kraenzlin M, Levasseur R et al.: Dairy in adulthood: From foods to nutrient interactions on bone and skeletal muscle health. J Am Coll Nutr 2013; 32(4): 251-263.

17. Zofková I: Hormonal aspects of the muscle-bone unit. Physiol Res 2008; 57: 159-169.
18. Macdonald H, Kontulainen S, Petit M et al.: Bone strength and its determinants in pre- and early pubertal boys and girls. Bone 2006; 39: 598-608.
19. Lang TF: The bone-muscle relationship in men and women. J Osteoporos 2011; 11: 702-735.
20. Mitchell SJ, Hilmer SN, Kirkpatrick CM et al.: Estimation of lean body weight in older women with hip fracture. J Nutr Health Aging 2012; 16(2): 188-192.
21. Rochefort GY, Pallu S, Benhamou CL: Osteocyte: the unrecognized side of bone tissue. Osteoporos Int 2010; 21: 1457-1469.
22. Matsumine H, Hirato K, Yanaihara T et al.: Aromatization by skeletal muscle. J Clin Endocrinol Metab 1986; 63: 717-720.
23. Coin A, Perissinotto E, Enzi G et al.: Predictors of low bone mineral density in the elderly: the role of dietary intake, nutritional status and sarcopenia. Eur J Clin Nutr 2008; 62: 802-809.
24. Seeman E, Hopper JL, Young NR et al.: Do genetic factors explain associations between muscle strength, lean mass, and bone density? A twin study. Am J Physiol 1996; 270: 320-327.
25. Marcus R: Relationship of age-related decreases in muscle mass and strength to skeletal status. J Gerontol 1995; 50: 86-87.
26. Ferrucci L, Penninx B, Volpato S et al.: Change in muscle strength explains accelerated decline of physical function in older women with high interleukin-6 serum levels. J Am Geriat Soc 2002; 50(12): 1947-1954.
27. Schleithoff SS, Zittermann A, Tenderich G et al.: Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind, randomized, placebo-controlled trial. Am J Clin Nutrit 2006; 83(4): 754-759.
28. Ebeling P, Sandgren M, DiMagno E et al.: Evidence of an age-related decrease in intestinal responsiveness to vitamin D: relationship between serum 1, 25-dihydroxyvitamin D_3 and intestinal vitamin D receptor concentrations in normal women. J Clin Endocrinol Metabol 1992; 75(1): 176-182.
29. Peake J, Della Gatta P, Cameron-Smith D: Aging and its effects on inflammation in skeletal muscle at rest and following exercise-induced muscle injury. Am J Physiol Regul Integr Comp Physiol 2010; 298(6): 14.
30. Cooper C: The crippling consequences of fractures and their impact on quality of life. Am J Med 1997; 103(2): 12-19.
31. Cawthon PM, Fox KM, Gandra SR et al.: Clustering of strength, physical function, muscle, and adiposity characteristics and risk of disability in older adults. J Am Geriat Soc 2011; 59(5): 781-787.
32. Janssen HC, Emmelot-Vonk MH, Verhaar HJ et al.: Vitamin D and muscle function: is there a threshold in the relation? JAMDA 2013; 14(8): 27.
33. Bischoff-Ferrari HA, Dietrich T, Orav EJ et al.: Positive association between 25-hydroxy vitamin D levels and bone mineral density: A population-based study of younger and older adults. Am J Med 2004; 116(9): 634-639.
34. Zamboni M, Zoico E, Tosoni P et al.: Relation between vitamin D, physical performance and disability in elderly persons. J Gerontol 2002; 57(1): 7-11.
35. Roubenoff R: Sarcopenic obesity: does muscle loss cause fat gain? Lessons from rheumatoid arthritis and osteoarthritis. Ann NY Acad Sci 2000; 904: 553-557.
36. Layne JE, Nelson ME: The effects of progressive resistance training on bone density: a review. Med Sci Sports Exerc 1999; 31(1): 25-30.
37. Bergmann P, Body JJ, Boonen S et al.: Loading and skeletal development and maintenance. J Osteoporos 2011, Article ID 786752.
38. Chesnut CH: Bone mass and exercise. Am J Med 1993; 95(5A): 34-36.

received/otrzymano: 07.12.2016
accepted/zaakceptowano: 28.12.2916