Osteosarcopenia and risk of falls: a concise review

Alessandro de Sire [1,2], Dario Calafiore [3], Claudio Curci [3], Lorenzo Lippi [4], Marco Invernizzi [5,6]

[1] Physical and Rehabilitative Medicine, Department of Medical and Surgical Sciences, University of Catanzaro "Magna Graecia", Catanzaro, Italy; [2] Research Center on Musculoskeletal Health, MusculoSkeletalHealth@UMG, University of Catanzaro "Magna Graecia", Catanzaro, Italy; [3] Physical Medicine and Rehabilitation Unit, Department of Neurosciences, ASST Carlo Poma, Mantua, Italy; [4] Department of Scientific Research, Campus LUdeS, Off-Campus Semmelweis University of Budapest, Budapest, Hungary; [5] Department of Health Sciences, University of Eastern Piedmont "A. Avogadro", Novara, Italy; [6] Translational Medicine, Dipartimento Attività Integrate Ricerca e Innovazione (DAIRI), Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

ABSTRACT

Falls in the elderly are a major cause of injury resulting in disability and hospitalization. They have a significant impact on both the individual (loss of quality of life, nursing home admissions) and society (healthcare costs). Even though falls in the elderly are common, there are some well-studied risk factors for them. Muscle wasting and loss of bone mineral density should be highlighted in particular. Frailty, a complex syndrome including, by definition, conditions such as osteoporosis, sarcopenia, and metabolic diseases, is associated with a high risk of falls.

There are several well-evaluated fall prevention approaches that either target a single fall risk factor or focus on multiple risk factors. It is known that physical exercise can play a key role not only in improving the functioning of patients suffering from osteosarcopenia, but also in terms of modulating the composition of bone tissue and muscle mass.

In conclusion, the correlation between osteosarcopenia, frailty, and fall risk is well known, but future research and further studies are necessary to fully understand the underlying mechanisms and optimize the therapeutic management.

KEYWORDS

Sarcopenia, osteoporosis, frailty, risk of falls, elderly, rehabilitation.

Introduction

Sarcopenia has been defined as an aging-related loss of skeletal muscle mass (SMM) and strength. Several prospective studies have reported that SMM decreases by 6% per decade after mid-life [1]. Sarcopenia is thought to involve several pathophysiological processes, such as denervation, mitochondrial dysfunction, and inflammatory and hormonal changes that may lead to adverse health outcomes including functional decline, frailty, and falls [2]. A fall is defined as an event that results in a person coming to rest inadvertently on the ground, floor or a lower level [3]. Falls are known to be multifactorial incidents caused by a complex interaction of intrinsic problems, extrinsic factors, and exposure to various risk factors [4]. Falls happen during different activities, and may occur when lying, sitting, standing, walking, or running [5]. They can lead to a high level of disability in elderly people definable as frail. The prevalence rates of falls in sarcopenic patients and their relationships with the risk of fracture have actually been the subject of only a few investigations. Thus, the aim of the present concise review was to evaluate the correlation between sarcopenia, risk of falls, and risk of fracture.

Sarcopenia and risk of falls

To date, literature has shown that sarcopenia is associated with multiple adverse health outcomes, including falls, hospitalization, functional decline, poor quality of life, and, in some instances, mortality [6]. This condition is frequent in elderly people, who tend to lose muscle mass and strength, and are therefore at increased risk of falling. Several studies have reported that 33% of people over 65 years of age fall each year, and the rate of injuries caused by falls increases with age [7]. Fall-related injuries negatively impact up to 50% of over-80s [7]. These numbers should be considered worrying, constituting a public health problem that deserves careful consideration [8]. A recent meta-analysis examining the association between sarcopenia and falls among community-dwelling older adults or older nursing home residents showed that the association of sarcopenia with falls was statistically significant [9]. Gait variability and impaired balance are both major fall risk factors [10] that, while considered separate clinical entities, are often intertwined and depend on several factors, making balance and gait disorders heterogeneous and multifactorial [11]. Thus, on the basis of the assumption that muscle mass and muscle strength are related to gait and balance, sarcopenia emerges as one of the main risk factors for falls among older people [8]. Falls ultimately lead to difficulties in self-care, declining functionality, loss of quality of life, kinesiophobia, increased comorbidities associated with immobility, fear of falling again, and decreased

Article history

Received 11 Jun 2024 – Accepted 21 Aug 2024

Contact

Alessandro de Sire; alessandro.desire@unicz.it

Associate Professor of Physical and Rehabilitative Medicine

Department of Medical and Surgical Sciences, University of Catanzaro "Magna Graecia", Catanzaro, Italy

average life expectancy [12]. Several authors agree that falls in the elderly have increased in the last 10 years [13]. Implementing efficient strategies can reduce fall risk, fall-related injuries, and related healthcare costs [14].

Sarcopenia and osteoporosis

Osteoporosis and sarcopenia are common age-associated diseases that often coexist. In the context of an aging population, the prevalence of both these conditions is expected to rise in the future, increasing the risk of fragility fractures, which are themselves associated with significant morbidity and mortality [15]. Hence, reduced independence seen in later life is associated with both bone and muscle loss [16]. The mechanical interaction between muscle and bone is described by the "mechanostat" theory, which states that muscle imposes mechanical forces on bone, and if these exceed a set threshold the bone turnover balance shifts away from bone resorption in favor of bone formation [17]. As both bone and muscle mass are intrinsically linked to the reduction in physical performance observed with aging, this lends credence to the importance of mechanical loading in the maintenance of the bone-muscle unit [18]. A recent bidirectional randomized controlled trial (RCT) concluded that osteoporosis and sarcopenia might have a significant causal effect on each other, identifying a significant positive causal effect of femoral neck and lumbar spine bone mineral density (BMD) on appendicular lean mass (ALM) and a significant positive causal effect of ALM on lumbar spine BMD. On the other hand, there was no evidence for a causal association between BMD and low grip strength. The molecular mechanisms linking bone to muscle function, known as bone-muscle crosstalk, are less well defined [19]. The hormones identified as playing a key role in the development of osteosarcopenia include growth hormone/insulin-like growth factor-1 (GH/IGF1) and gonadal sex hormones [20]. Human muscle and bone cells both express estrogen receptors, hence hormone replacement therapy in post-menopausal women is able to preserve both bone and muscle mass [21]. Furthermore, early menopause without treatment with exogenous estrogen is a strong risk factor for future fragility fracture [22]. The pathogenesis of male age-related osteoporosis and sarcopenia is less well characterized, but it is thought that estrogens derived from the metabolism of androgens play a role in preserving bone mass and that low testosterone results in reduced protein synthesis with subsequent loss of muscle mass [23]. Indeed, low testosterone levels in older men are predictive of frailty and incident falls [24]. From a clinical perspective, the coexistence of sarcopenia and osteoporosis has been associated cross-sectionally with depression, malnutrition, peptic ulcer disease, inflammatory arthritis, and reduced mobility [25]. In fact, several studies have demonstrated that individuals with both osteoporosis and sarcopenia are at higher risk of falls, fractures and 1-year mortality after hip fractures than those with osteoporosis or sarcopenia alone [26].

Osteoporosis and risk of falls

Osteoporosis is characterized by an increase in osteoclast function, which subsequently increases bone resorption, with a corresponding decrease in bone formation [27]. The most prevalent causes of osteoporosis are menopause and age, as the bone remodeling process is regulated by estrogen, parathyroid hormone, inflammatory cytokines, and vitamin D [28]. Bone is a plastic substance that undergoes continual remodeling in response to both physiological and extracorporeal factors; increased bone resorption and concomitant bone loss, regardless of the underlying mechanisms [29], constitute a complex pathophysiology that can be influenced by genetic predisposition, as well as pharmaceuticals (e.g., glucocorticoids), lifestyle, and diet [30,31].

Increasing evidence indicates that bone metabolism influences fall risk and should be taken into account in efforts to understand and treat osteoporosis. Recent studies suggest that fall-related bone fractures are among the most important factors affecting morbidity and quality of life in osteoporotic patients [32]. Several fall risk factors have been defined, including impaired walking, a sedentary lifestyle, vestibulopathy, balance dysfunction, increased postural oscillation, and decreased muscle mass. According to research findings, fall risk reduction is an essential component of both primary and secondary fragility fracture prevention strategies [33], which usually involve a multidimensional approach, including calcium and vitamin D supplementation, medication review, anti-osteoporotic drugs, fall risk assessment, and exercise/rehabilitation [34]. Additionally, multiple studies have demonstrated the efficacy of therapeutic physical activity in reducing falls [35,36]. A recent meta-analysis of RCTs investigating moderate-intensity multicomponent physical activity (aerobic, balance, and strength training) 3 times a week for 1 year or more reported significant fall risk reductions: a 22% lower risk of falls and a 26% lower risk of injurious falls. The risk of fractures was reduced by 16%, although the significance of this finding is weakened by the small number of fractures in the study ($p = .05$) [37].

Fall risk and physical exercise

Physical exercise can contribute significantly to preventing and treating various chronic conditions, including osteoporosis and sarcopenia, playing a crucial role in reducing the risk of falls in elderly people [38]. Moreover, physical exercise has a significant impact not only improving the functional activity of osteosarcopenic patients, but also in terms of modulating the composition of skeletal tissue and muscle mass [39]. Thus, it is recommended by multiple guidelines as one of the primary therapeutic options for the management of this condition [40,41,42].

Recent research studies have shown that physical exercise can modulate oxidative stress and inflammatory responses, leading to enhanced metabolism and energy expenditure [43]. However, the existing literature on these topics is still debated and therefore further observational studies are needed to determine whether modulation of osteosarcopenia through therapeutic exercise can reduce the risk of falls in elderly people and consequently improve patient functionality [44].

Future perspectives

The main challenges faced by clinicians in the area of osteosarcopenia treatment and fall risk reduction are poor adherence to multimodal treatment and the need to facilitate outcome evaluation. Easier clinical monitoring is mandatory in order to reduce the risk of fracture in elderly people, and it can include

a variety of approaches including video consultations and follow-up visits (i.e., telemedicine), remote patient monitoring using electronic applications, patient education incorporating distance learning to encourage self-management, and virtual physician-physician consultations (i.e., eConsults) [45]. The new technology used in telehealth services can help the clinician in this field [46]. Although the use of these services in the general population has been facilitated by increasingly ubiquitous access to technology, uptake of them has been slower in some groups, including people aged 65 years and older, due to issues such as lower digital literacy [47]. In this context, technological advances and digital solutions might offer a sustainable means of improving the remote assessment of elderly patients, overcoming barriers to in-person management and providing alternatives to inpatient and outpatient supervised rehabilitation [48,49]. Several studies have assessed the role of different wearable and smart technology devices in patients undergoing total joint replacement, suggesting that wearable technology has promising implications for the remote measurement of patients' functional outcomes [50]. The authors remarked that studies in the literature are now focusing on accelerometer, gyroscope, and smartphone devices, with encouraging results in terms of functional outcomes [50].

Conclusion

Taken together, the findings in the recent literature demonstrate that there a close correlation between osteosarcopenia, frailty, and fall risk. This nevertheless remains a hot research topic that deserves attention, especially from a daily clinical practice perspective. Further studies are mandatory to fully understand the therapeutic strategies possible in both osteosarcopenia and fall prevention in elderly people, also in terms of new technology applied in the context of rehabilitation programs.

References

1. Cruz-Jentoft AJ, Bahat G, Bauer J, et al; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31 [published correction appears in Age Ageing. 2019;48(4):601].
2. Cho MR, Lee S, Song SK. A review of sarcopenia pathophysiology, diagnosis, treatment and future direction. J Korean Med Sci. 2022;37(18):e146.
3. Zhang K, Ju Y, Yang D, Cao M, Liang H, Leng J. Correlation analysis between body composition, serological indices and the risk of falls, and the receiver operating characteristic curve of different indexes for the risk of falls in older individuals. Front Med (Lausanne). 2023;10:1228821.
4. Iolascon G, de Sire A, Calafiore D, et al. Multifactorial assessment of risk of falling in 753 post-menopausal women: a multicenter cross-sectional study by the Italian Group for the Study of Metabolic Bone Diseases. Clin Interv Aging. 2020;15:1077-84.
5. Olokunlade T, Benden ME, Han G, Sherman LD, Smith ML. Factors associated with incident and recurrent falls among men enrolled in evidence-based fall prevention programs: an examination of race and ethnicity. J Appl Gerontol. 2024:7334648241251735.
6. Beaudart C, Rizzoli R, Bruyère O, Reginster JY, Biver E. Sarcopenia: burden and challenges for public health. Arch Public Health. 2014;72(1):45.
7. Álvarez-Barbosa F, del Pozo-Cruz J, del Pozo-Cruz B, Alfonso-Rosa RM, Rogers ME, Zhang Y. Effects of supervised whole body vibration exercise on fall risk factors, functional dependence and health-related quality of life in nursing home residents aged 80+. Maturitas. 2014;79(4):456-63.
8. Rodrigues F, Domingos C, Monteiro D, Morouço P. A review on aging, sarcopenia, falls, and resistance training in community-dwelling older adults. Int J Environ Res Public Health. 2022;19(2):874.
9. Zhang X, Huang P, Dou Q, et al. Falls among older adults with sarcopenia dwelling in nursing home or community: a meta-analysis. Clin Nutr. 2020;39(1):33-9.
10. Lopez P, Pinto RS, Radaelli R, et al. Benefits of resistance training in physically frail elderly: a systematic review. Aging Clin Exp Res. 2018;30(8):889-99.
11. Pirker W, Katzenschlager R. Gait disorders in adults and the elderly: a clinical guide. Wien Klin Wochenschr. 2017;129(3-4):81-95.
12. Kuh D, Bassey EJ, Butterworth S, Hardy R, Wadsworth ME; Musculoskeletal Study Team. Grip strength, postural control, and functional leg power in a representative cohort of British men and women: associations with physical activity, health status, and socioeconomic conditions. J Gerontol A Biol Sci Med Sci. 2005;60(2):224-31.
13. Sharif SI, Al-Harbi AB, Al-Shihabi AM, Al-Daour DS, Sharif RS. Falls in the elderly: assessment of prevalence and risk factors. Pharm Pract (Granada). 2018;16(3):1206.
14. Maidan I, Droby A, Jacob Y, Giladi N, Hausdorff JM, Mirelman A. The neural correlates of falls: alterations in large-scale resting-state networks in elderly fallers. Gait Posture. 2020;80:56-61.
15. Edwards MH, Dennison EM, Aihie Sayer A, Fielding R, Cooper C. Osteoporosis and sarcopenia in older age. Bone. 2015;80:126-30.
16. Clynes MA, Gregson CL, Bruyère O, Cooper C, Dennison EM. Osteosarcopenia: where osteoporosis and sarcopenia collide. Rheumatology (Oxford). 2021;60(2):529-37.
17. Kaji H. Interaction between muscle and bone. J Bone Metab. 2014;21(1):29-40.
18. Coll PP, Phu S, Hajjar SH, Kirk B, Duque G, Taxel P. The prevention of osteoporosis and sarcopenia in older adults. J Am Geriatr Soc. 2021;69(5):1388-98.
19. Liu C, Liu N, Xia Y, Zhao Z, Xiao T, Li H. Osteoporosis and sarcopenia-related traits: a bi-directional Mendelian randomization study. Front Endocrinol (Lausanne). 2022;13:975647.
20. Sullivan SD, Sarrel PM, Nelson LM. Hormone replacement therapy in young women with primary ovarian insufficiency and early menopause. Fertil Steril. 2016;106(7):1588-99.
21. Olmos Martínez JM, Hernández Martínez P, González Macías J. Frailty, sarcopenia and osteoporosis. Med Clin (Barc). 2024;163(2):e17-e23.
22. Falsetti I, Palmini G, Donati S, Aurilia C, Iantomasi T, Brandi ML. Irisin and its role in postmenopausal osteoporosis and sarcopenia. Biomedicines. 2024;12(4):928.
23. Vandenput L, Mellström D, Laughlin GA, et al. Low testosterone, but not estradiol, is associated with incident falls in older men: the International MrOS Study. J Bone Miner Res. 2017;32(6):1174-81.
24. Cho SW, Baek S, Han S, et al. Metabolic phenotyping with computed tomography deep learning for metabolic syndrome, osteoporosis and sarcopenia predicts mortality in adults. J Cachexia Sarcopenia Muscle. 2024;15(4):1418-29.
25. Asavamongkolkul A, Adulkasem N, Chotiyarnwong P, et al. Prevalence of osteoporosis, sarcopenia, and high falls risk in healthy community-dwelling Thai older adults: a nationwide cross-sectional study. JBMR Plus. 2024;8(2):ziad020 [published correction appears in JBMR Plus. 2024;8(4):ziae040]
26. Xu X, Li D, Zhang S. Retrospective study for correlation analysis of nutritional status with osteoporosis, sarcopenia and cognitive impairment in elderly patients with coronary heart disease. Front Cardiovasc Med. 2024;10:1335572.

27. Tarantino U, Iolascon G, Cianferotti L, et al. Clinical guidelines for the prevention and treatment of osteoporosis: summary statements and recommendations from the Italian Society for Orthopaedics and Traumatology. J Orthop Traumatol. 2017;18(Suppl 1):3-36.
28. Reid IR, Bolland MJ, Grey A. Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis. Lancet. 2014;383(9912):146-55.
29. Watson SL, Weeks BK, Weis LJ, Harding AT, Horan SA, Beck BR. High-intensity resistance and impact training improves bone mineral density and physical function in postmenopausal women with osteopenia and osteoporosis: the LIFTMOR randomized controlled trial. J Bone Miner Res. 2018;33(2):211-20 [published correction appears in J Bone Miner Res. 2019;34(3):572].
30. de Sire A, Lippi L, Aprile V, et al. Pharmacological, nutritional, and rehabilitative interventions to improve the complex management of osteoporosis in patients with chronic obstructive pulmonary disease: a narrative review. J Pers Med. 2022;12(10):1626.
31. Hu Y, Han J, Ding S, Liu S, Wang H. Identification of ferroptosis-associated biomarkers for the potential diagnosis and treatment of postmenopausal osteoporosis. Front Endocrinol (Lausanne). 2022;13:986384.
32. Curtis EM, Moon RJ, Harvey NC, Cooper C. The impact of fragility fracture and approaches to osteoporosis risk assessment worldwide. Bone. 2017;104:29-38.
33. Iolascon G, de Sire A, Curci C, et al. Osteoporosis guidelines from a rehabilitation perspective: systematic analysis and quality appraisal using AGREE II. Eur J Phys Rehabil Med. 2021;57(2):273-9.
34. Lippi L, Uberti F, Folli A, et al. Impact of nutraceuticals and dietary supplements on mitochondria modifications in healthy aging: a systematic review of randomized controlled trials. Aging Clin Exp Res. 2022;34(11):2659-74.
35. Ferrillo M, Migliario M, Marotta N, et al. Oral health in breast cancer women with vitamin D deficiency: a machine learning study. J Clin Med. 2022;11(16):4662.
36. Liu-Ambrose T, Davis JC, Best JR, et al. Effect of a home-based exercise program on subsequent falls among community-dwelling high-risk older adults after a fall: a randomized clinical trial. JAMA. 2019;321(21):2092-100 [published correction appears in JAMA. 2019;322(2):174].
37. de Souto Barreto P, Rolland Y, Vellas B, Maltais M. Association of long-term exercise training with risk of falls, fractures, hospitalizations, and mortality in older adults: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(3):394-405.
38. Lippi L, de Sire A, Mezian K, et al. Impact of exercise training on muscle mitochondria modifications in older adults: a systematic review of randomized controlled trials. Aging Clin Exp Res. 2022;34(7):1495-510.
39. Shen Y, Shi Q, Nong K, et al. Exercise for sarcopenia in older people: a systematic review and network meta-analysis. J Cachexia Sarcopenia Muscle. 2023;14(3):1199-211.
40. van den Bergh JP, Geusens P, Appelman-Dijkstra NM, et al. The Dutch multidisciplinary guideline osteoporosis and fracture prevention, taking a local guideline to the international arena. Arch Osteoporos. 2024;19(1):23.
41. Montero-Odasso MM, Kamkar N, Pieruccini-Faria F, et al; Task Force on Global Guidelines for Falls in Older Adults. Evaluation of clinical practice guidelines on fall prevention and management for older adults: a systematic review. JAMA Netw Open. 2021;4(12):e2138911.
42. Benedetti MG, Furlini G, Zati A, Letizia Mauro G. The effectiveness of physical exercise on bone density in osteoporotic patients. Biomed Res Int. 2018;2018:4840531.
43. Lippi L, Turco A, Folli A, et al. Technological advances and digital solutions to improve quality of life in older adults with chronic obstructive pulmonary disease: a systematic review. Aging Clin Exp Res. 2023;35(5):953-68.
44. Inceoglu SC, Ayyildiz A, Sahin T, et al. The impact of combination of aerobic and resistive exercise on activities of daily living and risk of fall in osteosarcopenic patients. Sisli Etfal Hastan Tip Bul. 2024;58(1):68-74.
45. Paolucci T, de Sire A, Ferrillo M, et al. Telerehabilitation proposal of mind-body technique for physical and psychological outcomes in patients with fibromyalgia. Front Physiol. 2022;13:917956.
46. Beheshti L, Kalankesh LR, Doshmangir L, Farahbakhsh M. Telehealth in primary health care: a scoping review of the literature. Perspect Health Inf Manag. 2022;19(1):1n. eCollection 2022 Winter.
47. Mann DM, Chen J, Chunara R, Testa PA, Nov O. COVID-19 transforms health care through telemedicine: evidence from the field. J Am Med Inform Assoc. 2020;27(7):1132-5.
48. Havran MA, Bidelspach DE. Virtual physical therapy and telerehabilitation. Phys Med Rehabil Clin N Am. 2021;32(2):419-28.
49. Tsekoura M, Kastrinis A, Nomikou E, Katsoulaki M. Telerehabilitation and fall prevention in older adults. Adv Exp Med Biol. 2023;1425:485-9.
50. Iovanel G, Ayers D, Zheng H. The role of wearable technology in measuring and supporting patient outcomes following total joint replacement: review of the literature. JMIR Perioper Med. 2023;6:e39396.

Conflict of interest: *The authors declare that there are no conflicts of interest.*