



OPEN ACCESS

EDITED AND REVIEWED BY
Tzvi Dwolatzky,
Technion Israel Institute of Technology, Israel

*CORRESPONDENCE
Bagher Larjani
✉ emrc@tums.ac.ir

†These authors have contributed equally to this work and share first authorship

RECEIVED 26 November 2023
ACCEPTED 29 November 2023
PUBLISHED 18 December 2023

CITATION
Tabatabaei-Malazy O, Khashayar P,
Quyyumi AA, Nabipour I, Dabbaghmanesh MH,
Zakraoui L and Larjani B (2023) Editorial:
Community series - reducing the burden of
age-related disease in relation to osteoporosis,
sarcopenia and osteosarcopenia, volume II.
Front. Med. 10:1344694.
doi: 10.3389/fmed.2023.1344694

COPYRIGHT
© 2023 Tabatabaei-Malazy, Khashayar,
Quyyumi, Nabipour, Dabbaghmanesh, Zakraoui
and Larjani. This is an open-access article
distributed under the terms of the [Creative
Commons Attribution License \(CC BY\)](#). The use,
distribution or reproduction in other forums is
permitted, provided the original author(s) and
the copyright owner(s) are credited and that
the original publication in this journal is cited, in
accordance with accepted academic practice.
No use, distribution or reproduction is
permitted which does not comply with these
terms.

Editorial: Community series - reducing the burden of age-related disease in relation to osteoporosis, sarcopenia and osteosarcopenia, volume II

Ozra Tabatabaei-Malazy^{1†}, Patricia Khashayar^{2,3†},
Arshed Ali Quyyumi⁴, Iraj Nabipour⁵,
Mohammad Hossein Dabbaghmanesh⁶, Leith Zakraoui⁷ and
Bagher Larjani^{8*}

¹Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran, ²Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran, ³Center for Microsystems Technology, Imec & Ghent University, Zwijnaarde-Gent, Belgium, ⁴Emory Clinical Cardiovascular Research Institute, Emory University, Atlanta, GA, United States, ⁵The Persian Gulf Marine Biotechnology Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran, ⁶Endocrinology and Metabolism Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, ⁷Department of Rheumatology, Mongi Slim Hospital, La Marsa, Tunis, Tunisia, ⁸Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

KEYWORDS

osteoporosis, sarcopenia, osteosarcopenia, aging, frailty, risk factors, bone mineral density, resistance exercise

Editorial on the Research Topic

[Community series - reducing the burden of age-related disease in relation to osteoporosis, sarcopenia and osteosarcopenia, volume II](#)

Considering the accelerated aging rate, doubled to 1.5 billion by 2050, the cost and burden of related health problems are increasing. One of the more prevalent health problems among the elderly population is frailty that finally can result in sarcopenia and osteoporosis which may increase the fracture rate. This issue therefore aimed to report novel advancements in these two areas, focusing on new preventive measures and treatment options. The effect of certain co-morbidities on these two conditions were also highlighted, suggesting that preventing osteoporosis/sarcopenia can also reduce other co-morbidities among the elderly, improving their quality of life.

Three of the articles published in this issue were focused on sarcopenia (Merchant et al., Diniz de Salles et al., Hou et al.). The beneficial effects of nutrition in the pre-frailty phase on the prevention or reduction of frailty and disability risk in older adults is well known (1). Leucine, and leucine-enriched protein supplements in the range of the recommended dietary allowance (RDA) for protein in older adults (0.8 g/kg per day), together with resistance exercise, have been shown to be beneficial for muscle mass, physical function, and systemic inflammation. However, the effect of an additional dose of protein on RDA when combined with exercise in the elderly population is not yet known. In a non-randomized trial study,

Merchant et al. assessed the short-term effect (3 months) of a diet enriched with an additional protein and leucine supplementation with/without exercise on the physical function, muscle mass, and systemic inflammation in prefrail older adults who had received RDA protein. They found a significant improvement in body cell mass, and systemic inflammation in both groups; short physical performance battery (SPPB) test, gait speed, 5× sit-to-stand (STS), and muscle mass, however, improved significantly only in the nutrition+ exercise group. Since these effects were not sustained after a 3-month follow-up, their findings should be confirmed in future randomized trials with a larger number of at-risk elderly.

Elderly patients are at increased risk of postoperative complications (2), which require rapid recognition and treatment. Otherwise, they can lead to a cascade of events that may result in loss of independence, some degrees of disability, worsening of quality of life, higher treatment-related costs, and higher mortality. Diniz de Salles et al. aimed to evaluate the association between sarcopenia and frailty in an elderly population admitted to hospital for non-emergency surgical procedures. This is while the association between sarcopenia and frailty is still unclear, while several studies have shown the influence of sarcopenia on frailty over time (1, 3). The secondary objective of the study was to evaluate the correlation of sarcopenia and frailty with postsurgical outcomes. This is mainly because sarcopenia and frailty are believed to have significant adverse effects on the postoperative outcomes (4). In this observational study, frailty was assessed using the modified frailty index (MFI-11). Sarcopenia, on the other hand, was measured through (a) thickness and echogenicity on ultrasound; (b) handgrip strength on dynamometry; and (c) gait speed. They found sarcopenia, in all its domains, was associated with frailty. Unfavorable surgical outcomes were also associated with these two conditions. Diniz de Salles et al. also suggested that screening for sarcopenia and frailty in the elderly patients undergoing elective surgery is relevant, easy to perform, and helps with perioperative risk reduction in this population.

Sarcopenia can be defined by various signs and symptoms, one of which is low muscle strength. There are several tools and methods to diagnose the mass and strength of muscle in sarcopenic people (5) such as handgrip strength test, and dual-energy X-ray absorptiometry (DEXA). Hou et al. in a cohort study with a 600-day follow-up determined the impact of the uremic toxins on the frequency of low handgrip strength in 75 participants divided into three groups: control, chronic kidney disease (CKD), and end-stage renal disease (ESRD). Although, they found a similar rate of sarcopenia between groups, handgrip strength and serum level of indoxyl sulfate, a protein-bound uremic toxin were lower and higher accordingly in ESRD patients. Indoxyl sulfate can impair the function of mitochondria of skeletal muscle cells and muscle anabolism by inducing oxidative stress (6). Moreover, the hospitalization rate was higher in patients with ESRD. They concluded the low handgrip strength to be predictive of hospitalization.

The other articles were focused mainly on osteoporosis. Osteoporosis is a systemic skeletal disease characterized by loss of bone mass and micro architectural integrity that leads to increased bone fragility and risk of fracture (7). With the advancements in science and technology, the quality of life and health status

have significantly improved in the past decades. There are still huge differences in the living style, socioeconomic conditions, and medical status, such as smoking, education level, economic disparity, and chronic diseases, in various regions of China (8, 9). Such differences may have contributed to the disparities in the prevalence of osteoporosis in these regions. To address this issue, Wang J. et al. assessed the prevalence of osteoporosis and osteopenia as well as the associated risk factors in the China Community-based Cohort of Osteoporosis (CCCO). The multicenter cross-sectional study was conducted on 19,848 middle-aged and elderly permanent residents of seven representative Chinese regions (10, 11). The bone mineral density at the lumbar vertebrae and hip was determined using the dual-energy X-ray absorptiometry densitometer. Serum levels of bone metabolism markers were also measured. This study revealed dramatic regional differences in the prevalence of osteoporosis in China, with females, those aged 60 or older, with low BMI, low education level, current regular smokers, and with a history of fracture being at a higher risk of osteoporosis. They suggested that more preventive measures and treatment options should be focused on populations with such risk factors.

The maintenance of bone mass is negatively affected by metabolic dysfunctions such as chronic hyperglycemia (12). As a result, osteoporosis is more prevalent among patients with diabetes mellitus. In addition, it is well known that lipid profile disturbances especially high-density lipoprotein cholesterol (HDL-C) and apolipoprotein A1 (APOA1), its major protein component, have key roles in bone mass maintenance through affecting osteoblasts differentiation (13). However, there are controversies regarding their association with bone mineral density (BMD) values. Wang W. et al. investigated Chinese postmenopausal diabetic women for such associations. They found a remarkable association between APOA1 and osteocalcin level (which inhibits bone formation), lumbar BMD, and osteoporosis in contrast to HDL-C.

Cardiovascular disease and osteoporosis are common diseases in older adults, and both are associated with high morbidities (14). Yang and Huang study performed a multivariate logistic regression and stratified analysis to explore the possible relationship between BMD and the risk of CVD in older adults aged over 60 years. This study is expected to provide more guidance on early monitoring and clinical prevention. The cross-sectional study of 2,097 people aged over 60 years speculated that DXA examination or targeted prevention strategies, such as increased sun exposure, appropriate physical exercise, and calcium or vitamin D supplements, should be considered for CVD patients. Meanwhile, for osteoporotic patients or those at high risk of fracture, active anti-osteoporosis drug therapy can increase BMD, improve bone quality, and reduce cardiovascular complications to a certain extent. Negative non-linear relationship was noted between the femur BMD levels and the prevalence of CVD in people aged over 60 years with an inflection point of 0.741 gm/cm². No significant differences were found between age, gender, and the comorbidities subgroups. Bone loss therefore was considered as a new risk factor for CVD. This is while future studies are needed to make a comprehensive assessment of combined dietary and biochemical indicators. This also points out the importance of preventive measures for

osteoporosis to indirectly reduce the prevalence of CVD, the world's biggest killer of humans.

Current osteoporosis medications have drawbacks such as possible side effects and having slow onset, therefore developing osteoporosis drugs with faster onset and fewer side effects is essential. Therefore, the [Shih et al.](#) study investigated the effects of topical SDDL-E (15) applied for 20 days in ovariectomized (OVX)-induced osteoporosis rat models. The changes in estradiol, various bone turnover markers such as serum alkaline phosphatase (ALP) activity (16), serum and urinary calcium (17), bone mineral density (BMD), various bone mechanics indicators and bone histology were assessed to understand the mechanism of action and the therapeutic efficacy of SDDL-E on osteoporosis. The results demonstrated that the 20-day treatment with topical SDDL-E can improve bone strength and trabecular bone structure in OVX-induced osteoporosis rats. The underlying mechanisms include restoring estradiol levels as well as reducing bone turnover, net bone resorption, bone calcium loss, and calcium excretion through the kidneys. These findings suggest topical application of the plant extract is an efficient potential new approach for rapid treatment of osteoporosis.

One of the most common osteoporotic complications is osteoporotic vertebral fracture (OVF). OVF can lead to loss of height, acute and chronic pain, decreased quality of life, and increased fracture risk (18). Since, falls are known as the main risk factor for fracture in patients with OVF, improving body balance by exercise is believed to have an important role in reducing the future fracture risk (19). [Li et al.](#) conducted a systematic review and meta-analysis to assess the effects of resistance and balance exercises in patients with OVF. They found exercising improved quality of life, visual analog pain scale, Timed Up and Go, falls efficacy scale international, kyphosis, and functional reach. These beneficial effects were considerable when training continued for at least 10 weeks.

Odontoid fractures are another relatively common fracture of the spine (C2) vertebral body among the elderly. Despite its prevalence, there are controversies in its treatment. Several studies have suggested surgical management, suggesting it can result in more biochemical stability and fusion compared to the conventional therapies (20). This is while the surgical risks are high among the elderly population. As a result, maintaining the right balance between the risks and benefits of the surgery is challenging. [Lenga et al.](#) in a retrospective study with a 5-year follow-up assessed the morbidity and mortality rate of peri- and post-surgery of C1/C2 posterior screw fixation technique against the associated risk factors

and mortality. Although they found a high rate of morbidity and mortality in octogenarians, they recommended spine surgery to achieve bone union and preserve of neurological status.

To conclude, all articles of this Research Topic sum up the current information and highlight the current research gaps and elucidate the path for future research on the topic. The findings of the published studies in the current Research Topic have been proposed some acceptable modalities and strategies for management of Osteoporosis, Sarcopenia and Osteosarcopenia, and also improvement of the patients' quality of life.

Author contributions

OT-M: Validation, Writing—original draft, Writing—review & editing. PK: Validation, Writing—original draft, Writing—review & editing. AQ: Validation, Writing—review & editing. IN: Validation, Writing—review & editing. MHD: Validation, Writing—review & editing. LZ: Validation, Writing—review & editing. BL: Supervision, Validation, Writing—review & editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Hashemi R, Motlagh AD, Heshmat R, Esmailzadeh A, Payab M, Yousefinia M, et al. Diet and its relationship to sarcopenia in community dwelling Iranian elderly: a cross sectional study. *Nutrition*. (2015) 31:97–104. doi: 10.1016/j.nut.2014.05.003
2. Polanczyk CA, Marcantonio E, Goldman L, Rohde LEP, Orav J, Mangione CM, et al. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. *Ann Intern Med*. (2001) 134:637–3. doi: 10.7326/0003-4819-134-8-200104170-00008
3. Álvarez-Bustos A, Carnicero-Carreño JA, Davies B, Garcia-Garcia FJ, Rodríguez-Artalejo F, Rodríguez-Mañas L, et al. Role of sarcopenia in the frailty transitions in

older adults: a population-based cohort study. *J Cachexia Sarcopenia Muscle*. (2022) 13:2352–60. doi: 10.1002/jcsm.13055

4. Shen Y, Hao Q, Zhou J, Dong B. The impact of frailty and sarcopenia on postoperative outcomes in older patients undergoing gastrectomy surgery: a systematic review and meta-analysis. *BMC Geriatr*. (2017) 17:188. doi: 10.1186/s12877-017-0569-2

5. Darvishi A, Hemami MR, Shafiee G, Daroudi R, Mohseni M, Shekarabi FH, et al. Sarcopenia screening strategies in older people: a cost effectiveness analysis in Iran. *BMC Public Health*. (2021) 21:926. doi: 10.1186/s12889-021-10511-7

6. Duranton F, Cohen G, De Smet R, Rodriguez M, Jankowski J, Vanholder R, et al. Normal and pathologic concentrations of uremic toxins. *J Am Soc Nephrol.* (2012) 23:1258–70. doi: 10.1681/ASN.2011121175
7. Panahi N, Saeedi Moghaddam S, Fahimfar N, Rezaei N, Sanjari M, Rashidi MM, et al. Trend in global burden attributable to low bone mineral density in different WHO regions: 2000 and beyond, results from the Global Burden of Disease (GBD) study 2019. *Endocr Connect.* (2023) 12:e230160. doi: 10.1530/EC-23-0160
8. Maddah M, Sharami SH, Karandish M. Educational difference in the prevalence of osteoporosis in postmenopausal women: a study in northern Iran. *BMC Public Health.* (2011) 11:845. doi: 10.1186/1471-2458-11-845
9. Vaidya SV, Ekbote VH, Khadilkar AV, Chiplonkar SA, Pillay D, Divave U. Bone status of women over 40 years of age from two socioeconomic strata. *Endocr Res.* (2012) 37:25–34. doi: 10.3109/07435800.2011.601384
10. Lorentzon M, Mellström D, Haug E, Ohlsson C. Smoking is associated with lower bone mineral density and reduced cortical thickness in young men. *J Clin Endocrinol Metab.* (2007) 92:497–503. doi: 10.1210/jc.2006-1294
11. Kassi EN, Stavropoulos S, Kokkoris P, Galanos A, Moutsatsou P, Dimas C, et al. Smoking is a significant determinant of low serum vitamin D in young and middle-aged healthy males. *Hormones.* (2015) 14:245–50. doi: 10.14310/horm.2002.1521
12. Ebrahimipur M, Sharifi F, Nezhad FA, Bagherzadeh M, Ostovar A, Shafiee G, et al. Effect of diabetes on BMD and TBS values as determinants of bone health in the elderly: Bushehr Elderly Health program. *J Diabetes Metab Disord.* (2019) 18:99–106. doi: 10.1007/s40200-019-00395-1
13. Triantaphyllidou IE, Kalyvioti E, Karavia E, Lilis I, Kypreos KE, Papachristou DJ. Perturbations in the HDL metabolic pathway predisposes to the development of osteoarthritis in mice following long-term exposure to a western-type diet. *Osteoarthr Cartil.* (2013) 21:322. doi: 10.1016/j.joca.2012.11.003
14. Fahimfar N, Parsaiyan H, Khalagi K, Shafiee G, Sanjari M, Mansourzadeh MJ, et al. The association of cardiovascular diseases risk scores and osteosarcopenia among older adult populations: the results of bushehr elderly health (BEH) program. *Calcif Tissue Int.* (2023) 112:422–9. doi: 10.1007/s00223-022-01059-8
15. Yousefzadeh N, Kashfi K, Jeddi S, Ghasemi A. Ovariectomized rat model of osteoporosis: a practical guide. *EXCLI J.* (2020) 19:89–107. doi: 10.17179/excli2019-1990
16. Chapurlat RD, Confavreux CB. Novel biological markers of bone: from bone metabolism to bone physiology. *Rheumatology.* (2016) 55:1714–25. doi: 10.1093/rheumatology/kev410
17. Antonucci DM, Sellmeyer DE, Bilezikian JP, Palermo L, Ensrud KE, Greenspan SL, et al. Elevations in serum and urinary calcium with parathyroid hormone (1-84) with and without alendronate for osteoporosis. *J Clin Endocrinol Metab.* (2007) 92:942–7. doi: 10.1210/jc.2006-1788
18. Rajabi M, Ostovar A, Sari AA, Sajjadi-Jazi SM, Mousavi A, Larijani B, et al. Health-related quality of life in osteoporosis patients with and without fractures in Tehran, Iran. *J Bone Metab.* (2023) 30:37–46. doi: 10.11005/jbm.2023.30.1.37
19. Yu WY, Hwang HF, Chen CY, Lin MR. Situational risk factors for fall-related vertebral fractures in older men and women. *Osteoporos Int.* (2021) 32:1061–70. doi: 10.1007/s00198-020-05799-x
20. White A, Hashimoto R, Norvell D, Vaccaro A. Morbidity and mortality related to odontoid fracture surgery in the elderly population. *Spine.* (2010) 35:S146. doi: 10.1097/BRS.0b013e3181d830a4