

## Review Article

# Similarities in Acquired Factors Related to Postmenopausal Osteoporosis and Sarcopenia

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Postmenopausal population is at increased risk of musculoskeletal impairments. Sarcopenia and osteoporosis are associated with significant morbidity and social and health-care costs. These two conditions are uniquely linked with similarities in pathophysiology and diagnostic methods. Uniform diagnostic criteria for sarcopenia are still evolving. Postmenopausal sarcopenia and osteoporosis share many environmental risk- and preventive factors. Moreover, geriatric frailty syndrome may result from interaction of osteoporosis and sarcopenia and may lead to increased mortality. The present paper reviews the factors in evolution of postmenopausal sarcopenia and osteoporosis.

## 1. Introduction

One of the biggest challenges for public health care is the maintenance of health, independence, and mobility as well as prevention and postponement of disability of the aging population [1]. There are sex dependent differences in morbidity and disability among the elderly population which become more evident with age [2, 3]. Among middle-aged women, menopausal transition, caused by physiological exhaustion of ovarian function [4, 5], evokes increase in musculoskeletal, cardiovascular, and mental impairments and cancer [6–8]. This increased female vulnerability related to aging, together with predominance of female elderly population, makes them an important target for research and preventive health care measures [7].

Sarcopenia, that is, muscle wasting, and osteoporosis, that is, fragile bone disease, are significant health burdens among the postmenopausal women. The prevalence of sarcopenia has been reported to be 10% to 40% in postmenopausal population depending on the reference method used and the population [8]. Osteoporosis affects approximately 30% of female population over 50 years [9]. Sarcopenia results in decline in activities of daily living, quality

of life, and self-rated health and increases falls and related skeletal fractures [10–15] which have been estimated to have deep impact of social and healthcare-related costs of the postmenopausal population [16–19].

The present paper focuses on similarities in acquired factors associated with postmenopausal osteoporosis and sarcopenia concentrating on decades after the menopausal transition. Consequently, essential aspects on the effects of aging on sarcopenia and osteoporosis will be covered.

## 2. Contemporary Definition of Sarcopenia and Osteoporosis

Evaluation of the evidence behind the synergism between postmenopausal sarcopenia and osteoporosis requires a clear definition for both conditions. Unfortunately, uniform criteria for sarcopenia are still evolving, and methods as well as different measurement cutoffs have been used across studies. Majority of the diagnostic thresholds for sarcopenia have been developed based on muscle mass measurements with similar methods applied for diagnosis of osteoporosis. Moreover, the diagnosis of osteoporosis has shifted from

salience of DXA towards independent risk factors for osteoporosis.

**2.1. Sarcopenia.** Among the elderly, genetics, hormonal changes, and lifestyle factors related to physical activity and nutritional factors have been linked to development of sarcopenia. From physiologic viewpoint, these lead to alterations in muscle protein turnover, muscle tissue remodeling, loss of alpha motor neurons, muscle cell recruitment, apoptosis, and muscle's fat content [20–22]. The multifactorial etiology of sarcopenia emphasizes and differentiates the three divisions of sarcopenia, that is, *muscle mass*, *muscle strength*, and *muscle function*. Conceptually, this is supported by the evidence that muscle strength does not correlate directly with muscle mass, and the relationship between strength may not be linear [23, 24]. In fact, some have argued, that with regards to terminology, dynapenia would be a better acronym to describe age-related decline in muscle strength and function [25]. This, however, has not yet been uniformly incorporated into clinical use.

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes related to physical ability, quality of life, or even death [23, 26]. According to the consensus of the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia may be categorized into *presarcopenia* (loss of muscle mass), *sarcopenia* (loss of muscle mass and strength or functional ability), and *severe sarcopenia* (loss of muscle mass, strength, and functional ability) [20]. This categorization may be considered clinically sound and holistically aligns the concept of multiple facets of muscle wasting.

There are several methods for assessment of muscle mass, strength, and function. *Muscle mass* may accurately be assessed by dual X-ray absorptiometry (DXA) with very low radiation dose (1-2 micro-Sieverts). The operational definitions of sarcopenia have generally used DXA-based skeletal muscle mass index (SMI) [27]. Muscle mass below 2 SD of the mean of young reference population has been considered pathognomic for sarcopenia. Other methods available for assessment of muscle mass include bioimpedance analysis (BIA) [28–31], magnetic resonance imaging (MRI), and computed tomography (CT) [32, 33]. In addition, anthropometric measurements, such as calf circumference, arm circumference, and skin fold thickness, may be used for evaluation of muscle mass [27, 34].

*Muscle strength* may be measured by variety of methods. Grip strength has been found to be a reproducible method for assessment of muscle strength [35–37]. Isometric knee extensor strength has also been commonly used for assessment of muscle strength and has shown feasibility in frail older subjects [38, 39], although there is limited reference data available [40–42].

The international working group has recently recommended a series of tasks, entitled short physical performance battery (SPPB) as the standard evaluation of *physical performance* in research and clinical use [43, 44]. Other physical performance tests routinely used among the elderly include

gait speed [43], timed get-up-and-go test (TGUG) [45], stair climb power test (SCPT) [46].

**2.2. Osteoporosis.** Osteoporosis affects approximately 30% of the postmenopausal population. Osteoporosis is characterized by reduced bone mineral density (BMD) [47–51] and increased rate of bone loss [52]. The main determinants of BMD are the peak bone mass achieved by early adulthood, the bone loss associated with age, and menopause in women [53, 54]. Although the risk of fractures is greater among women with low BMD, it explains only part of the increased fracture tendency among the elderly [55]. This suggests that also other BMD-independent risk factors should be taken into account while evaluating the risk of fragility fractures [56]. The pathophysiology behind osteoporosis is, as with sarcopenia, multifactorial. Genetics, nutritional factors, lifestyle factors, and comorbidities have been shown to be associated with the disease [55–57]. In addition, factors related to falls have independent role in development of fragility fractures.

By definition, osteoporosis is a disease of increased skeleton fragility accompanied by low BMD and microarchitectural deterioration [58]. The golden standard for measuring bone material properties in clinical practice is axial DXA measurement from femur and spine. Bone mineral density (BMD) lower than  $-2.5$  SD below the young adults is considered osteoporotic and BMD between  $-1$  and  $-2.5$  osteopenic. Peripheral methods, for example, peripheral quantitative computed tomography (pQCT) for assessment of bone microarchitectural properties, have been developed, but they have not supplanted central DXA as diagnostic method.

### 3. Interaction between Postmenopausal Sarcopenia and Osteoporosis: The Potential Role of Common Acquired Risk Factors

Sarcopenia and osteoporosis have been thought to coexist [59]. Several studies have shown a positive association between lean mass and BMD in postmenopausal women [60–62]. Appendicular skeletal muscle-mass-related relative skeletal muscle mass index (RSMI), which has been used for definition of sarcopenia, has been suggested to be positively related to BMD [63]. The correlation of RSMI with BMD, however, may be significantly affected by differences in physical activity [63]. Nevertheless, the positive association between sarcopenia and osteoporosis has not been shown constantly across different studies [64]. Classically, it has been suggested that changes in bone mass are mediated through interaction with muscle strain via the sensory function of osteocytes [65]. This mechanostat theory has also emphasized the substantial role of estrogen in controlling the muscle-bone unit which makes postmenopausal women an especial target of interest. Consequently, there seem to be several factors that significantly contribute to the interaction between sarcopenia and osteoporosis.

The evidence behind the synergism between sarcopenia and osteoporosis should be viewed from the perspective of

the three modalities of sarcopenia, that is, muscle mass, strength, and function and the two modalities of osteoporosis, that is, BMD and fractures. Essentially, this interaction should also be considered from the view of common etiologic risk- and preventive factors. Indeed, many such factors are closely related to menopausal transition and age group of the postmenopausal population. The following paragraph concentrate on the common etiologic factors excluding secondary factors related to specific morbidities.

**3.1. Genetics.** Muscle and bone tissues have common mesenchymal precursor [66, 67]. During the growth, bone and muscle tissues exert significant allometry [68, 69]. Thereafter, during the adulthood, the functional properties between the two components of musculoskeletal system are functionally closely associated, and bone loss as well as muscle strength are positively correlated [70]. In the late years of the lifespan, the loss of both muscle and bone tissue shows parallel decline and may have genetic control [66, 71]. There are several gene candidates involved in the genetic control of musculoskeletal interactions [72–74] which are holistically reviewed in detail recently [69]. However, the whole process of maturation, development, and decline of musculoskeletal system is significantly affected, besides genetics, by environmental factors [75].

The heritability of lean mass, measured with DXA, has been estimated to vary between 56% and 84% [76, 77]. With regards to muscle strength and power, genetic effects explain 30%–50% in postmenopausal age group [77, 78]. Analogously, the heritability of bone strength, measured with section modulus of femoral neck, has been reported to be 40 to 55% [76]. Lean mass and areal BMD seem to have common genetic effects that contribute to the interaction between these traits [76, 79]. This association is likely to be multigenetic. A recent study found that muscle cross-sectional area and structural bone strength share genetic effects in the postmenopausal age group [80].

*To conclude, components of muscle and bone strength are significantly controlled by genes. Furthermore, bone and muscle strength may essentially share genetic effects.*

**3.2. Aging and Hormonal Changes in Menopause.** Peak muscle strength is achieved in the early 40s after which muscle strength gradually declines [81, 82]. After the age of 50, muscle mass has been reported to decline 1–2% per year [83] and muscle strength 1.5% to 3% per year [84–87]. Elderly women lose muscle performance more rapidly than do their male counterparts [88, 89]. It has been estimated that the decline of muscle strength attributable to the menopause accounts for an approximately 10–15% extraloss in addition to that purely related to age [88, 89]. The loss of muscle strength during the menopause has been linked to estrogen depletion [90, 91], evoked by exhaustion of ovarian function during the perimenopausal years. Plasma estrone and estradiol levels have been reported to be associated with muscle mass in women [92]. This effect may be mediated directly through estrogen receptors in skeletal muscle [93] or indirectly through the effects of proinflammatory cytokines [94]. In

addition, it has been shown that hormone therapy maintains muscle strength and performance [95–98] although this affect has not been observed constantly across studies [99, 100]. The natural menopausal transition seems, however, not to accelerate the decline in functional ability (such as get-up-and-go test or modified Cooper test) to the same extent in comparison to muscle strength [88]. These findings emphasize the different roles of muscle mass, strength, and function in development and evaluation of sarcopenia. In addition to menopause-related female hormonal changes, several other mechanisms, related to hormonal changes, accumulation of free radicals, nutrition, and physical activity among the others, may also contribute to sarcopenia in aging population which partly occurs simultaneously with menopause [91]. Consequently the exact contribution and mechanism by which menopause affects muscle tissue is still not fully resolved.

Menopausal transition is the most important and inevitable single factor in the evolution of postmenopausal osteoporosis [53, 54]. At the beginning of menopause, the acute loss of the restraining effect of estrogen on receptors on the membranes of osteoblasts and osteoclasts leads to accelerated bone turnover, uncoupling bone formation from resorption [101–103]. The closer molecular mechanisms of estrogen-depletion-related bone loss have been linked to the overproduction of bone resorptive cytokines (RANKL) [103]. In addition, imbalance between calcium secretion and absorption following the estrogen depletion has been suggested to influence the accelerated bone loss rate [104]. It has been shown that menopausal transition is associated with both increased bone loss rate, reduced BMD, and increased fracture incidence [105–110]. The phase of the most accelerated bone loss takes place at the very beginning of menopause (amenorrhea phase) after which the bone loss rate becomes progressively diminished for several years during the early postmenopause [105–111]. Some differences have been observed in the pattern of menopausal bone loss between different skeletal sites which may be related to the different composition of these sites with respect to cortical and trabecular bone [112, 113]. Perimenopausal bone loss rates of over –2 percent/year in spinal and over –1 percent/year in the femoral region have generally been reported [105, 106, 110, 111, 114]. In postmenopausal women, age-related bone loss continues at age-specific rate after the initial fastening during the menopausal transition [112]. In women over the age of 60 years, the risk of fracture has been shown to increase 6% per year [115]. The significant role of female hormones for bone health is further supported by the finding that HT prevents postmenopausal bone loss and decreases the risk of fractures [116–120] with 34% reduction in vertebral and 13% reduction in nonvertebral fracture incidence [121].

*To conclude, female hormones essentially regulate both muscle and bone health during the postmenopause and thus play significant role in development of sarcopenia and osteoporosis. These may be, to some extent, prevented by HT. Aging aggravates the effects of estrogen depletion on bone and muscle loss.*

**3.3. Body Weight and Composition.** In postmenopausal age group, there is a significant positive correlation between body weight, fat mass, lean tissue mass with BMD [70]. However, there are some specific differences in response of muscle and bone tissue to weight, weight change, and fatness.

In healthy young subject, bone and muscle grow in harmony with weight increase because of gravity-stimulated mechanoreceptors [122, 123]. However, being overweight impairs physical activity in all age groups. High BMI has been previously found to predict poorer quality of life particularly in the areas of physical functioning and health perceptions [124, 125]. Increase in BMI in postmenopausal population is predominantly due to increase in fat mass with significantly lower contribution of lean mass [126]. The increased prevalence of functional limitations and disability with increasing BMI has been repeatedly reported, although the relative increase in muscle mass with increasing BMI might explain some discrepancies between genders [127–130]. The decline in physical activity due to obesity may contribute to the development of sarcopenia [131]. In addition, the fat and muscle tissue may be inversely controlled through certain metabolic pathways, including inflammatory cytokines [132], insulin resistance [133, 134], and effects of growth hormone [135]. These factors may result in condition termed “sarcopenic obesity” [136, 137]. The prevalence of sarcopenic obesity has been suggested to be around 4 to 12 percent [136, 138]. Sarcopenic obesity has been proposed to be associated with disability and functional decline [138, 139]. Other studies, however, have linked this disability to only obesity itself [138].

Weight loss has been suggested to contribute to the development in sarcopenia in aging population although it has been argued that, during weight change, a greater proportion of lean mass than fat mass is conserved [140]. However, weight loss interventions combining adequate diet and exercise have been suggested to improve muscle strength and quality with simultaneous fat loss [141]. This also aligns the conception that there is a tight connection between adiposity and muscle function. Weight-loss-related bone loss has been found to be reduced in postmenopausal subjects with good muscle strength [142].

Body weight and weight changes are positively linked to BMD and its changes in postmenopausal women. Weight and weight increase are associated with the maintenance of BMD and reduced bone loss whereas thinness and weight loss lead to low BMD and enhanced bone loss in early and later postmenopause [143–145]. In addition, high body weight is a strong independent predictor of lower postmenopausal fracture incidence, especially of the hip [146]. These effects may partly be linked with fat-tissue-related estrogen production [5]. It has been found that HT may counteract weight-loss-related bone loss in postmenopausal women, which supports the role of estrogen in fat-bone interaction [147]. Mechanical load as such is likely to lead to bone strengthening with mobility-induced weight-bearing stress. In addition, hormones that regulate fat tissue metabolism, leptins, have been suggested to be involved in the regulation of bone metabolism [148, 149]. The heavier population also has a higher nutritional intake and may

thus consume more calcium and other bone-preserving products. In addition, the differentiating role of muscles and fat in weight-related bone mass changes remains unclear. It has been hypothesized that lower hip fracture incidence among the obese is related to higher soft tissue padding, not bone strength itself [150]. Indeed, increased fracture risk in appendicular sites has been linked to obesity [150]. Part of the observed BMD changes related to weight alterations may be due to methodological difficulties encountered in the measurement techniques adopted to deal with body compositional factors, most importantly fat tissue [62, 151].

*To conclude, fatness is related to higher lean and bone mass, and weight loss generally causes bone and muscle loss in postmenopausal age group. However, obese women may have unique etiology behind sarcopenia (sarcopenic obesity) and increased risk of osteoporotic fractures (appendicular fractures).*

**3.4. Physical Activity and Exercise.** Bone cross-sectional area is associated with muscle cross-sectional area [152], and lean mass correlates with areal BMD [153]. In addition, muscle volume and estimated torque of muscles have been suggested to explain differences in structural bone strength [154]. Consequently, the positive association between muscle and bone tissue has been suggested to be a result of the forces that muscles exert on the bones [155].

Inactivity is a well-demonstrated cause of significant loss of muscle mass and strength at all ages [156, 157]. Moreover, there are differences in effects of different types of physical activity with regards to response of muscle tissue. While aerobic exercise contributes less to muscle hypertrophy in comparison to resistance training, it has significant impact on protein synthesis, satellite cell activation, and increased muscle fiber area [158–160]. Aerobic exercise may also decrease the body fat infiltration of muscle tissue improving the functional properties of muscle system relative to body weight. Resistance training, however, significantly improves the muscle mass, strength, and their interaction in postmenopausal age group [27, 161]. Interestingly, the effects of resistance training may have muscle-quality-improving effects even among the frail older population [162–168]. However, the amount of training, whether aerobic or resistance type in nature, may need intensity more than typical for leisure type of physical activity in order to have significant effects [169]. From the clinical viewpoint, an important facet of the effects of exercise on muscle tissue is that prevention of sarcopenia with exercise may not have sufficient power to occur at short period of time, especially among the elderly [170, 171]. Consequently, it is widely accepted that prevention of sarcopenia should be carried out throughout the lifespan.

It has been postulated that both decreasing muscle activity and muscle mass are the main causes of bone loss during aging [172]. Furthermore, in experimental models, mature skeleton is less sensitive to exercise-induced peak muscle strain than growing bone [173]. In adult bone exercise most likely induces conservation rather than gains in strength [174]. According to previous studies, muscle strength, impact, and nonimpact exercise as well as the overall physical activity level are positively associated with

BMD, bone loss rate, and fracture risk [5, 62, 144–177]. Analogously, immobilization has been demonstrated to accelerate bone loss rate [178]. Certain appendicular muscle strength measures, most importantly grip strength, have been demonstrated to correlate well with the overall muscle performance and strength [35, 179]. Grip strength may have diagnostic value for prediction of fractures [176] and selection of patients to BMD measurements [180]. It has been suggested, that in elderly women's lean mass correlates with BMD irrespective of body site but that the association between muscle strength and BMD is site-specific [62].

Functional capacity has been shown to be associated with higher BMD and predict fractures in postmenopausal women [180, 181]. Kärkkäinen et al. found that standing on one foot (SOOF) less than 10 seconds increased the risk of hip fracture 9-fold, and self-assessed ability to walk less than 100 m increased the risk of clinical vertebral fractures 4-fold and hip fracture 11-fold in postmenopausal population [181]. Moreover, a recent Cochrane review on the effects of exercise on preventing and treating postmenopausal osteoporosis concluded that especially weight-bearing exercise is effective in increasing BMD, although exercise seems not to prevent fractures during the first two years of therapy [182].

*To conclude, muscle and bone strength are directly positively linked. Physical exercise has both muscle and bone tissue maintaining capabilities in postmenopausal women.*

**3.5. Vitamin D.** There are two forms of vitamin D, ergocalciferol (vitamin D<sub>2</sub>) and cholecalciferol (vitamin D<sub>3</sub>). Cholecalciferol is the metabolically active form of vitamin D. Vitamin D is produced with either the effect of ultraviolet B radiation or ingested with nutrition, and the metabolically active form is produced in the kidneys.

Vitamin D receptor is present in skeletal muscle [183]. Vitamin D deficiency affects predominantly weight-bearing muscles of the lower limb [184, 185]. Previous studies have shown that vitamin D levels are positively associated with muscle power, function, and physical performance [186, 187]. Doses of 400 IU vitamin D may not be sufficient to improve muscle function in nondepleted population. Nevertheless, in vitamin-D-deficient subjects, vitamin D 400 IU, with calcium 800 mg, has been reported to improve gait speed and body sway [188]. In the age group of the postmenopausal population, vitamin D 800 IU with calcium 1000 mg has shown to improve muscle function [189, 190]. Patients with low 25(OH)D levels have been shown to have impaired functional performance, psychomotor function, muscle strength and increased falling tendency [191, 192]. Previously, vitamin D has been reported to improve postural and dynamic balance [193]. Although it has been suggested that calcium supplementation is necessary for optimal action of vitamin D [194], combined vitamin D with calcium is superior to calcium alone in reducing the number of falls [190]. In the postmenopausal age group, low vitamin D and calcium intake and renal insufficiency may result in mild secondary hyperparathyroidism [195]. Indeed, low vitamin D and high parathyroid hormone levels have been found to increase the risk of low muscle mass and strength in postmenopausal population [195].

Vitamin D, combined to calcium, has been shown to decrease bone loss in adults and the elderly [196]. It has been postulated that serum 25(OH)D is a more important predictor of hip BMD than calcium intake [197], and correction of vitamin D hypovitaminosis has been demonstrated to result in increases in BMD [198]. Nevertheless, the protective effects of vitamin D have not been showed constantly [199], and, in postmenopausal women with adequate vitamin D levels, calcium supplementation may be as effective as vitamin D [200]. A recent Cochrane review on effects of vitamin D and vitamin D analogues on prevention fractures associated with involutional and postmenopausal osteoporosis concluded that vitamin D alone is unlikely to prevent fractures while supplementation with calcium does appear to prevent fracture in institutional care [201].

*To conclude, vitamin D is essential in physiological-processes-related muscle strength, function, and bone strength. Vitamin D substitution may prevent fractures and functional decline in postmenopausal women.*

#### **4. Interactive Consequences of Osteoporosis and Sarcopenia: Falls and Frailty Syndrome**

**4.1. Falls.** An important common consequence of sarcopenia is tendency to fall which, together with osteoporosis, lead to fragility fractures. One-third of individuals aged 65 and older fall at least once each year, and about half of these fall twice or more [202, 203]. Of these falls 3–6% lead to fractures [202, 204] typically distal radius, proximal humerus, and hip [205–207]. Falls have complex and diverse causes. Maintenance of posture requires visual, tactile, proprioceptive, and vestibular competence, central processing, and coordinated motor response [208, 209]. Furthermore, ankle flexibility, plantar tactile sensation, and muscle strength have role in balance [210]. In addition, there are several comorbidities and medication that increase the risk of falling.

It has been shown that the upper and lower body weakness is adversely related to falls [211]. Lower extremity weakness is better predictor of falls than weakness of the upper body. Moreover, several single-intervention strategies for fall prevention have proven to be beneficial. Strength and balance training reduces both noninjurious and injurious falls [212–217]. However, multifactorial fall prevention has not been shown to have positive effect constantly [218, 219].

There are two main determinants for fragility fractures: bone material quality and tendency to fall. Vertebral fractures in the elderly population may occur without falls, while the incidence of other fractures is dependent on the tendency to fall. The most number of fragility fractures occur among women without osteoporotic BMD [220] although the risk of fracture is higher in women with low BMD. The risk of falling has been more closely related with limb fracture risk than BMD [221], and postmenopausal women with the highest physical activity level may have moderately higher wrist fracture incidence despite of lower bone loss rate [222].

*To conclude, falls are more frequent in sarcopenic subjects and especially increase the functional decline among osteoporotic subjects.*

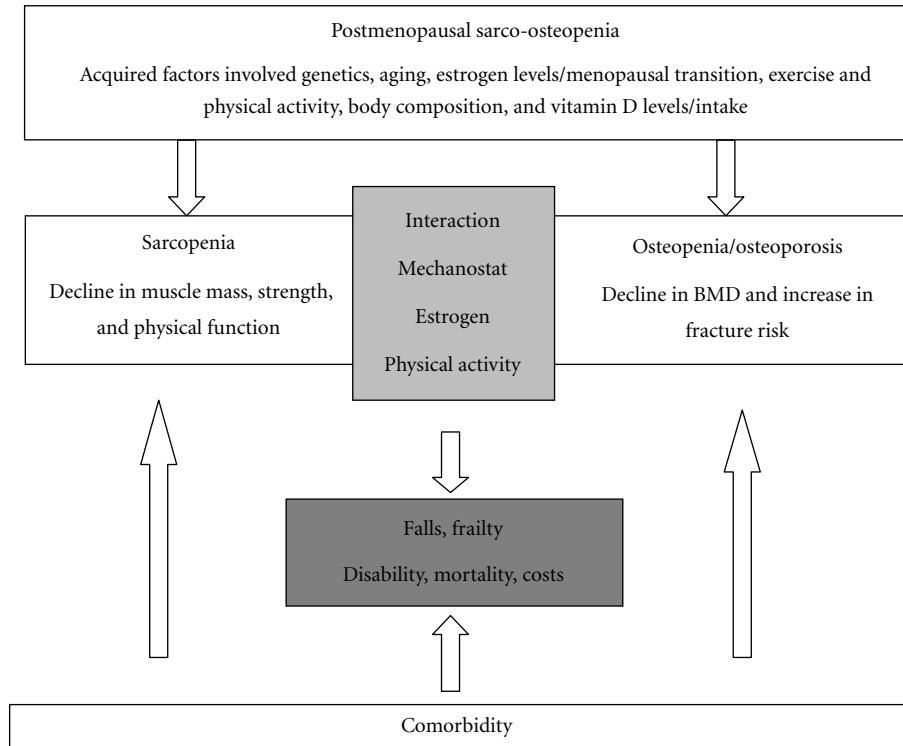


FIGURE 1: Dimensions of postmenopausal sarcopenia, osteoporosis, and frailty syndrome.

**4.2. Frailty Syndrome.** By definition, central element defining frailty is a state of great vulnerability of an aged subject when confronted by a stressor. Components of sarcopenia are substantially included into the concept of frailty among the elderly. Frailty syndrome has been defined as a clinical syndrome in which three or more of the following criteria are present: unintentional significant weight loss, self-reported exhaustion, weakness (measured with grip strength), slow walking speed, and low physical activity [223]. Given this frame, it has been postulated that sarcopenia and related poor muscle strength limits mobility and physical activity and thereby reduces total energy expenditure and nutritional intake, which, in turn, lead to weight loss and further aggravate sarcopenia [224]. Previous studies have indicated that the components of both sarcopenia and frailty syndrome are significant and independent risk factors of disability and death [225, 226]. A recent study found a strong association between this commonly used definition for the frailty syndrome and lower extremity indexes of body composition [226]. Frail's older persons had lower muscle density and muscle mass and higher fat mass. Moreover, in an analysis of the single criterion composing the frailty score, physical inactivity was the strongest correlate of body composition. However, as with definition of sarcopenia, the uniform criteria for frailty syndrome have not fully developed and should be reassessed across populations. Furthermore, osteoporosis and bone fragility may be considered to further aggravate the consequences of frailty syndrome. Presently, the criteria of frailty syndrome does not include assessment of osteoporosis or BMD. However, previous studies have shown associations between components of osteoporosis and

frailty syndrome [227] and have been reviewed thoroughly recently [228]. Furthermore, a recent study by Frisoli et al. has demonstrated, that osteoporosis plus sarcopenia have concomitant impact on frailty status in elderly women [229]. It was found that, in the presence of both sarcopenia and osteoporosis, the odds for frailty were over two times higher (OR 6.4) than those in presence of either syndrome alone (OR 3.1 for sarcopenia and OR 2.1 for osteoporosis). It must be reminded, however, that clinically significant frailty generally occurs decades after the menopausal transition itself.

*To conclude, frailty syndrome presents the most aggravated form of increased morbidity among sarcopenic plus osteoporotic subjects.*

## 5. Conclusions

Figure 1 summarizes the associations between postmenopausal osteoporosis, sarcopenia, falls, and frailty syndrome.

Postmenopausal women are at risk of both osteoporosis and sarcopenia. There is evidence that these two conditions coexists and share similar risk factors. Both sarcopenia and osteoporosis are strongly linked not only to aging but also to estrogen depletion and thereby to menopausal transition. This makes the postmenopausal population a significant target group for prevention of both sarcopenia and osteoporosis.

While the associations between muscle strength, muscle mass, and functional capacity with clinically relevant endpoint of osteoporosis, that is, BMD and fractures, have been

reported, there are no studies addressing the associations between three stages of clinical sarcopenia, that is, presarcopenia, sarcopenia, and severe sarcopenia. The associations of the three modalities of sarcopenia with osteopenia, osteoporosis, and severe osteoporosis remain unexplored. An essential part of the diagnosis of both osteoporosis and sarcopenia includes DXA, which allows simultaneous assessment of both conditions. The future research should concentrate on exploring the clinically relevant dimensions and interactions of sarcopenia and osteoporosis.

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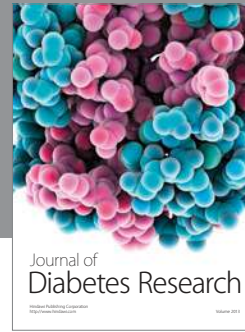
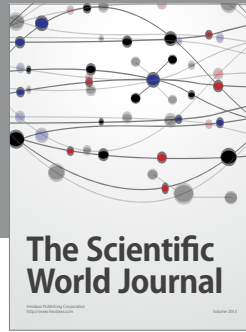
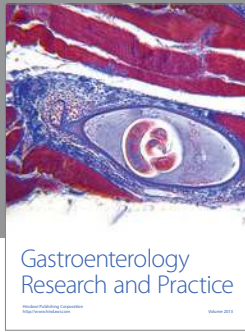
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