

1 *Review*

## 2 **How Exercise and Dietary Intervention Affect the** 3 **Outcome of Osteosarcopenic Obesity Syndrome?**

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9 **Abstract:** Osteosarcopenic obesity (OSO) is described by the simultaneous presence of  
10 osteopenia/osteoporosis, sarcopenia, and increased adiposity. Over time, older adults with OSO  
11 syndrome might be at greater risk for loss of physical function and bone fractures. Furthermore, a  
12 sedentary lifestyle, inadequate nutrition, pharmaceutical drugs and chronic conditions encompass  
13 the multifactorial nature of OSO syndrome. Physical activity and a healthy diet play a crucial role  
14 in management and treatment of OSO syndrome. Research has shown that even low-intensity  
15 physical activity or daily habitual activity can maintain bone mineral density, muscle strength and  
16 improve muscle quality, and reduce adiposity. However, older adults with high risk of fall and  
17 injuries require tailored exercise intensity. Also, balanced daily intake of vitamin D, calcium and  
18 protein is important in prevention and treatment of OSO syndrome in postmenopausal women.  
19 Effective measurement of bone mass, muscle mass and strength is required when detecting OSO  
20 syndrome and to evaluate the balance, strength and endurance of elder individuals and severity of  
21 the condition.

22 **Keywords:** Osteosarcopenic Obesity; Exercise; Diet; Aging; Fall

23

### 24 **1. Introduction**

25 Osteosarcopenic obesity (OSO) syndrome is accompanied by changes in body composition  
26 including deterioration of bone mass (manifested as osteopenia/osteoporosis), decline in muscle  
27 strength and muscle mass (sarcopenia), and increased presence of adipose tissue or fat redistribution  
28 in the abdominal region and its infiltration into bone and muscle [1,2]. Although OSO syndrome has  
29 been previously diagnosed among younger individuals [3], the older adults (specifically  
30 postmenopausal women over the age of 65) and patients with chronic conditions have a particular  
31 higher risk for OSO syndrome [2,4]. Specifically, in older women, there is an age-related loss of bone,  
32 lean mass and muscle strength, and gain in adiposity [4]. It is important to take into consideration  
33 that young obese individuals with decreased lean body mass have a higher chance of developing  
34 OSO syndrome and frailty earlier than healthy lean individuals [3].

35 Given the severe consequences of OSO syndrome on general health status and quality of life the  
36 elderly population, early prevention measures are required to evaluate its progression and halt its  
37 advancement. Therefore, the purpose of this document is to give an overview of the literature  
38 regarding the precise pathophysiologic processes, diagnostic criteria, and effective physical  
39 measurements to evaluate the severity of OSO syndrome. The current review will look into the  
40 management of OSO syndrome through diet and exercise, as well as its relationship with fall risk.

41 Aging is not only associated with increased adiposity, but also with fat redistribution and  
42 infiltration into the bone and muscle tissues [1,5]. Skeletal muscle, bone and fat masses are all derived  
43 from shared mesenchymal stem cells [6]. When the body is affected by systemic low-grade  
44 inflammation, it will result in exacerbated adipogenesis and suppressed osteoblastogenesis and  
45 myogenesis in adults [7–10]. Visceral adiposity has a negative impact on bone and muscle health by  
46 promoting low-grade chronic inflammation [11,12]. Adipose tissue is involved in secreting pro-

47 inflammatory cytokines such as tumor necrosis factor-alpha, interleukin 1 and 6, and C-reactive  
 48 protein [7,13–16]. Therefore, excess adiposity, which itself is associated with increased secretion of  
 49 inflammatory mediators may decrease osteogenesis and myogenesis [7,9].

## 50 2. Diagnostic Criteria

51 The criteria for the diagnosis of OSO syndrome is based on the combination of diagnostic criteria  
 52 reflecting bone, muscle, and fat impairment. Ilich *et al.*, [2] used a combination of several criteria for  
 53 diagnosing OSO syndrome which include: a) *T*-scores  $\leq -1.0$  SD of the lumbar spine (L<sub>1</sub>-L<sub>4</sub>) and/or  
 54 femoral neck [17], b) The 20<sup>th</sup> percentile of the residual distribution for appendicular lean mass (ALM)  
 55 with cut-off point  $\leq -1.43$  for diagnosing sarcopenia [18] and c) body fat  $\geq 32\%$  DXA [18]. The current  
 56 diagnostic criteria are based on several recent studies [19–23]. Refer to **Table 1** for detailed diagnostic  
 57 criteria of OSO syndrome based on *T*-score and body composition.

58 **Table 1.** Diagnostic criteria of OSO syndrome based on bone density and body composition.

Condition	<i>T</i> -score $\leq -1.0$ SD at the femoral neck, or lumbar spine	<20 <sup>th</sup> percentile of ALM for women	Fat mass $\geq 32\%$ for women
Osteopenia/ osteoporosis	Yes	No	No
Sarcopenia	No	Yes	No
Obesity	No	No	Yes
OSO	Yes	Yes	Yes

59 ALM: appendicular lean mass; OSO: osteosarcopenic obesity

60  $ALM = -17.4 + 18.3 \times \text{height (m)} + 0.16 \times \text{body fat (kg)}$

## 61 3. Diet and Exercise in OSO Population

62 Elderly population face a challenge to follow a healthy diet due to diminished appetite, changes  
 63 in taste and smell, poor dentition and chronic diseases [24]. Moreover, absorption of many nutrients  
 64 decreases with aging [4,24]. Diet plays a vital role in maintaining bone health and body composition.  
 65 A recent study showed women with OSO syndrome have a lower daily intake of vitamin D and  
 66 calcium (diet and supplements) in comparison to those who were osteopenic obese, only osteopenic,  
 67 sarcopenic, or obese [20], suggesting potential health benefits of maintaining an adequate intake of  
 68 vitamin D and calcium. Moreover, low serum vitamin D concentration has been observed in  
 69 population with the OSO syndrome [25]. Insufficient protein intake can increase muscle wasting in  
 70 aging adults [26,27]. Based on a recent recommendation for OSO population, high protein diet (1.4-  
 71 1.6g/kg/day) is required to maintain the muscle quality and muscle mass [28]. Also, a recent study on  
 72 postmenopausal women showed a significant positive correlation between the total amount of  
 73 protein intake and right femoral neck bone mineral density and *T*-score [20]. However, it is important  
 74 to balance high protein diet with calcium and vitamin D, as extensive high protein diet is associated  
 75 with increased urinary calcium excretion, which may affect bone mineral density [29,30]. Aside from  
 76 energy imbalance and lower protein intakes, it has been revealed that high level of simple  
 77 carbohydrates and low omega-3 polyunsaturated fatty acids may also contribute to OSO syndrome  
 78 [28,31]. It is also worth noting that elderly including frail women living in an assisted living facility  
 79 or living alone tend to rely on someone else for food preparation. This life-style may result in reduced  
 80 protein and total energy intake [32,31].

81 Considerable evidence exists regarding the fact that low physical activity combined with  
 82 inadequate nutrients intake may further aggravate the decline in muscle protein synthesis and  
 83 contribute to muscle loss in older adults [31,33,34]. Resistance training may reduce fat mass [35] while  
 84 improving bone mineral density [36,37]. A recent study by Cunha *et al.*, showed that 12-week  
 85 resistance training is effective to improve the risk factors of OSO syndrome among older women ( $\geq$   
 86 60 years old) [38]. In another study with a longer duration of intervention (12-month exercise  
 87 program combining aerobic step, flexibility/postural control training and resistance training) on

88 postmenopausal Caucasian women revealed an increase in skeletal muscle mass [39]. It is clear that  
89 resistance and aerobic exercises require at least some level of functionality in the elderly population.  
90 However, aging is often associated with comorbidities, in addition to the physical changes to bone,  
91 and body composition [4,40]. There are many barriers to exercise for frail population due to their  
92 physical limitations [41]. Therefore, conventional resistance and aerobic exercises may not be the best  
93 viable option for OSO population as the first line of treatment. Unconventional activities (Tai chi,  
94 Yoga, Pilates, etc.) might be more suitable for older population [28,42]. The results of several studies  
95 on the effects of Tai Chi in sedentary obese women suggest that it could result in fat mass loss [43,44].  
96 Moreover, Tai Chi may help in maintaining bone mineral density and improving body composition  
97 [42]. Similarly, a 6-month study with Yoga exercise intervention showed a significant improvement  
98 in balance (timed one-legged stand and forward flexibility) in the elderly population (65-85 years)  
99 [45]. In addition, an 8-week Pilates exercise program on postmenopausal women (>60 years old)  
100 revealed a significant decrease in percent body fat and increase in lean body mass [46]. The effect of  
101 Tai chi, Yoga and Pilates on OSO population has not been widely studied. Regardless, there is enough  
102 evidence to suggest that these activities have the potential to be used for treatment or prevention of  
103 OSO [42,47]. Nevertheless, more research is needed in this area.

104 On a different note, in the past few years, research has looked into the effects of whole body  
105 vibration on bone mineral density and body composition. Whole body vibration seems to be an  
106 alternative treatment option for older population who are not able to perform conventional exercise  
107 due to chronic conditions such as chronic obstructive pulmonary disease [48], chronic heart failure  
108 [49], etc. Three whole body vibration sessions per week for 12 weeks may increase leg power and  
109 bone formation in older individuals [50]. Moreover, the results of several meta-analyses suggest that  
110 whole body vibration may improve bone mineral density in postmenopausal women and reduce the  
111 risk of fall and fracture [51,52]. Therefore whole body vibration seems to be a promising intervention  
112 for treatment of OSO syndrome.

113 Prescribing exercise (even in the form of low intensity or habitual activity) is needed to maintain  
114 or improve bone mineral density [42,53–56], maintain muscle strength and muscle quality, reduce  
115 adiposity and improve balance [42,57,47]. A significant negative correlation has been reported  
116 between total hours of unconventional physical activity/week and waist circumference in  
117 postmenopausal women. In addition, total hours of habitual physical activity (gardening,  
118 housework, etc.) and the average number of steps climbed were negatively correlated with total body  
119 fat percentage, body mass index (BMI), hip and abdominal circumference [20]. Thus, even low-  
120 intensity exercise or habitual activities may maintain the bone mineral density and muscle mass and  
121 reduce the risk of obesity for OSO syndrome. A recent recommendation for OSO population has  
122 emphasized the importance of comprehensive exercise program matched with the balance and  
123 strength of each individual [28,42]. The goal is to improve functionality, quality of life, and most  
124 importantly preventing falls.

#### 125 **4. Physical and Functional Performance Tests to Evaluate OSO Syndrome**

126 Decreased physical function by aging can indicate an increased risk for morbidity and long-term  
127 disability [34,58]. Specific measurements are required to evaluate balance, strength and endurance in  
128 the older population. Handgrip strength, knee isometric strength, sit-to-stand test (to measure lower  
129 body strength, balance and range of motion), 4-meter timed normal and brisk walk tests (to measure  
130 locomotion), 2-minute walk test (to measure endurance), and timed one leg stance (to measure  
131 balance) are all parts of the recommended measurements for OSO syndrome [2,59–61]. These tests  
132 are valuable measurements to assess fall risk and evaluate changes or deficits in body composition  
133 preceding OSO syndrome.

134 Handgrip strength has been used as a powerful predictor of functional abilities in older adults  
135 [62,63]. Several studies reported that loss of handgrip strength is associated with lower bone mineral  
136 density [64,65]. Moreover, poorer handgrip strength is associated with increased risk of falls [62,63].  
137 Women identified with OSO syndrome have a poorer handgrip score in comparison to only obese

138 population [22]. Furthermore, lower handgrip strength is reported to be associated with malnutrition,  
139 which exacerbates the loss of bone and lean mass [66,67].

140 Some researchers view muscle quality as a more reliable measurement of functional status than  
141 strength alone [68]. Muscle quality can be measured as maximal force production per unit of muscle  
142 mass [68]. A one-repetition max from the knee extension divided by leg lean mass (kg) has been used  
143 as a measurement of muscle quality [69]. Results of a recent study revealed that older adults with  
144 OSO syndrome had significantly lower knee extension scores than the individuals identified by only  
145 obese or osteopenic obese which may further reinforce the association between the combined impact  
146 of bone loss, sarcopenia and obesity with the overall loss of fitness [19]. Although aging, myosteatorsis  
147 and chronic diseases affect the muscle quality, strength training can improve the condition [4,68,70].

148 Also, the sit-to-stand test has been used to measure balance and range of motion in the lower  
149 extremities [71–73]. Based on Center for Disease Control and Prevention (CDC) recommendation cut-  
150 off point of ten sit-to-stands in 30 seconds was used to determine the risk of fall [74]. Women ages 75-  
151 79 years who performed less than ten sit-to-stands were classified as “below average strength” for  
152 lower body evaluation. Poorer sit-to-stand test scores have been associated with slower walking pace  
153 [65,75]. Drey *et al.*, [76] found a statistically significant decline in sit-to-stand score in osteosarcopenic  
154 population in comparison to only osteopenic or only obese individuals. The sit-to-stand test has also  
155 been used to evaluate OSO population; lower sit-to-stand scores in older adults with OSO were  
156 reported in comparison to osteopenic obese, only osteopenic and only sarcopenic [19].

157 Walking speed is another predictor of functional status and frailty in older populations [77–79].  
158 Higher fat accumulation in the lower extremities is correlated with slower walking speeds [65]. In  
159 addition, higher femoral neck bone mineral density is associated with faster walking speed [64]. In a  
160 study conducted on postmenopausal women (age of  $61.6 \pm 7.4$  years), the OSO population presented  
161 the slowest normal and brisk walking speed in comparison to sarcopenic obese and osteopenic obese  
162 population [34].

163 In addition, the one-leg stance is a reliable assessment of balance in older adults [64,65]. The  
164 scores for this test decrease with age [2,80]. Balance impairment is associated with reduced gait speed  
165 [81]. A study conducted by Shin *et al.*, [65] revealed a 21% decrease in ability to stand with each leg  
166 (30 seconds) as total body and gynoid region fat increase by 1% in the older population.

167 Overall, the physical and functional test results of several studies reinforce the concept that older  
168 women with OSO syndrome are more prone to greater functional decline than those who have each  
169 aspect of this syndrome separately. A significant weakening in the OSO population in regard to sit-  
170 to-stand and knee extension scores and slower walking speed indicates a greater loss of strength in  
171 the quadriceps muscles.

## 172 5. Fall Prevention in OSO Syndrome

173 The increased risk of falls and hip fractures is probably of the greatest concern for the OSO  
174 population [34,47]. Fall-related injuries are one of the major causes of mortality and disability among  
175 the older individuals [82]. The intensity of exercise should never surpass the physical ability of older  
176 adult and it should not increase the risk of fall, as according to CDC falls are leading cause of injury  
177 and death in American older adults [83] and the second leading cause of accidental or unintentional  
178 injury deaths globally [84]. In addition, each year an estimated 646,000 individuals die from falls  
179 worldwide [84]. One out of every five falls causes serious injury such as head injury or bone fracture  
180 [83]. Moreover, one out of three fall-related deaths were attributable to low bone mineral density [82].  
181 Bone fractures, especially in the elderly, can lead to long-term disability, institutionalization and even  
182 mortality [85,86].

183 A number of risk factors related to falls have been identified. Being a female, independent living,  
184 previous history of falls, physical disability, use of a walking aid, fear of falling, Parkinson’s disease,  
185 vertigo and visual/sensory deficits were associated with higher risk of fall in community-dwelling  
186 older adults [87]. Moreover, a study on Mexican older adults (>60 years old) has shown obesity,  
187 depressive symptoms and urinary incontinence were significant factors associated with falls [88]. Fall  
188 risk factors can be classified as extrinsic factors which reflect medication and home hazards or



189 intrinsic factors which include overall functional status [47]. The previous history of falls, muscle  
190 strength, postural instability and fear of falling are independent predictors of fall in the older  
191 population [89–91]. It has also been reported that obesity concurrent with low muscle strength is  
192 associated with higher fall risk score among older adults [92]. Furthermore, persistent vitamin D  
193 deficiency in the elderly is associated with increased risk of falls and fractures [93]. The association  
194 of osteoporosis and sarcopenia with fall risk factors has been reported previously [94].

195 As OSO syndrome is a fundamental health challenge, a multifactorial approach should be  
196 considered to reduce the risk of fall and fracture. OSO individuals may benefit from comprehensive  
197 physical activity program, nutritional intervention and pharmacological treatment for preventing fall  
198 [28,47]. Since extensive diet-induced weight loss in older obese adults can lead to further impaired  
199 physical function by accelerating bone loss [97] and fat-free mass loss [98], a proper nutritional intake  
200 is principal in preventing fall and fracture. It is of paramount importance for the management of  
201 osteoporosis and the prevention of falls to achieve an adequate intake of calcium and vitamin D and  
202 also engage with healthy life-style habits. Active life-style and avoidance of tobacco, alcohol and drug  
203 consumption such as long-term use of corticosteroids (unless there is an indication) all have an  
204 important role in reducing the risk of fall and fracture [28,47,88]. It has also been described that  
205 vitamin D supplement may improve muscle strength, and reduce the risk of falls and mortality in  
206 postmenopausal women [99,100]. Moreover, active vitamin D treatment may prevent and treat both  
207 osteoporosis and sarcopenia [101].

208 Although physical activity alone has been described to have beneficial effects on reducing the  
209 risk of fall [102], combining exercise with other strategies including education has been shown to be  
210 even more effective [103]. The long-term balance training program and Tai Chi as an alternative have  
211 shown to be effective in improving functional balance and reducing the risk of fall in elderly women  
212 [104,105]. Furthermore, it has been described that a whole body vibration intervention reduces fall  
213 risk factors [106].

214 Also, a dramatic increase in the number of falls and fractures at the beginning of menopause has  
215 been linked to the decrease in estradiol serum concentrations [107]. Initiation of  
216 hormone replacement therapy soon after the menopause, has shown positive effects on balance,  
217 leading to a decrease in the risk of falls [108,109]. However, the results are still controversial [107],  
218 therefore more clinical trials are needed to approve the use of hormone replacement therapy to  
219 improve body composition and reduce the risk of fall.

220 As it has been previously discussed in the literature, increased body fat promotes damage to  
221 bone and muscle tissues simultaneously, weakening the bone structure and changing the muscle  
222 quality [1,4,40,110,111]. Compared to those who are only obese or sarcopenic, older adults with  
223 sarcopenic obesity have less physical strength and functional capacity and are at greater risk of falls  
224 and consequently long-term disability [95,112,113]. Finally, considering the complex nature of OSO  
225 syndrome, a multifactorial approach is recommended to reduce the risk of fall among elderly  
226 individuals.

## 227 6. Discussion and Summary

228 Aging causes numerous physiological changes in body composition, including a decrease in  
229 both muscle and bone mass and a gradual increase in fat mass [4,40,114]. An ultimate consequence is  
230 the development of OSO syndrome [40]. One of the main risks related to changes in body composition  
231 is the higher chance of fall and fracture. Physical activity and a healthy diet may slow the progression  
232 of OSO syndrome and reduce the risk of fall. It is worth considering that low-intensity exercises such  
233 as Tai chi, Yoga, Pilates, etc. or whole body vibration can be used as alternatives for conventional  
234 exercise (aerobic and resistance training) in prevention and treatment of OSO syndrome in older  
235 adults. It is recommended that practitioners consider the individuals' chronic conditions and  
236 limitations so that exercise could be altered according to the level of fitness and strength. Finally,  
237 OSO population should be monitored for daily levels of calcium, vitamin D and protein intake to  
238 ensure maintaining an optimal diet.

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