

# Sarcopenia in Menopausal Women: Current Perspectives

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**Abstract:** Menopause is associated with hormonal changes, which could accelerate or lead to sarcopenia. Functional impairment and physical disability are the major consequences of sarcopenia. In order to hamper these negative health outcomes, it appears necessary to prevent and even treat sarcopenia, through healthy lifestyle changes including diet and regular physical activity or through hormonal replacement therapy when appropriate. Therefore, the purpose of this narrative review will be 1) to present the prevalence of sarcopenia in postmenopausal women; 2) to address the risk factors related to sarcopenia in this specific population; and 3) to discuss how to manage sarcopenia among postmenopausal women.

**Keywords:** sarcopenia, menopause, hormones, physical activity, nutrition

## Introduction

Menopause is a non-pathologic condition occurring in all women and involving the permanent cessation of menses resulting from estrogen deficiency.<sup>1</sup> Clinically, a woman is considered to have menopause in absence of menses during at least 12 consecutive months. When the ovaries are removed through an ovariectomy, women who have not yet experienced natural menopause are considered to have surgical menopause.<sup>2</sup> During aging and menopausal transition, a progressive muscle degeneration occurs<sup>3</sup> which can lead to sarcopenia. Sarcopenia is a progressive and generalized skeletal muscle disorder that is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality.<sup>4</sup> According to the EWGSOP 2 (European Working Group on Sarcopenia in Older People), the criteria for defining sarcopenia are 1) low muscle strength, 2) low muscle quantity or quality, 3) low muscle performance.<sup>4</sup> The AWGS (Asian Working Group for Sarcopenia) estimates that sarcopenia should be described as 1) low muscle mass plus 2) low muscle strength and/or low physical performance.<sup>5</sup> Based on the ESPEN-SIG (European society of clinical nutrition and metabolism, Special interest group), the criteria for sarcopenia are: 1) low skeletal muscle mass and 2) low muscle strength (which they advised could be assessed by walking speed).<sup>6</sup> Sarcopenia is defined by The International Working Group on Sarcopenia (IWGS) as 1) the presence of low skeletal muscle mass and 2) low muscle function (which they advised could be assessed by walking speed).<sup>7</sup> Aging causes skeletal muscle atrophy. Age-related muscle atrophy (also called sarcopenia) is related to muscular and neuromuscular factors.<sup>8</sup> In fact, it has been demonstrated that in older adults, changes in exercise (inactivity, sedentarity and bed rest, etc.) and nutrition (malnutrition, protein deficiency, etc.) behaviors in addition to hormonal changes (estrogen or testosterone decreased<sup>9</sup>) lead to neuromuscular junction insufficiency, myofiber loss, mitochondrial dysfunction (fission, fusion, autophagy, mitophagy, Parkin, etc.), impairment on capillary blood flow, difficulty to repair and regeneration muscle capacity (mostly due to muscle satellite cell number decreased), fat infiltration, immune-senescence (ie, neutrophil migration such as PI3K) or inflammatory state (GDF-15; IL-6, TNF-alpha, etc.).<sup>10-13</sup> Overall these physiological alterations result to muscle protein degradation exceeding synthesis but also changes in muscle architecture or muscle composition (fat infiltration), muscle contraction.<sup>10-14</sup> As menopause is characterized by important changes in hormonal status, it is relevant to investigate the link between these changes and sarcopenia. In addition, developing efficient intervention for the management of

sarcopenia among postmenopausal women may be of great interest for both researchers and clinicians. This narrative review will (1) summarize the epidemiology of sarcopenia, and, especially in postmenopausal women; (2) present the risk factors related to sarcopenia in this specific population and (3) discuss how to manage sarcopenia among postmenopausal women.”

## Epidemiology

### Prevalence of Sarcopenia with Age

From the age of 30, muscle mass decreases by around 3% to 8% per decade and this decrease accelerates after the age of 60.<sup>15–17</sup> Indeed, after the age of 70, the loss of muscle mass declines by 0.5% to 1.0% per year.<sup>18</sup> However, this decline differs by sex. After 75 years, the loss is close to 1% per year in men while it is 0.7% per year in women.<sup>18</sup> A total muscle mass less than 2 standard deviations below the mean for young healthy reference populations is called « sarcopenia ».<sup>4</sup>

In general population, estimates of sarcopenia prevalence vary from 9.9% to 40.4%, depending on the definition used.<sup>19</sup> The prevalence of sarcopenia in community-dwelling older adults aged over 60 years is greater in men [11% (95% CI: 8–13%)] than in women [9% (95% CI: 7–11%)].<sup>20</sup> The prevalence of sarcopenia increases also with age.<sup>20</sup> Thus, the prevalence is 2.6% and 1.2%, respectively, in women and men aged 70–74 years while it is 31.6% and 17.4% in women and men older than 80 years.<sup>20</sup> The prevalence of sarcopenia also depends on the home setting. In nursing home, the prevalence of sarcopenia is 51% (95% CI: 37–66%) in men and 31% (95% CI: 22–42%) in women.<sup>21</sup> Among hospitalized older adults (>60 years), the prevalence is 23% (95% CI: 15–30%) in men and 24% (95% CI: 14–35%) in women.<sup>21</sup> In addition to age, sex and home setting, the prevalence of sarcopenia is also influenced by ethnicity. For example, the prevalence of sarcopenia is higher among non-Asian (men: 19%; women: 20%) than Asian (men: 10%; women: 11%) individuals in both sex.<sup>22</sup> Finally, women with Polycystic ovary syndrome (PCOS) have a high prevalence of sarcopenic obesity (ie, 53% of women with PCOS are classified as sarcopenic obese).<sup>23</sup>

### Prevalence of Sarcopenia Among Postmenopausal Women

An acceleration of muscle mass loss with the menopausal transition is observed.<sup>24</sup> Indeed, during the menopausal transition, lean body mass (LBM) decreased by 0.5% (a mean annual absolute loss of 0.2kg) while fat mass increased by 1.7% per year (mean absolute gain of 0.45kg).<sup>25</sup> Compared with postmenopausal women, premenopausal women have a greater appendicular lean mass (ALM:  $18.2 \pm 2.2$  vs  $17.8 \pm 2.1$  kg,  $p < 0.001$ ).<sup>26</sup> Moreover, being postmenopausal is associated with a higher risk of presenting with sarcopenia (odds ratio [OR] 2.99, 95% CI, 1.38–6.51).<sup>27</sup> In addition, in postmenopausal women, a significant difference in the prevalence of sarcopenia is reported according to the age: 1.4% in the 60–69 y group, 4.9% in the 70–79 y group and 12.5% in the  $\geq 80$  y group.<sup>28</sup> In younger postmenopausal women ( $57.8 \pm 4.5$  years), the proportion of pre-sarcopenic, sarcopenic, and nonsarcopenic women are 11.8%, 2.7%, and 85.6%, respectively.<sup>29</sup> Furthermore, the effects of hormone therapy (HT) on sarcopenia are controversial in the available literature. Some authors show that the prolonged use (<13 months) of HT is associated with a lower prevalence of sarcopenia in postmenopausal women (odds ratio: 0.60; 95% confidence interval: 0.41–0.88;  $P = 0.01$ ).<sup>24</sup> It has been also observed that even years after cessation of the therapy, a history of HT is positively associated with negating the loss in muscle quantity and quality<sup>30</sup> and in muscle mass.<sup>31</sup> Conversely, other authors state that sarcopenia is as common in non-obese women who are long-term HT users as in community-dwelling women not using HT, suggesting that HT does not protect against the muscle loss of aging.<sup>32</sup> Finally, the loss of skeletal muscle can possibly be improved by the re-establishment of young ovarian influence in aged mice.<sup>33</sup> These findings also reveal the complex concept of germ cell independent influence on sarcopenia.<sup>33</sup>

### Risk Factors for Sarcopenia Among Menopausal Women

In addition to well-known and no sex-specific factors such as low protein intake, low vitamin D intake, low physical activity, hormonal changes occurring during menopause are also important risk factors leading to sarcopenia.<sup>15,34,35</sup> The effects regarding hormonal changes of surgical menopause will be similar to those of natural menopause, but they may be more acute. This is because the hormonal changes will happen suddenly rather than over several years. The changes will generally start as soon as the procedure is over. The impact and role of the sexual and anabolic hormones involved are detailed below.

## The Decrease of Estrogens

First of all, it is important to differentiate 4 types of estrogens and their specific roles:

- Estrone (E1): Estrone (E1) can be converted into estradiol (E2), and serves mainly as a precursor or metabolic intermediate of estradiol.<sup>36</sup>
- Estradiol (E2): Estradiol is the most potent and most abundant estrogen during a woman's reproductive years. It has a beneficial effect on the skeletal muscle by stimulating satellite cell proliferation. Skeletal muscle can respond to estrogenic hormonal control due to the presence of specific receptors for E2 at the level of muscle fibers. Additionally, estradiol can limit inflammatory stress damage on skeletal muscle.<sup>3</sup>
- Estriol (E3): Levels of estriol rise during pregnancy, as it helps the uterus grow and prepares the body for delivery. Thus, estriol levels peak just before birth. In addition, emerging evidence indicates that estriol has potential immunomodulatory benefits for many disease states including autoimmune, inflammatory, and neurodegenerative conditions.<sup>37</sup>
- Estrerol (E4): Estrerol is produced, at detectable levels, only a few months during life, by the fetal liver during pregnancy and reaching the maternal circulation through the placenta. Its function is presently unknown.<sup>38</sup>

Estrogen, mainly E2, may be directly involved in muscle metabolism by binding to estrogen receptors expressed on skeletal muscle, as well as indirectly by altering the secretion of growth hormone (GH) and insulin growth factor 1 (IGF-1).<sup>39</sup> Estrogen may also play a role in regulating carbohydrate and lipid metabolism by relieving muscle glycogen and inducing lipid oxidation, which may influence skeletal muscle composition in postmenopausal women.<sup>40</sup> Therefore, the important decrease in estrogen levels with menopause may play a potential role in the muscle mass decline observed after the 5th decade of life.<sup>41</sup> In fact, the decrease in estrogen concentration is associated with an increase in pro-inflammatory cytokines [ie, tumor necrosis factor-alpha (TNF $\alpha$ ); interleukin-6 (IL-6)], which might explain the apparition of sarcopenia after menopause.<sup>42</sup> Another potential explanation is that loss of muscle estrogen receptors. Indeed, the number of estrogen receptors in muscle is higher among children, men and young women than in postmenopausal women.<sup>34</sup> Muscle strength and muscle power are also correlated with estrogen levels.<sup>43</sup> A significant decrease in muscle power is demonstrated in postmenopausal women.<sup>44</sup> Thus, it is known that the decline of estrogen levels and receptors contributes to the loss of muscle function and the development of sarcopenia in postmenopausal women.<sup>24</sup> The levels of E2 in postmenopausal women depend on confounding factors (eg, fat mass, fat distribution, ethnicity, HT). Obese postmenopausal women have higher E2 levels compared to non-obese ones.<sup>45</sup> The evidence also suggests that in postmenopausal women, fat loss can result in substantial decreases in estradiol levels.<sup>46</sup> Among postmenopausal women, fat mass follow a U-shaped distribution according to E2 levels.<sup>47</sup> Moreover, Non-Hispanic White women had higher total and bioavailable E2 levels than Hispanics, independently of age, type of menopause, waist circumference, alcohol intake or current smoking.<sup>48</sup> Hispanic women also have higher levels of bioavailable E2 than American-African women.<sup>48</sup> Compared with White women, Japanese American women had higher E2 and bioavailable E2 levels.<sup>49</sup> Mean levels in E2 in Hispanic women are similar to those of White women.<sup>49</sup> But in all cases, total levels of estrone, and estradiol, are significantly higher in HT users than in non-users.<sup>50</sup>

## The Decrease of Testosterone (Androgen Sexual Hormones)

Testosterone is a pleiotropic hormone that plays an important role in the human body. This sexual hormone plays a crucial role in the maintenance and growth of muscle in both men and women.<sup>51</sup> In addition, literature highlights direct anabolic effects of androgens on mammalian skeletal muscle.<sup>52</sup> Most testosterone circulates tightly bound to sex hormone-binding globulin (SHBG) or weakly bound to albumin. A minor amount circulates as free testosterone, and it is believed that this is the metabolically active fraction.<sup>53</sup> With aging, free-testosterone levels are decreased in men and this decline parallels the decrease in muscle mass and muscle strength.<sup>54</sup> In women, free-testosterone levels are decreased and this decrease is more important during the first years after menopause.<sup>55</sup> Thus, the decline in free-testosterone could also play a role in the accelerated muscle mass loss with menopause. There is a relationship between fat mass, fat distribution and free-testosterone levels. Indeed, both premenopausal and postmenopausal overweight women have higher free-testosterone levels compared with normal weight premenopausal and

postmenopausal women.<sup>56</sup> In addition, the evidence suggests that fat loss can result in substantial decreases in postmenopausal testosterone level.<sup>46</sup> Moreover, free-testosterone is positively associated with visceral fat, independent of confounding factors.<sup>57</sup> This suggests that testosterone could play a role in regional fat distribution.<sup>57</sup> There is also a relationship between ethnicity and free-testosterone levels. The literature reports that non-Hispanic white women have higher testosterone levels than Hispanic women independently of age, type of menopause, waist circumference, alcohol intake or current smoking.<sup>48</sup>

## The Decrease of Dehydroepiandrosterone (DHEA)

Dehydroepiandrosterone (DHEA) and its sulfate ester (DHEA-S) are the most abundant steroids in humans.<sup>58</sup> It is the main pro-hormone related to biosynthesis of testosterone and estrogen.<sup>59</sup> Its biological functions are: 1) DHEA, like other androgens, are responsible for the androgenic effects of adrenarche;<sup>59</sup> 2) DHEA is also a weak estrogen. It can be transformed into potent estrogens (eg, estradiol) in certain tissues and thereby produces estrogenic effects in these tissues;<sup>59,60</sup> 3) As a steroid and neurotrophin, DHEA has also important effects in the central nervous system.<sup>61</sup> DHEA, has a higher production between 25 and 35 years old and then gradually decrease over time,<sup>62</sup> especially at the time of menopause in women, reaching values sometimes as low as 10–20% of those encountered in young individuals.<sup>34</sup> Sarcopenia is thought to be related to discordant secretions of DHEA.<sup>63</sup> In fact, DHEA decline is associated with a decrease in muscle mass and physical performance.<sup>64</sup> The skeletal muscle is able to convert DHEA into active androgens and estrogens, and to stimulate IGF-1, which is important in muscle growth and recovery.<sup>65</sup> There is an association between levels of DHEA and obesity or ethnicity. Regarding obesity, several authors suggest that postmenopausal women with severe obesity are unable to increase the DHEA adrenal production rate in order to parallel the increase in the hormone metabolic clearance rate (due to enlargement of body fat mass per se).<sup>66</sup> The deficiency of this mechanism might itself contribute to the progressive fat accumulation in severe obesity.<sup>66</sup> Indeed, DHEA may be the cause of fatty liver, obesity (especially abdominal obesity) and diabetes in postmenopausal women.<sup>67</sup> Regarding ethnicity, after adjustment for age, smoking, and BMI, DHEA levels are higher among Chinese and Japanese postmenopausal women and lower among African Americans and Hispanic postmenopausal women.<sup>68</sup>

## The Decrease of Progesterone

Progesterone is an endogenous steroid hormone, one of two female sex hormones (the other being estrogen). Its main functions are regulating menstruation and supporting pregnancy and embryogenesis in the female body.<sup>69</sup> Production stops during menstrual cycles when there is no ovulation and after final menstrual period. Thus, by menopause, ovarian progesterone production is stopped.<sup>70</sup> Decline in progesterone by aging leads to the loss of muscular function, the loss of muscle mass and sarcopenia.<sup>71</sup> Indeed, presence and activity of progesterone receptor are shown in different cell types of skeletal muscle.<sup>71</sup> However, skeletal muscle contractile characteristics are not affected by the fluctuations in progesterone levels.<sup>71</sup> The current literature does not make it possible to show ethnicity differences in progesterone levels among postmenopausal women.<sup>72</sup>

## The Decrease of Growth Hormone (GH) and Insulin Like Growth Factor I (IGF-I)

GH is responsible for growth regulation during childhood but it also regulates body composition, metabolism and aerobic capacity throughout life.<sup>73</sup> Circulating GH levels show a significant decline with ageing.<sup>74</sup> With the age-dependent decline in GH secretion, changes in body composition are observed (ie, a decrease in LBM and an increase in total body fat, especially intra-abdominal fat).<sup>74</sup> Among women, the secretion of GH remains relatively stable until the menopause. Thereafter, GH levels significantly fall.<sup>74</sup> IGF-1 plays an important role in childhood growth, and has anabolic effects in adults. Circulating IGF-1 levels show also a significant decline with ageing.<sup>74</sup> With the age-dependent decline in IGF-1 secretion, changes in body composition are observed (ie, a decrease in LBM and an increase in total body fat, especially intra-abdominal fat).<sup>74</sup> Serum levels of IGF-1 reduced by menopause.<sup>75</sup> Given the diurnal variation in GH, measurement of insulin-like growth factor 1 (IGF1) produced by the liver in response to GH is a more stable marker of GH secretion.<sup>76</sup> On the one hand, GH levels are associated with sarcopenia in the elderly.<sup>77</sup> In fact, GH deficiency leads to the loss of muscle mass but not muscle strength.<sup>9</sup> On the other hand, IGF-1 levels are also associated with sarcopenia in the elderly.<sup>77</sup> IGF-1 is independently associated with the reduction of skeletal muscle mass, along with BMI and sex.<sup>77</sup> IGF-1 is also positively associated with aerobics and muscle

endurance measurements.<sup>78</sup> Body composition could influence the levels of GH and IGF-1. In postmenopausal women, GH and IGF-1 are significantly inversely correlated with trunk fat and percent body fat.<sup>50</sup> Weight gain is not consistent with increases in IGF-I levels among postmenopausal individuals.<sup>79</sup> The use of HT could also influence the levels of GH and IGF-1. In HT users, GH levels are lower in obese than in non-obese women.<sup>50</sup> IGF-1 levels are lower in obese HT users than in non-obese non-users HT women.<sup>50</sup> Finally, ethnicity could influence GH and IGF-1 levels. Compared with white postmenopausal women, African American postmenopausal women are more likely to have high IGF-I levels.<sup>79</sup>

## The Increase of Cortisol

Though widely known as the body's stress hormone, cortisol has a variety of effects on different functions throughout the body.<sup>80</sup> Beginning in the third decade of life, cortisol levels increase gradually with age.<sup>81</sup> This increase is not specifically related to the stage of the menopausal transition.<sup>82</sup> A relative increase in cortisol may reflect the presence of stress and stimulate muscle catabolism, which could lead to sarcopenia.<sup>63</sup> However, there are still few studies involving the relationship between sarcopenia and changes in cortisol levels circulating in the body. Cortisol measures demonstrate a U-shaped relationship with BMI and are associated with visceral adipose tissue and total fat mass.<sup>83</sup> Moreover, postmenopausal women with visceral fat accumulation have elevated cortisol secretion due to an increased sensitivity along the hypothalamic-pituitary-adrenal axis, and that this may be causing their abnormal fat depot distribution.<sup>84</sup> To date, no studies assessed differences in cortisol levels by ethnicity in postmenopausal women.

## Management of Sarcopenia Among Postmenopausal Women

A healthy lifestyle, including nutrition and physical activity but also HT (natural or not) when appropriate can help to prevent or even to treat sarcopenia in postmenopausal women.

### Nutrition

Menopause is associated with increased prevalence of sarcopenia and obesity.<sup>85</sup> Optimal dietary intake of protein, vitamin D and omega-3 (ie, Mediterranean diet) may prevent or attenuate these age-related alterations in musculoskeletal health and more specifically in postmenopausal women.<sup>86</sup>

### Protein Intake

The evidence suggests that total energy and protein intakes decreased across the menopausal transition.<sup>87</sup> Indeed, a decrease in energy intake in postmenopausal women (approximately 254 kcal/day) is observed.<sup>88</sup> However, the mean body weight changed minimally over time and this could be likely explained by a reduction in energy expenditure (approximately 200 kcal/day), mainly characterized by a decrease in physical activity.<sup>88</sup> A reduction in protein intake over time during the menopausal transition is also observed and could negatively impact satiety and therefore weight gain.<sup>89</sup> Healthy postmenopausal women consumed, on average, 1.1 g/kg/d protein, although 25% of them consumed less than the recommended daily allowance (RDA = 0.8g/kg/d protein).<sup>90</sup>

Adequate protein intakes are essential because proteins are the best contributors to sarcopenia and loss of strength in postmenopausal women.<sup>34</sup> In fact, dietary proteins have an impact on regulatory proteins and growth factors involved in muscle growth.<sup>86</sup> The Institute of Medicine recommends for all ages the protein allowance of 0.8 g/kg body weight.<sup>91</sup> The few available interventional studies focusing on postmenopausal women have shown that high protein intake did not promote lean muscle mass gain when compared to recommended dietary allowance (RDA).<sup>92</sup> Therefore, the current evidence suggests that RDA may be sufficient to maintain LBM in postmenopausal women. Nevertheless, postmenopausal women with protein intake below RDA have higher body fat and fat-to-lean ratio than their counterparts who reach the protein RDA.<sup>90</sup> Likewise, upper and lower extremity functions are impaired in postmenopausal women with protein intake below RDA.<sup>90</sup> Furthermore, the importance of the amount of dietary protein during low-calorie diets is controversial. In fact, several authors have shown that postmenopausal women who follow a low-caloric diet, in order to lose weight, have a lower muscle mass decline when they consume more protein.<sup>93</sup> They also showed that, in the case of hypocaloric diet, there is a significant correlation between protein intake (g/kg body weight/day) and absolute fat mass loss ( $r = 0.37$ ,  $P = 0.001$ ).<sup>93</sup> More recently, other authors have conversely shown that high protein weight-loss diet, without exercise, have no impact on preservation of fat-free mass but may



help to maintain muscle strength in postmenopausal women.<sup>94</sup> In this sense, a recent study reported that high protein intake (1.5 g protein/kg body weight) compared to normal protein intake (0.8 g protein/kg body weight) during a 12-weeks energy-restricted diets without exercise had no impact on preservation of lean mass.<sup>94</sup> It has been also observed that protein intake exceeding the RDA (1.6gr/kg/d vs 0.8gr/kg/d) did not increase LBM, strength, and physical performance in a sample of late postmenopausal woman consuming a low-glycemic index diet for 6 months.<sup>95</sup> In addition, when combined with a resistance exercise training during 10 weeks, authors concluded that in postmenopausal women, an increased on protein intake (1.2gr/kg/d) did not promote higher lean body mass gain when compared to RDA recommendation.<sup>92</sup> But others reported that in postmenopausal women, even a moderate increase in protein intake (~1.2 g protein·kg<sup>-1</sup>·d<sup>-1</sup>) when combined to 10 weeks of resistance exercise, could promote a small additional improvement in functional capacity but not in strength and lean mass.<sup>96</sup> Moreover, Longland et al showed that during a 4-weeks energy deficit consumption (~40%) a diet containing very high protein intake (2.4 g protein·kg<sup>-1</sup>·d<sup>-1</sup>) and combined with a high volume of resistance and anaerobic exercise was more effective to increase LBM than a diet containing a high protein intake (1.2 g protein·kg<sup>-1</sup>·d<sup>-1</sup>) and combined with a high volume of resistance and anaerobic exercise.<sup>97</sup> Finally, at long term (5-year follow-up), it appears that high protein intake (1.2g/kg/d) is associated with beneficial effects on muscle mass and size and bone mass in elderly women.<sup>95</sup>

In addition, the distribution of protein intake over the day is important and at least 20–25 g of high-quality protein with each main meal (breakfast, lunch, dinner) should be consumed during the day.<sup>98</sup> Beside the amount and distribution of protein throughout the day, the type of protein ingested is also important. Effectively, a vegetarian diet is associated with a lower muscle mass index than is an omnivorous diet at the same protein intake. Thus, animal protein intake is a factor promoting muscle mass index among women.<sup>99</sup> However, some authors consider that neither the amount nor the quality of protein ingested in omnivore, ovo-lacto-vegetarians or vegan diet is a limiting factor in determining the amount of muscle mass in postmenopausal women.<sup>100</sup>

It is also important to note that HT does not appear to influence protein synthesis. Thus, protein intakes should be similar in women with HT than in women without HT.<sup>101</sup>

Thus, it seems that the dose of proteins (very high dose compared to RDA) and the time of ingestion/diet habits (long-term effect) can help to preserve muscle function in postmenopausal women.

## Vitamin D Intake

Low vitamin D status is highly prevalent in postmenopausal women.<sup>102</sup> The prevalence of vitamin D deficiency in postmenopausal women varies in different countries. Indeed, in the European Union, 32.1% of women after menopause are estimated to have a circulating level of 25(OH)D lower than 20 ng/mL<sup>103</sup> whereas in India, China and the United States, the prevalence of vitamin D inadequacy is reported to be 53.3%,<sup>104</sup> 72.1%,<sup>105</sup> and 53%,<sup>106</sup> respectively. Estrogen increases the activity of the enzyme responsible for activating vitamin D and so declining estrogen levels during the menopausal transition could lead to vitamin D deficiency.<sup>107,108</sup> Vitamin D deficiency is associated with a loss of muscle mass and strength in older people, and a decline in physical performance.<sup>109</sup> Accumulating evidence from molecular and clinical studies suggests that vitamin D deficiency is associated with sarcopenic status in elderly women independent of body composition, diet and hormonal status.<sup>110,111</sup>

Vitamin D is essential for the optimal functioning of the musculoskeletal system as it stimulates dietary calcium absorption and has a major regulating role in muscle function.<sup>102</sup> Vitamin D promotes protein synthesis and calcium and phosphate transport in muscle, thus influencing muscle strength.<sup>109</sup> Current data provide evidence about the beneficial effect of vitamin D supplementation on muscle strength, physical performance and prevention of falls and fractures in older women.<sup>110</sup> Correction of vitamin D deficit has a favorable effect on muscle mass among sarcopenic obese postmenopausal women.<sup>112</sup>

The ESCEO recommends vitamin D supplementation at 800–1000 IU/d to maintain serum 25-(OH)D concentration >50 nmol/L in elderly or postmenopausal women at risk of vitamin D deficiency.<sup>109</sup> There is an inverse relationship between fat mass and serum 25(OH)D levels and, therefore, the dosage of supplementation should be adjusted according to the body mass index.<sup>113</sup> An adequate calcium intake (1000 mg/d) should also be respected.<sup>86</sup>

## Mediterranean Diet

A Mediterranean diet is characterized by a high monounsaturated: saturated fat ratio, a high intake of alpha-linolenic acid, a lower ratio of omega-6/omega-3 fatty acids, moderate ethanol intake, high intakes of dietary fiber, vitamins, minerals, antioxidants and a range of non-nutritive compounds including polyphenols, carotenoids and flavonoids; relatively low intakes of meat and dairy products; and moderate consumption of alcohol.<sup>114</sup> A decreased risk of physical frailty and sarcopenia is observed with greater adherence to a Mediterranean diet.<sup>115</sup> The potential explanation is that Mediterranean diet has positive effect on oxidative stress,<sup>116</sup> inflammation<sup>117</sup> and insulin resistance,<sup>118</sup> which are risk factors for muscle catabolism.<sup>119</sup> In addition, adherence to a Mediterranean diet could help to manage weight among postmenopausal women and is inversely associated with overweight/obesity in this population.<sup>120,121</sup> However, very few studies including global Mediterranean diet intervention and focusing on muscle mass gain or maintenance in postmenopausal women are available in the literature, expressing an important gap regarding this issue.<sup>119</sup>

Moreover, an important component of the Mediterranean diet is the high consumption Omega-3 polyunsaturated fatty acids (PUFAs). However, low dietary omega-3 PUFAs levels are inversely associated with sarcopenia.<sup>122</sup> Several evidences indicate that omega-3 PUFAs are able to reduce muscle wasting by increasing the functional capacity in the elderly by growing the intracellular metabolic signal.<sup>123</sup> The average intake level of omega-3 fatty acids in postmenopausal women is 1.31 g/day, which seemed to be slightly lower than that in premenopausal women (1.46 g/day) and men (1.76 g/day).<sup>124</sup> In addition, HT induces negative effects on fatty acid profile among women such as elevating saturated fatty acids and diminishing unsaturated fatty acids compared to women without HT.<sup>125</sup> There is growing evidence for a beneficial effect of omega-3 polyunsaturated fatty acids (PUFAs) supplementation in sarcopenic older persons, which may add to the effect of exercise and/or protein supplementation. Marine-derived omega-3 PUFAs can influence the exercise and nutritional response of skeletal muscle.<sup>126</sup> However, the exact dosage, frequency and use (alone or combined) in the treatment and prevention of sarcopenia still need further exploration.<sup>127</sup> A recent meta-analysis highlighted a significant relationship in favor of omega-3 PUFAs supplementation for LBM (effect size 0.27) and skeletal muscle mass (effect size 0.31)<sup>128</sup> in older people. In postmenopausal women, it has been shown that Omega-3 PUFAs have the potential to improve body composition and substrate oxidation.<sup>129</sup>

## Physical Activity

Menopausal transition is accompanied with a decline in energy expenditure, mainly characterized by a decrease in physical activity and a shift to a more sedentary lifestyle.<sup>130</sup> There is also a decrease in LBM in women after the menopause, which is associated with a decrease in resting metabolism rate.<sup>131</sup> Moreover, it has been shown that postmenopausal women have a lower fat oxidation and energy expenditure during exercise than premenopausal women,<sup>132</sup> further contributing to a lower capacity for substrate utilization by skeletal muscle after the menopause. Therefore, the menopausal transition is associated with a risk to increase body weight and adiposity. In addition, previous research has shown that physical inactivity contributes to the development of sarcopenia.<sup>133</sup> Since menopause occurs approximately with the onset of sarcopenia, aging non-physically active postmenopausal women should switch as soon as possible to an active lifestyle. Moreover, struggling the deleterious effects of inactivity is important in postmenopausal women. The benefits of physical activity are numerous in this population, the most important being the maintenance of muscle mass and therefore muscle strength.<sup>134,135</sup>

Globally, the physical activity practice for postmenopausal women should combine endurance (aerobic), strength and balance exercises.<sup>134</sup> It is recommended that postmenopausal women practice 150 min of moderate aerobic activity per week combined with resistance training 3 times a week.<sup>134</sup> Every woman should be aware of her target heart rate and should track exercise intensity.<sup>134</sup> In addition, body and mind exercises (eg, yoga, stretching) can help to manage menopause-related symptoms.<sup>134</sup> In more detail, it has been shown that low-volume of resistance training (ie, three sets of 8–12 repetitions at 70% of one repetition maximum (1RM) with 1.5 min of rest interval) between sets and exercises, three times a week improves muscular strength among postmenopausal women.<sup>136</sup> More specifically, while a low-volume RT improves fat mass and muscular strength, a high-volume resistance training is necessary to improve indicators of abdominal adiposity and lipid metabolism in postmenopausal women.<sup>136</sup> In addition, long-term periodized resistance training prevents aging sarcopenia and decreases body fat in postmenopausal elderly women.<sup>137,138</sup> The available literature also suggest that moderate-to-high-

intensity elastic band training and low-intensity elastic band training with blood flow restriction result in similar increases in strength, lean body mass and muscle thickness in postmenopausal women.<sup>139</sup> Unfortunately, the effects of resistance training on fat mass, muscle strength and functional capacities are attenuated in postmenopausal women with sarcopenic obesity<sup>140</sup> although progressive elastic band resistance exercise can reduce fat mass in this demographic.<sup>141,142</sup> Finally, based on a systematic review of randomized controlled trials, early postmenopausal women could benefit from 30 min of daily walking combined with a resistance training twice a week (ie, 8 to 10 repetitions of 8 to 10 exercises for major muscle groups, starting with 40% of one repetition maximum).<sup>143</sup>

## Physical Activity Combined with Nutrition

Based on a recent network systematic review, both exercise alone and the combination of exercise and nutrition have beneficial effects on muscle strength and physical performance in older adults with sarcopenia.<sup>144</sup> Thus, although few authors have focused on sarcopenic postmenopausal women, the effects of nutrition alone or physical activity alone on sarcopenia among postmenopausal women could be potentiated when the 2 interventions are combined.

Thereby, data suggest that exercise and amino acid supplementation together is effective in enhancing muscle strength, muscle mass and walking speed in sarcopenic women.<sup>145</sup> Then, adding soy to milk combined with 16 weeks of resistance training result in more significant increases in muscle strength.<sup>146</sup> However, soy protein supplementation when combined with resistance training does not influence the indicators of body composition compared to resistance training alone.<sup>147</sup> However, it exerts possible favorable effects on lipid profile in postmenopausal women.<sup>147</sup> It is also admit that the combination of exercise and tea catechin (polyphenolic) supplementation had a beneficial effect on physical function measured by walking ability and muscle mass among elderly sarcopenic women.<sup>148</sup>

When looking at data specific to obese postmenopausal women, resistance training appears effective in the prevention of all components of sarcopenic obesity in women, resulting in significant improvements in muscular mass, strength, and functional capacity plus loss of fat mass, especially when coupled with hypocaloric diets containing at least 0.8 g/kg body weight of protein.<sup>112</sup> With the same idea, whey protein combined with resistance training increases lean mass and decreases total and trunk fat mass, improving sarcopenia and decreasing sarcopenia obesity in older women.<sup>149</sup> Furthermore, aerobic exercise added to dietary weight loss can attenuate the loss of appendicular lean mass during weight loss, and may be effective for the prevention and treatment of sarcopenia among overweight and obese postmenopausal women.<sup>150</sup> Then, diet and exercise induce weight loss with higher protein and increased dairy product intakes promotes more favorable body composition changes in obese postmenopausal.<sup>151</sup> Anyway, a short weight loss program combining caloric restriction and aerobic exercise may significantly reduce fat mass and improve lipid-lipoprotein profile in obese women, independently of their sarcopenic status.<sup>152</sup>

## Hormone Replacement Therapy (Natural or Not)

The available literature demonstrates that HT has significant beneficial effects on skeletal muscle mass, strength and protection from damage in older women.<sup>153</sup> HT improves myosin function and strength in muscle that is devoid of sex hormones and the content of oestrogen receptors in muscle also increases.<sup>86</sup> HT seems to improve muscle power, regulation of muscle contraction and muscle composition.<sup>86</sup> In fact, HT is linked to the reversal of both menopause-related obesity and loss of lean mass, without overall change in body weight. The increase in LBM during HT is likely explained by muscle anabolism, which in turn, prevents disease in the elderly.<sup>154</sup> More benefits of HT are seen in younger postmenopausal females and those who initiate HRT proximal to menopause.<sup>153</sup>

Nonetheless, it seems that the effects of HT depend on several factors such the dosage or the level of physical activity of postmenopausal women. In fact, ultra-low-dose HT has no impact (neither improvement nor worsening) on muscle mass, body fat and physical performance.<sup>155</sup> Then, HT does not provide any additional beneficial effect on body composition in active postmenopausal women.<sup>156</sup> As a matter of fact, physically active women display greater total FFM, appendicular FFM, and muscle mass index compared to less active women ( $P < 0.05$ ) whereas HT provide no additional effect on any FFM.<sup>156</sup>

On the other hand, the European Menopause and Andropause Society (EMAS) suggests natural hormonal management of menopausal symptoms as an option for women who cannot or do not wish to take HT.<sup>157</sup> Thus, phytoestrogen-based



medications are commonly used by menopausal women, and especially by obese postmenopausal women, to relieve menopausal symptoms.<sup>158</sup> Soy protein and isoflavones can improve muscle density quality and reduce body weight. It is considered a breakthrough in preventing osteo-sarcopenia and obesity that may occur after menopause.<sup>159</sup> In fact, soy contains phytoestrogens, whose chemical structure is very similar to that of human estrogen.<sup>160</sup> Compounds called lignans and isoflavones in soybeans can mimic the sex hormone estrogen produced by the human body. Soy protein also contains branched chain amino acids (BCAA), which may have a positive effect on body weight regulation and muscle protein synthesis.<sup>161</sup> Isoflavone supplementation helps to increase fat-free mass in obese-sarcopenic postmenopausal women.<sup>162</sup> However, a recent systematic review suggests that some types of phytoestrogens, such as daidzein, but not soy products or isoflavone mix, could lead to modest adverse changes in body composition in menopausal women.<sup>158</sup> Diets with higher soy isoflavones content look promising to manage sarcopenic obesity in postmenopausal women.<sup>112,162</sup> However, according to some authors, isoflavones, irrespective of exercise, did not produce changes in muscle strength, function and quality.<sup>163</sup>

## Creatine Supplementation

It is known that women exhibiting 70–80% lower endogenous creatine stores compared to men. Thus, it appears that creatine supplementation could be a non-pharmacological solution to counteract muscle function decline in menopausal (pre and post) women. A recent review concluded that creatine supplementation appears to be effective for improving strength and exercise performance in premenopausal women.<sup>164</sup> In addition, Smith-Ryan et al reported that high doses of creatine (0.3 g·kg<sup>-1</sup>·d<sup>-1</sup>) during at least 7 days could lead to benefits in skeletal muscle size and function in postmenopausal women.<sup>164</sup> However, low-dose chronic supplementation with creatine (1 g/d for 52 weeks) among postmenopausal women failed to have an effect on FFM, bone density, bone turnover, or muscle function.<sup>165</sup> It has been also observed that creatine supplementation (5g/day) combined with a resistance training (2 sessions/week) during 24 weeks, increased lean mass (appendicular: arms+legs) and muscle function in postmenopausal women.<sup>166</sup> In addition, a meta-analysis performed by Chilibeck et al confirmed that creatine supplementation combined with resistance training improve lean mass and muscle strength (upper and lower body) in older adults.<sup>167</sup> One explanation is that muscle integrity has also been upregulated with creatine use, resulting in an increase in satellite cell activity, growth factors (ie, IGF-1), protein kinases and myogenic transcription factors.<sup>167</sup> Finally, creatine supplementation does not induce additional negative effects compared to placebo and is therefore considered safe.” Thus, alone or when combined with resistance training, creatine supplementation could be considered.

In summary, components of sarcopenia appear to be treatable by all these interventions (nutrition, exercise, HT (natural or not)<sup>168</sup>) in postmenopausal women and should be recommended to promote healthy ageing.

## Conclusion

The prevalence of sarcopenia highly depends on the definition used. But being a postmenopausal woman is associated with a higher risk of becoming sarcopenic. Etiology of sarcopenia is complex and multifactorial, accelerated by sedentary lifestyle, malnutrition, and various morbidities. Nevertheless, the accelerated development of sarcopenia during the menopause seems to be due to hormonal changes and mostly by estrogenic decrease. Fortunately, the risk of developing sarcopenia in postmenopausal women may be attenuated through healthy lifestyle changes (combined or not), including diet (ie, adequate protein intake, sufficient vitamin D intake, omega 3); regular physical activity and/or hormone therapy (natural or not).

## Disclosure

The authors report no conflicts of interest in this work.

## References

1. Peacock K, Ketvertis KM. *Menopause*, in *StatPearls*. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC; 2021.
2. Rodriguez M, Shoupe D. Surgical menopause. *Endocrinol Metab Clin North Am*. 2015;44(3):531–542. doi:10.1016/j.ecl.2015.05.003
3. Geraci A, Calvani R, Ferri E, et al. Sarcopenia and menopause: the role of estradiol. *Front Endocrinol*. 2021;12:682012. doi:10.3389/fendo.2021.682012

4. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2018;48(1):16–31. doi:10.1093/ageing/afy169
5. Chen L-K, Woo J, Assantachai P, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. 2020;21(3):300–307.e2. doi:10.1016/j.jamda.2019.12.012
6. Muscaritoli M, Anker SD, Argilés J, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) “cachexia-anorexia in chronic wasting diseases” and “nutrition in geriatrics”. *Clin Nutr*. 2010;29(2):154–159. doi:10.1016/j.clnu.2009.12.004
7. Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc*. 2011;12(4):249–256. doi:10.1016/j.jamda.2011.01.003
8. Pion CH, Barbat-Artigas S, St-Jean-Pelletier F, et al. Muscle strength and force development in high- and low-functioning elderly men: influence of muscular and neural factors. *Exp Gerontol*. 2017;96:19–28. doi:10.1016/j.exger.2017.05.021
9. Morley JE. Hormones and Sarcopenia. *Curr Pharm Des*. 2017;23(30):4484–4492. doi:10.2174/1381612823666161123150032
10. Dhillon RJ, Hasni S. Pathogenesis and management of sarcopenia. *Clin Geriatr Med*. 2017;33(1):17–26. doi:10.1016/j.cger.2016.08.002
11. Pascual-Fernández J, Fernández-Montero A, Córdova-Martínez A, et al. Sarcopenia: molecular pathways and potential targets for intervention. *Int J Mol Sci*. 2020;21(22):8844. doi:10.3390/ijms21228844
12. Alcazar J, Frandsen U, Prokhorova T, et al. Changes in systemic GDF15 across the adult lifespan and their impact on maximal muscle power: the Copenhagen Sarcopenia Study. *J Cachexia Sarcopenia Muscle*. 2021;12(6):1418–1427. doi:10.1002/jcsm.12823
13. St-Jean-Pelletier F, Pion CH, Leduc-Gaudet J-P, et al. The impact of ageing, physical activity, and pre-frailty on skeletal muscle phenotype, mitochondrial content, and intramyocellular lipids in men. *J Cachexia Sarcopenia Muscle*. 2017;8(2):213–228. doi:10.1002/jcsm.12139
14. Nishikawa H, Fukunishi S, Asai A, et al. Pathophysiology and mechanisms of primary sarcopenia (Review). *Int J Mol Med*. 2021;48(2). doi:10.3892/ijmm.2021.4989
15. Rolland Y, Vellas B. [Sarcopenia]. *Rev Med Interne*. 2009;30(2):150–160. French. doi:10.1016/j.revmed.2008.08.013
16. Holloszy JO. The biology of aging. *Mayo Clin Proc*. 2000;75(Suppl):S3–S8. doi:10.1016/S0025-6196(19)30634-2
17. Melton LJ 3rd, Khosla S, Crowson CS, et al. Epidemiology of sarcopenia. *J Am Geriatr Soc*. 2000;48(6):625–630. doi:10.1111/j.1532-5415.2000.tb04719.x
18. Mitchell WK, Williams J, Atherton P, et al. Sarcopenia, dynapenia, and the impact of advancing age on human skeletal muscle size and strength; a quantitative review. *Front Physiol*. 2012;3:260. doi:10.3389/fphys.2012.00260
19. Mayhew AJ, Amog K, Phillips S, et al. The prevalence of sarcopenia in community-dwelling older adults, an exploration of differences between studies and within definitions: a systematic review and meta-analyses. *Age Ageing*. 2019;48(1):48–56. doi:10.1093/ageing/afy106
20. Volpato S, Bianchi L, Cherubini A, et al. Prevalence and clinical correlates of sarcopenia in community-dwelling older people: application of the EWGSOP definition and diagnostic algorithm. *J Gerontol a Biol Sci Med Sci*. 2014;69(4):438–446. doi:10.1093/gerona/glt149
21. Papadopoulou SK, Tsintavis P, Potsaki G, et al. Differences in the prevalence of sarcopenia in community-dwelling, nursing home and hospitalized individuals. a systematic review and meta-analysis. *J Nutr Health Aging*. 2020;24(1):83–90. doi:10.1007/s12603-019-1267-x
22. Shafiee G, Keshkar A, Soltani A, et al. Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies. *J Diabetes Metab Disord*. 2017;16(1):21. doi:10.1186/s40200-017-0302-x
23. McBreairey LE, Chilibeck PD, Gordon JJ, et al. Polycystic ovary syndrome is a risk factor for sarcopenic obesity: a case control study. *BMC Endocr Disord*. 2019;19(1):70. doi:10.1186/s12902-019-0381-4
24. Kim SW, Kim R. The association between hormone therapy and sarcopenia in postmenopausal women: the Korea National Health and Nutrition Examination Survey, 2008–2011. *Menopause*. 2020;27(5):506–511. doi:10.1097/GME.0000000000001509
25. Greendale GA, Sternfeld B, Huang M, et al. Changes in body composition and weight during the menopause transition. *JCI Insight*. 2019;4(5). doi:10.1172/jci.insight.124865
26. Sipilä S, Törmäkangas T, Sillanpää E, et al. Muscle and bone mass in middle-aged women: role of menopausal status and physical activity. *J Cachexia Sarcopenia Muscle*. 2020;11(3):698–709. doi:10.1002/jcsm.12547
27. Monterrosa-Castro A, Ortiz-Banquéz M, Mercado-Lara M. Prevalence of sarcopenia and associated factors in climacteric women of the Colombian Caribbean. *Menopause*. 2019;26(9):1038–1044. doi:10.1097/GME.0000000000001347
28. Zanchetta MB, Abdala R, Massari F, et al. Postmenopausal women with sarcopenia have higher prevalence of falls and vertebral fractures. *Medicina*. 2021;81(1):47–53.
29. Orprayoon N, Wainipitapong P, Champaiboon J, et al. Prevalence of pre-sarcopenia among postmenopausal women younger than 65 years. *Menopause*. 2021;28(12):1351–1357. doi:10.1097/GME.0000000000001866
30. Onambélé-Pearson GL, Tomlinson DJ, Morse CI, et al. A prolonged hiatus in postmenopausal HRT, does not nullify the therapy’s positive impact on ageing related sarcopenia. *PLoS One*. 2021;16(5):e0250813. doi:10.1371/journal.pone.0250813
31. Greeves JP, Cable NT, Reilly T, et al. Changes in muscle strength in women following the menopause: a longitudinal assessment of the efficacy of hormone replacement therapy. *Clin Sci*. 1999;97(1):79–84. doi:10.1042/CS19980406
32. Kenny AM, Dawson L, Kleppinger A, et al. Prevalence of sarcopenia and predictors of skeletal muscle mass in nonobese women who are long-term users of estrogen-replacement therapy. *J Gerontol a Biol Sci Med Sci*. 2003;58(5):M436–40. doi:10.1093/gerona/58.5.M436
33. Habermehl TL, Mason JB. Decreased sarcopenia in aged females with young ovary transplants was preserved in mice that received germ cell-depleted young ovaries. *J Clin Med*. 2019;8(1):40. doi:10.3390/jcm8010040
34. Maltais ML, Desroches J, Dionne JJ. Changes in muscle mass and strength after menopause. *J Musculoskelet Neuronal Interact*. 2009;9(4):186–197.
35. Lang T, Streeter P, Cawthon P, et al. Sarcopenia: etiology, clinical consequences, intervention, and assessment. *Osteoporos Int*. 2010;21(4):543–559. doi:10.1007/s00198-009-1059-y
36. Kuhl H. Pharmacology of estrogens and progestogens: influence of different routes of administration. *Climacteric*. 2005;8(Suppl 1):3–63. doi:10.1080/13697130500148875
37. Ali ES, Mangold C, Peiris AN. Estriol: emerging clinical benefits. *Menopause*. 2017;24(9):1081–1085. doi:10.1097/GME.0000000000000855

38. Holinka CF, Diczfalussy E, Coelingh Bennink HJ. Estetrol: a unique steroid in human pregnancy. *J Steroid Biochem Mol Biol.* 2008;110(1–2):138–143. doi:10.1016/j.jsbmb.2008.03.027
39. Lemoine S, Granier P, Tiffocche C, et al. Estrogen receptor alpha mRNA in human skeletal muscles. *Med Sci Sports Exerc.* 2003;35(3):439–443. doi:10.1249/01.MSS.0000053654.14410.78
40. D'Eon T, Braun B. The roles of estrogen and progesterone in regulating carbohydrate and fat utilization at rest and during exercise. *J Womens Health Gend Based Med.* 2002;11(3):225–237. doi:10.1089/152460902753668439
41. Messier V, Rabasa-Lhoret R, Barbat-Artigas S, et al. Menopause and sarcopenia: a potential role for sex hormones. *Maturitas.* 2011;68(4):331–336. doi:10.1016/j.maturitas.2011.01.014
42. Roubenoff R. Catabolism of aging: is it an inflammatory process? *Curr Opin Clin Nutr Metab Care.* 2003;6(3):295–299. doi:10.1097/01.mco.0000068965.34812.62
43. Lowe DA, Baltgalvis KA, Greising SM. Mechanisms behind estrogen's beneficial effect on muscle strength in females. *Exerc Sport Sci Rev.* 2010;38(2):61–67. doi:10.1097/JES.0b013e3181d496bc
44. Phillips SK, Rook KM, Siddle NC, et al. Muscle weakness in women occurs at an earlier age than in men, but strength is preserved by hormone replacement therapy. *Clin Sci.* 1993;84(1):95–98. doi:10.1042/cs0840095
45. Freeman EW, Sammel MD, Lin H, et al. Obesity and reproductive hormone levels in the transition to menopause. *Menopause.* 2010;17(4):718–726. doi:10.1097/gme.0b013e3181cec85d
46. Jones ME, Schoemaker M, Rae M, et al. Changes in estradiol and testosterone levels in postmenopausal women after changes in body mass index. *J Clin Endocrinol Metab.* 2013;98(7):2967–2974. doi:10.1210/jc.2013-1588
47. Colleluori G, Chen R, Napoli N, et al. Fat mass follows a U-shaped distribution based on estradiol levels in postmenopausal women. *Front Endocrinol.* 2018;9:315. doi:10.3389/fendo.2018.00315
48. Kim C, Golden SH, Mather KJ, et al. Racial/ethnic differences in sex hormone levels among postmenopausal women in the diabetes prevention program. *J Clin Endocrinol Metab.* 2012;97(11):4051–4060. doi:10.1210/jc.2012-2117
49. Setiawan VW, Haiman CA, Stanczyk FZ, et al. Racial/ethnic differences in postmenopausal endogenous hormones: the multiethnic cohort study. *Cancer Epidemiol Biomarkers Prev.* 2006;15(10):1849–1855. doi:10.1158/1055-9965.EPI-06-0307
50. Figueroa A, Going SB, Milliken LA, et al. Body composition modulates the effects of hormone replacement therapy on growth hormone and insulin-like growth factor-I levels in postmenopausal women. *Gynecologic and Obstetric Investigation.* 2002;54(4):201–206. doi:10.1159/000068383
51. Tyagi V, Scordo M, Yoon RS, et al. Revisiting the role of testosterone: are we missing something? *Rev Urol.* 2017;19(1):16–24. doi:10.3909/riu0716
52. Herbst KL, Bhasin S. Testosterone action on skeletal muscle. *Curr Opin Clin Nutr Metab Care.* 2004;7(3):271–277. doi:10.1097/00075197-200405000-00006
53. Shea JL, Wong PY, Chen Y. Free testosterone: clinical utility and important analytical aspects of measurement. *Adv Clin Chem.* 2014;63:59–84.
54. van den Beld AW, de Jong FH, Grobbee DE, et al. Measures of bioavailable serum testosterone and estradiol and their relationships with muscle strength, bone density, and body composition in elderly men. *J Clin Endocrinol Metab.* 2000;85(9):3276–3282. doi:10.1210/jcem.85.9.6825
55. Lee CE, McArdle A, Griffiths RD. The role of hormones, cytokines and heat shock proteins during age-related muscle loss. *Clin Nutr.* 2007;26(5):524–534. doi:10.1016/j.clnu.2007.05.005
56. Stanikova D, Zsido RG, Luck T, et al. Testosterone imbalance may link depression and increased body weight in premenopausal women. *Transl Psychiatry.* 2019;9(1):160. doi:10.1038/s41398-019-0487-5
57. Janssen I, Powell LH, Kazlauskaitė R, et al. Testosterone and visceral fat in midlife women: the Study of Women's Health Across the Nation (SWAN) fat patterning study. *Obesity.* 2010;18(3):604–610. doi:10.1038/oby.2009.251
58. Samaras N, Samaras D, Frangos E, et al. A review of age-related dehydroepiandrosterone decline and its association with well-known geriatric syndromes: is treatment beneficial? *Rejuvenation Res.* 2013;16(4):285–294. doi:10.1089/rej.2013.1425
59. Labrie F, Luu-The V, Labrie C, et al. DHEA and its transformation into androgens and estrogens in peripheral target tissues: intracrinology. *Front Neuroendocrinol.* 2001;22(3):185–212. doi:10.1006/frne.2001.0216
60. Webb SJ, Geoghegan TE, Prough RA, et al. The biological actions of dehydroepiandrosterone involves multiple receptors. *Drug Metab Rev.* 2006;38(1–2):89–116. doi:10.1080/03602530600569877
61. Vieira-Marques C, Arbo BD, Cozer AG, et al. Sex-specific effects of dehydroepiandrosterone (DHEA) on glucose metabolism in the CNS. *J Steroid Biochem Mol Biol.* 2017;171:1–10. doi:10.1016/j.jsbmb.2016.11.014
62. de Menezes KJ, Peixoto C, Nardi AE, et al. Dehydroepiandrosterone, its sulfate and cognitive functions. *Clin Pract Epidemiol Ment Health.* 2016;12(1):24–37. doi:10.2174/1745017901612010024
63. Yanagita I, Fujihara Y, Kitajima Y, et al. A high serum cortisol/DHEA-S ratio is a risk factor for sarcopenia in elderly diabetic patients. *J Endocr Soc.* 2019;3(4):801–813. doi:10.1210/js.2018-00271
64. Labrie F, Luu-The V, Belanger A, et al. Is dehydroepiandrosterone a hormone? *J Endocrinol.* 2005;187(2):169–196. doi:10.1677/joe.1.06264
65. Maggio M, Lauretani F, Ceda GP. Sex hormones and sarcopenia in older persons. *Curr Opin Clin Nutr Metab Care.* 2013;16(1):3–13. doi:10.1097/MCO.0b013e32835b6044
66. De Pergola G, Giagulli VA, Garruti G, et al. Low dehydroepiandrosterone circulating levels in premenopausal obese women with very high body mass index. *Metabolism.* 1991;40(2):187–190. doi:10.1016/0026-0495(91)90172-S
67. Saruç M, Yüceyar H, Ayhan S, et al. The association of dehydroepiandrosterone, obesity, waist-Hip ratio and insulin resistance with fatty liver in postmenopausal women—a hyperinsulinemic euglycemic insulin clamp study. *Hepatogastroenterology.* 2003;50(51):771–774.
68. Lasley BL, Santoro N, Randolph JF, et al. The relationship of circulating dehydroepiandrosterone, testosterone, and estradiol to stages of the menopausal transition and ethnicity. *J Clin Endocrinol Metab.* 2002;87(8):3760–3767. doi:10.1210/jcem.87.8.8741
69. Cable JK, Grider MH. *Physiology, Progesterone, in StatPearls.* Treasure Island (FL): StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC; 2022.
70. Roeca C, Al-Safi Z, Santoro N, et al. MDText.com. In: Feingold KR, editor. *The Postmenopausal Women, in Endotext.* South Dartmouth (MA): Inc. Copyright © 2000–2022 MDText.com; 2022.

71. Kim YJ, Tamadon A, Park HT, et al. The role of sex steroid hormones in the pathophysiology and treatment of sarcopenia. *Osteoporos Sarcopenia*. 2016;2(3):140–155. doi:10.1016/j.afos.2016.06.002
72. Pinheiro SP, et al. Racial differences in premenopausal endogenous hormones. *Cancer Epidemiol Biomarkers Prev*. 2005;14(9):2147–2153. doi:10.1158/1055-9965.EPI-04-0944
73. Brinkman JE, Holmes MD, Pollak MN, et al. *Physiology, Growth Hormone*. Treasure Island (FL): StatPearls Publishing; Copyright © 2022, StatPearls Publishing LLC; 2022.
74. Fanciulli G, Delitala A, Delitala G. *Growth hormone, menopause and ageing: no definite evidence for 'rejuvenation' with growth hormone*. *Hum Reprod Update*. 2009;15(3):341–358. doi:10.1093/humupd/dmp005
75. Nasu M, Sugimoto T, Chihara M, et al. Effect of natural menopause on serum levels of IGF-I and IGF-binding proteins: relationship with bone mineral density and lipid metabolism in perimenopausal women. *Eur J Endocrinol*. 1997;136(6):608–616. doi:10.1530/eje.0.1360608
76. McKee A, Morley JE, Matsumoto AM, et al. Sarcopenia: an endocrine disorder? *Endocr Pract*. 2017;23(9):1140–1149. doi:10.4158/EP171795.RA
77. Bian A, Ma Y, Zhou X, et al. Association between sarcopenia and levels of growth hormone and insulin-like growth factor-I in the elderly. *BMC Musculoskelet Disord*. 2020;21(1):214. doi:10.1186/s12891-020-03236-y
78. Nindl BC, Santtila M, Vaara J, et al. Circulating IGF-I is associated with fitness and health outcomes in a population of 846 young healthy men. *Growth Horm IGF Res*. 2011;21(3):124–128. doi:10.1016/j.ghir.2011.03.001
79. Jung SY, Hursting SD, Guindani M, et al. Bioavailable insulin-like growth factor-I inversely related to weight gain in postmenopausal women regardless of exogenous estrogen. *Cancer Epidemiol Biomarkers Prev*. 2014;23(3):534–544. doi:10.1158/1055-9965.EPI-13-1053
80. Thau L, Gandhi J, Sharma S. *Physiology, Cortisol, in StatPearls*. Treasure Island (FL): StatPearls Publishing; Copyright © 2022, StatPearls Publishing LLC; 2022.
81. Woods NF, Mitchell ES, Smith-Dijulio K. Cortisol levels during the menopausal transition and early postmenopause: observations from the Seattle Midlife Women's Health Study. *Menopause*. 2009;16(4):708–718. doi:10.1097/gme.0b013e318198d6b2
82. Woods NF, Carr MC, Tao EY, et al. Increased urinary cortisol levels during the menopausal transition. *Menopause*. 2006;13(2):212–221. doi:10.1097/01.gme.0000198490.57242.2e
83. Schorr M, Lawson EA, Dichtel LE, et al. Cortisol measures across the weight spectrum. *J Clin Endocrinol Metab*. 2015;100(9):3313–3321. doi:10.1210/JC.2015-2078
84. Márin P, Darin N, Amemiya T, et al. Cortisol secretion in relation to body fat distribution in obese premenopausal women. *Metabolism*. 1992;41(8):882–886. doi:10.1016/0026-0495(92)90171-6
85. Nappi RE, Simoncini T. Menopause transition: a golden age to prevent cardiovascular disease. *Lancet Diabetes Endocrinol*. 2021;9(3):135–137. doi:10.1016/S2213-8587(21)00018-8
86. Rizzoli R, Stevenson JC, Bauer JM, et al. The role of dietary protein and vitamin D in maintaining musculoskeletal health in postmenopausal women: a consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). *Maturitas*. 2014;79(1):122–132. doi:10.1016/j.maturitas.2014.07.005
87. Duval K, Prud'homme D, Rabasa-Lhoret R, et al. Effects of the menopausal transition on dietary intake and appetite: a MONET Group Study. *Eur J Clin Nutr*. 2014;68(2):271–276. doi:10.1038/ejcn.2013.171
88. Abdulnour J, Doucet É, Brochu M, et al. The effect of the menopausal transition on body composition and cardiometabolic risk factors: a Montreal-Ottawa New Emerging Team group study. *Menopause*. 2012;19(7):760–767. doi:10.1097/gme.0b013e318240f6f3
89. Paddon-Jones D, Westman E, Mattes RD, et al. Protein, weight management, and satiety. *Am J Clin Nutr*. 2008;87(5):1558s–1561s. doi:10.1093/ajcn/87.5.1558S
90. Gregorio L, Brindisi J, Kleppinger A, et al. Adequate dietary protein is associated with better physical performance among post-menopausal women 60–90 years. *J Nutr Health Aging*. 2014;18(2):155–160. doi:10.1007/s12603-013-0391-2
91. Trumbo P, Schlicker S, Yates AA, et al. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. *J Am Diet Assoc*. 2002;102(11):1621–1630. doi:10.1016/S0002-8223(02)90346-9
92. Rossato LT, Nahas P, de Branco F, et al. Higher protein intake does not improve lean mass gain when compared with RDA recommendation in postmenopausal women following resistance exercise protocol: a randomized clinical trial. *Nutrients*. 2017;9(9):1007. doi:10.3390/nu9091007
93. Bopp MJ, Houston DK, Lenchik L, et al. Lean mass loss is associated with low protein intake during dietary-induced weight loss in postmenopausal women. *J Am Diet Assoc*. 2008;108(7):1216–1220. doi:10.1016/j.jada.2008.04.017
94. Englert I, Bosy-Westphal A, Bischoff S, et al. Impact of protein intake during weight loss on preservation of fat-free mass, resting energy expenditure, and physical function in overweight postmenopausal women: a randomized controlled trial. *Obes Facts*. 2021;14(3):259–270. doi:10.1159/000514427
95. Silva TR, Lago SC, Yavorivski A, et al. Effects of high protein, low-glycemic index diet on lean body mass, strength, and physical performance in late postmenopausal women: a randomized controlled trial. *Menopause*. 2021;28(3):307–317. doi:10.1097/GME.0000000000001692
96. Nahas PC, Rossato LT, Martins FM, et al. Moderate increase in protein intake promotes a small additional improvement in functional capacity, but not in muscle strength and lean mass quality, in postmenopausal women following resistance exercise: a randomized clinical trial. *Nutrients*. 2019;11(6):1323. doi:10.3390/nu11061323
97. Longland TM, Oikawa SY, Mitchell CJ, et al. Higher compared with lower dietary protein during an energy deficit combined with intense exercise promotes greater lean mass gain and fat mass loss: a randomized trial. *Am J Clin Nutr*. 2016;103(3):738–746. doi:10.3945/ajcn.115.119339
98. Paddon-Jones D, Rasmussen BB. Dietary protein recommendations and the prevention of sarcopenia. *Curr Opin Clin Nutr Metab Care*. 2009;12(1):86–90. doi:10.1097/MCO.0b013e32831cef8b
99. Aubertin-Leheudre M, Adlercreutz H. Relationship between animal protein intake and muscle mass index in healthy women. *Br J Nutr*. 2009;102(12):1803–1810. doi:10.1017/S0007114509991310
100. Andrich DE, Filion M-E, Woods M, et al. Relationship between essential amino acids and muscle mass, independent of habitual diets, in pre- and post-menopausal US women. *Int J Food Sci Nutr*. 2011;62(7):719–724. doi:10.3109/09637486.2011.573772
101. Toth MJ, Sites CK, Matthews DE. Role of ovarian hormones in the regulation of protein metabolism in women: effects of menopausal status and hormone replacement therapy. *Am J Physiol Endocrinol Metab*. 2006;291(3):E639–E646. doi:10.1152/ajpendo.00050.2006



102. Capatina C, Carsote M, Caragheorgheopol A, et al. Vitamin d deficiency in postmenopausal women - biological correlates. *Maedica*. 2014;9(4):316–322.
103. Bruyère O, Malaise O, Neuprez A, et al. Prevalence of vitamin D inadequacy in European postmenopausal women. *Curr Med Res Opin*. 2007;23(8):1939–1944. doi:10.1185/030079907X219562
104. Tandon VR, Sharma S, Mahajan S, et al. Prevalence of vitamin d deficiency among Indian menopausal women and its correlation with diabetes: a first Indian cross sectional data. *J Midlife Health*. 2014;5(3):121–125. doi:10.4103/0976-7800.141188
105. Li S, Ou Y, Zhang H, et al. Vitamin D status and its relationship with body composition, bone mineral density and fracture risk in urban central south Chinese postmenopausal women. *Ann Nutr Metab*. 2014;64(1):13–19. doi:10.1159/000358340
106. Chlebowski RT, Johnson KC, Lane D, et al. 25-hydroxyvitamin D concentration Vitamin D intake and joint symptoms in postmenopausal women. *Maturitas*. 2011;68(1):73–78.
107. Buchanan JR, Santen R, Cauffman S, et al. The effect of endogenous estrogen fluctuation on metabolism of 25-hydroxyvitamin D. *Calcif Tissue Int*. 1986;39(3):139–144. doi:10.1007/BF02555109
108. LeBlanc ES, Desai M, Perrin N, et al. Vitamin D levels and menopause-related symptoms. *Menopause*. 2014;21(11):1197–1203. doi:10.1097/GME.0000000000000238
109. Rizzoli R, Boonen S, Brandi M-L, et al. Vitamin D supplementation in elderly or postmenopausal women: a 2013 update of the 2008 recommendations from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). *Curr Med Res Opin*. 2013;29(4):305–313. doi:10.1185/03007995.2013.766162
110. Anagnostis P, Dimopoulou C, Karras S, et al. Sarcopenia in post-menopausal women: is there any role for vitamin D? *Maturitas*. 2015;82(1):56–64. doi:10.1016/j.maturitas.2015.03.014
111. Park S, Ham JO, Lee BK. A positive association of vitamin D deficiency and sarcopenia in 50 year old women, but not men. *Clin Nutr*. 2014;33(5):900–905. doi:10.1016/j.clnu.2013.09.016
112. Petroni ML, Caletti MT, Dalle Grave R, et al. Prevention and treatment of sarcopenic obesity in women. *Nutrients*. 2019;11(6):1302. doi:10.3390/nu11061302
113. Pérez-López FR, Chedraui P, Pilz S. Vitamin D supplementation after the menopause. *Ther Adv Endocrinol Metab*. 2020;11:2042018820931291. doi:10.1177/2042018820931291
114. Buckinx F, Aubertin-Leheudre M. Nutrition to prevent or treat cognitive impairment in older adults: a GRADE recommendation. *J Prev Alzheimers Dis*. 2021;8(1):110–116. doi:10.14283/jpad.2020.40
115. Granic A, Sayer AA, Robinson SM. Dietary patterns, skeletal muscle health, and sarcopenia in older adults. *Nutrients*. 2019;11(4):745. doi:10.3390/nu11040745
116. Baumann CW, Kwak D, Liu HM, et al. Age-induced oxidative stress: how does it influence skeletal muscle quantity and quality? *J Appl Physiol*. 2016;121(5):1047–1052. doi:10.1152/japplphysiol.00321.2016
117. Cruz-Jentoft AJ, Romero-Yuste S, Chamizo Carmona E, et al. Sarcopenia, immune-mediated rheumatic diseases, and nutritional interventions. *Aging Clin Exp Res*. 2021;33(11):2929–2939. doi:10.1007/s40520-021-01800-7
118. Francaux M, Demeulder B, Naslain D, et al. Aging reduces the activation of the mTORC1 pathway after resistance exercise and protein intake in human skeletal muscle: potential role of REDD1 and Impaired Anabolic Sensitivity. *Nutrients*. 2016;8(1):47. doi:10.3390/nu8010047
119. Silva TR, Oppermann K, Reis FM, et al. Nutrition in menopausal women: a narrative review. *Nutrients*. 2021;13(7):2149. doi:10.3390/nu13072149
120. Barrea L, Pugliese G, Laudisio D, et al. Mediterranean diet as medical prescription in menopausal women with obesity: a practical guide for nutritionists. *Crit Rev Food Sci Nutr*. 2021;61(7):1201–1211. doi:10.1080/10408398.2020.1755220
121. Sayón-Orea C, Santiago S, Cuervo M, et al. Adherence to Mediterranean dietary pattern and menopausal symptoms in relation to overweight/obesity in Spanish perimenopausal and postmenopausal women. *Menopause*. 2015;22(7):750–757. doi:10.1097/GME.0000000000000378
122. Zhang Y, Guo H, Liang J, et al. Relationship between dietary omega-3 and omega-6 polyunsaturated fatty acids level and sarcopenia. A meta-analysis of observational studies. *Front Nutr*. 2021;8:738083. doi:10.3389/fnut.2021.738083
123. Tachtsis B, Camera D, Lacham-Kaplan O. Potential roles of n-3 PUFAs during skeletal muscle growth and regeneration. *Nutrients*. 2018;10(3):309. doi:10.3390/nu10030309
124. Chae M, Park K. Association between dietary omega-3 fatty acid intake and depression in postmenopausal women. *Nutr Res Pract*. 2021;15(4):468–478. doi:10.4162/nrp.2021.15.4.468
125. Cybulska AM, Skonieczna-żydecka K, Drozd A, et al. Fatty acid profile of postmenopausal women receiving, and not receiving, hormone replacement therapy. *Int J Environ Res Public Health*. 2019;16(21):4273. doi:10.3390/ijerph16214273
126. Jeromson S, Gallagher I, Galloway S, et al. Omega-3 fatty acids and skeletal muscle health. *Mar Drugs*. 2015;13(11):6977–7004. doi:10.3390/md13116977
127. Dupont J, Dedeyne L, Dalle S, et al. The role of omega-3 in the prevention and treatment of sarcopenia. *Aging Clin Exp Res*. 2019;31(6):825–836. doi:10.1007/s40520-019-01146-1
128. Bird JK, Troesch B, Warnke I, et al. The effect of long chain omega-3 polyunsaturated fatty acids on muscle mass and function in sarcopenia: a scoping systematic review and meta-analysis. *Clin Nutr ESPEN*. 2021;46:73–86. doi:10.1016/j.clnesp.2021.10.011
129. Aubree Hawley AT, Sam W, Xinya L, Jamie B, Baum J. The Impact of whey protein and/or omega-3 fatty acid supplementation on body composition, energy expenditure and metabolic health in postmenopausal women (SHAPE Study). *Curr Dev Nutr*. 2021;5(2):500. doi:10.1093/cdn/nzab041\_015
130. Duval K, Prud'homme D, Rabasa-Lhoret R, et al. Effects of the menopausal transition on energy expenditure: a MONET Group Study. *Eur J Clin Nutr*. 2013;67(4):407–411. doi:10.1038/ejcn.2013.33
131. Cunningham JJ. Body composition and resting metabolic rate: the myth of feminine metabolism. *Am J Clin Nutr*. 1982;36(4):721–726. doi:10.1093/ajcn/36.4.721
132. Abildgaard J, Pedersen AT, Green CJ, et al. Menopause is associated with decreased whole body fat oxidation during exercise. *Am J Physiol Endocrinol Metab*. 2013;304(11):E1227–E1236. doi:10.1152/ajpendo.00492.2012
133. Evans WJ. Skeletal muscle loss: cachexia, sarcopenia, and inactivity. *Am J Clin Nutr*. 2010;91(4):1123s–1127s. doi:10.3945/ajcn.2010.28608A
134. Mishra N, Mishra VN. Devanshi exercise beyond menopause: Dos and Don'ts. *J Midlife Health*. 2011;2(2):51–56.



135. Juppi H-K, Sipilä S, Cronin NJ, et al. Role of menopausal transition and physical activity in loss of lean and muscle mass: a follow-up study in middle-aged Finnish women. *J Clin Med*. 2020;9(5):1588. doi:10.3390/jcm9051588
136. Nunes PR, Barcelos LC, Oliveira AA, et al. Effect of resistance training on muscular strength and indicators of abdominal adiposity, metabolic risk, and inflammation in postmenopausal women: controlled and randomized clinical trial of efficacy of training volume. *Age*. 2016;38(2):40. doi:10.1007/s11357-016-9901-6
137. Botero JP, Shiguemoto GE, Prestes J, et al. Effects of long-term periodized resistance training on body composition, leptin, resistin and muscle strength in elderly post-menopausal women. *J Sports Med Phys Fitness*. 2013;53(3):289–294.
138. Vasconcelos KS, Dias JMD, Araújo MC, et al. Effects of a progressive resistance exercise program with high-speed component on the physical function of older women with sarcopenic obesity: a randomized controlled trial. *Braz J Phys Ther*. 2016;20(5):432–440. doi:10.1590/bjpt-rbf.2014.0174
139. Thiebaud RS, Loenneke JP, Fahs CA, et al. The effects of elastic band resistance training combined with blood flow restriction on strength, total bone-free lean body mass and muscle thickness in postmenopausal women. *Clin Physiol Funct Imaging*. 2013;33(5):344–352. doi:10.1111/cpf.12033
140. de Oliveira Silva A, Dutra M, De Moraes WM, et al. Resistance training-induced gains in muscle strength, body composition, and functional capacity are attenuated in elderly women with sarcopenic obesity. *Clin Interv Aging*. 2018;13:411–417. doi:10.2147/CIA.S156174
141. Huang SW, Ku J-W, Lin L-F, et al. Body composition influenced by progressive elastic band resistance exercise of sarcopenic obesity elderly women: a pilot randomized controlled trial. *Eur J Phys Rehabil Med*. 2017;53(4):556–563. doi:10.23736/S1973-9087.17.04443-4
142. Liao CD, Tsao J-Y, Lin L-F, et al. Effects of elastic resistance exercise on body composition and physical capacity in older women with sarcopenic obesity: a CONSORT-compliant prospective randomized controlled trial. *Medicine*. 2017;96(23):e7115. doi:10.1097/MD.00000000000007115
143. Asikainen TM, Kukkonen-Harjula K, Mäkelä S. Exercise for health for early postmenopausal women: a systematic review of randomised controlled trials. *Sports Med*. 2004;34(11):753–778. doi:10.2165/00007256-200434110-00004
144. Wu PY, Huang K-S, Chen K-M, et al. Exercise, nutrition, and combined exercise and nutrition in older adults with sarcopenia: a systematic review and network meta-analysis. *Maturitas*. 2021;145:38–48. doi:10.1016/j.maturitas.2020.12.009
145. Kim HK, Suzuki T, Saito K, et al. Effects of exercise and amino acid supplementation on body composition and physical function in community-dwelling elderly Japanese sarcopenic women: a randomized controlled trial. *J Am Geriatr Soc*. 2012;60(1):16–23. doi:10.1111/j.1532-5415.2011.03776.x
146. Orsatti FL, Maestà N, de Oliveira EP, et al. Adding soy protein to milk enhances the effect of resistance training on muscle strength in postmenopausal women. *J Diet Suppl*. 2018;15(2):140–152. doi:10.1080/19390211.2017.1330794
147. Maesta N, Nahas EAP, Nahas-Neto J, et al. Effects of soy protein and resistance exercise on body composition and blood lipids in postmenopausal women. *Maturitas*. 2007;56(4):350–358. doi:10.1016/j.maturitas.2006.10.001
148. Kim H, Suzuki T, Saito K, et al. Effects of exercise and tea catechins on muscle mass, strength and walking ability in community-dwelling elderly Japanese sarcopenic women: a randomized controlled trial. *Geriatr Gerontol Int*. 2013;13(2):458–465. doi:10.1111/j.1447-0594.2012.00923.x
149. Nabuco HCG, Tomeleri CM, Fernandes RR, et al. Effect of whey protein supplementation combined with resistance training on body composition, muscular strength, functional capacity, and plasma-metabolism biomarkers in older women with sarcopenic obesity: a randomized, double-blind, placebo-controlled trial. *Clin Nutr ESPEN*. 2019;32:88–95. doi:10.1016/j.clnesp.2019.04.007
150. Mason C, Xiao L, Imayama I, et al. Influence of diet, exercise, and serum vitamin d on sarcopenia in postmenopausal women. *Med Sci Sports Exerc*. 2013;45(4):607–614. doi:10.1249/MSS.0b013e31827aa3fa
151. Josse AR, Atkinson SA, Tarnopolsky MA, et al. Increased consumption of dairy foods and protein during diet- and exercise-induced weight loss promotes fat mass loss and lean mass gain in overweight and obese premenopausal women. *J Nutr*. 2011;141(9):1626–1634. doi:10.3945/jn.111.141028
152. Barbat-Artigas S, Garnier S, Joffroy S, et al. Caloric restriction and aerobic exercise in sarcopenic and non-sarcopenic obese women: an observational and retrospective study. *J Cachexia Sarcopenia Muscle*. 2016;7(3):284–289. doi:10.1002/jcsm.12075
153. Tiidus PM. Benefits of estrogen replacement for skeletal muscle mass and function in post-menopausal females: evidence from human and animal studies. *Eurasian J Med*. 2011;43(2):109–114. doi:10.5152/eajm.2011.24
154. Sørensen MB, Rosenfalck AM, Højgaard L, et al. Obesity and sarcopenia after menopause are reversed by sex hormone replacement therapy. *Obes Res*. 2001;9(10):622–626. doi:10.1038/oby.2001.81
155. Kenny AM, Kleppinger A, Wang Y, et al. Effects of ultra-low-dose estrogen therapy on muscle and physical function in older women. *J Am Geriatr Soc*. 2005;53(11):1973–1977. doi:10.1111/j.1532-5415.2005.53567.x
156. Aubertin-Leheudre M, Audet M, Goulet EDB, et al. HRT provides no additional beneficial effect on sarcopenia in physically active postmenopausal women: a cross-sectional, observational study. *Maturitas*. 2005;51(2):140–145. doi:10.1016/j.maturitas.2004.06.017
157. Mintzioris G, Lambrinoudaki I, Goulis DG, et al. EMAS position statement: non-hormonal management of menopausal vasomotor symptoms. *Maturitas*. 2015;81(3):410–413. doi:10.1016/j.maturitas.2015.04.009
158. Glisic M, Kastrati N, Musa J, et al. Phytoestrogen supplementation and body composition in postmenopausal women: a systematic review and meta-analysis of randomized controlled trials. *Maturitas*. 2018;115:74–83. doi:10.1016/j.maturitas.2018.06.012
159. Tang S, Du Y, Oh C, et al. Effects of soy foods in postmenopausal women: a focus on osteosarcopenia and obesity. *J Obes Metab Syndr*. 2020;29(3):180–187. doi:10.7570/jomes20006
160. Adlercreutz H. Phytoestrogens: epidemiology and a possible role in cancer protection. *Environ Health Perspect*. 1995;103(Suppl 7):103–112. doi:10.1289/ehp.95103s7103
161. Galleano M, Calabro V, Prince PD, et al. Flavonoids and metabolic syndrome. *Ann N Y Acad Sci*. 2012;1259(1):87–94. doi:10.1111/j.1749-6632.2012.06511.x
162. Aubertin-Leheudre M, Lord C, Khalil A, et al. Six months of isoflavone supplement increases fat-free mass in obese-sarcopenic postmenopausal women: a randomized double-blind controlled trial. *Eur J Clin Nutr*. 2007;61(12):1442–1444. doi:10.1038/sj.ejcn.1602695
163. Choquette S, Dion T, Brochu M, et al. Soy isoflavones and exercise to improve physical capacity in postmenopausal women. *Climacteric*. 2013;16(1):70–77. doi:10.3109/13697137.2011.643515

164. Smith-Ryan AE, Cabre HE, Eckerson JM, et al. Creatine supplementation in women's health: a lifespan perspective. *Nutrients*. 2021;13(3):877. doi:10.3390/nu13030877
165. Lobo DM, Tritto AC, da Silva LR, et al. Effects of long-term low-dose dietary creatine supplementation in older women. *Exp Gerontol*. 2015;70:97–104. doi:10.1016/j.exger.2015.07.012
166. Gualano B, Macedo AR, Alves CRR, et al. Creatine supplementation and resistance training in vulnerable older women: a randomized double-blind placebo-controlled clinical trial. *Exp Gerontol*. 2014;53:7–15. doi:10.1016/j.exger.2014.02.003
167. Chilibeck PD, Kaviani M, Candow D, et al. Effect of creatine supplementation during resistance training on lean tissue mass and muscular strength in older adults: a meta-analysis. *Open Access J Sports Med*. 2017;8:213–226. doi:10.2147/OAJSM.S123529
168. Fragala MS, Dam T-TL, Barber V, et al. Strength and function response to clinical interventions of older women categorized by weakness and low lean mass using classifications from the Foundation for the National Institute of Health sarcopenia project. *J Gerontol a Biol Sci Med Sci*. 2015;70(2):202–209. doi:10.1093/gerona/glu110

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