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REVIEW ARTICLE

Effects of Resistance Exercise on Older Individuals with Sarcopenia: Sex Differences in Humans

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Sarcopenia affects tens of millions of adults worldwide, with a reported prevalence of 10-50% among older adults. A decrease in muscle strength and function due to aging reduces physical performance, causing pain and disease. Accordingly, interest in the treatment or prevention of sarcopenia through resistance exercises, which have been found to be effective in improving muscle strength and hypertrophy, is increasing. However, given the individual differences, it is difficult to determine the optimal RE method. Currently, the importance of personalized resistance exercise (RE) prescriptions is emphasized, and research on sex/gender differences needs to be conducted. Our review focused on the effects of resistance exercise on muscle strength, muscle hypertrophy, and muscle function in older adults in relation to sex differences. In this review, we aimed to analyze sex differences in the effect of RE on older adults with sarcopenia and provide meaningful information for future research on exercise programs for individuals with sarcopenia.

Key words: Sex difference, Resistance exercise, Sarcopenia, Muscular function

INTRODUCTION

In 1989, Rosenberg defined sarcopenia as the decline in muscle mass and function due to aging [1]. Sarcopenia affects tens of millions of adults worldwide, with a reported prevalence range of 10-50% among older people [2,3]. Muscle mass reaches a peak in healthy adults in their 20s and 30s, and then decreases thereafter by approximately 1% per year, with an accelerated rate after the age of about 50 years. A decrease in muscle strength and function due to aging reduces physical performance, causing pain and disease [4]. The older population is rapidly increasing worldwide; the longer life expectancy and the sizeable "baby boomer" generation have resulted in the older population accounting for a large proportion of the world's population. By 2050, one-quarter of the world's population is expected to be over 60 years of age. Aging of the population is linked to an increase in the prevalence of impairment and disability and is expected to impose a tremendous strain on the healthcare system [5,6]. Owing to these latent results, interest in the treatment or prevention of sarcopenia through resistance exercises, which have been found to be effective in improving muscle strength and hypertrophy, is increasing.

Currently, there is no effective pharmacological intervention for the treatment of sarcopenia. However, physical activity or resistance exercise (RE) as a non-pharmacological intervention is an effective tool for improving physical constitution and muscle function in older individuals, and it has positive effects, such as improving the quality of life and reducing falls through increasing muscle mass and muscle strength in older individuals with muscle loss [7,8]. RE is possible in all age groups and plays an important role in improving and maintaining bone density. It is also used to prevent and treat chronic diseases and provides benefits in terms of functional movements, physical performance, and psychological facets [9,10]. The U.S. Department of Health and Human Services recommends exercising more than twice a week, in a way that incorpo-

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rates all major muscles. However, muscle adaptability varies, depending on frequency, strength, volume, age, sex, etc. Thus, given the individual differences, it is difficult to determine the optimal RE method [11,12]. Therefore, studies of the relationship of training methods with age and sex can provide useful information for RE prescriptions for older individuals.

Sex is also relevant to RE prescriptions. Sex has been included as an auxiliary analysis in studies that have experimented with various resistance movements. However, studies comparing resistance training results between older men and women have yielded inconsistent results. For example, some studies have shown significant differences between the sexes in terms of muscle mass or muscle strength after RE [13,14], whereas other studies found no difference in the effect of RE between older men and women [15,16]. Further studies are needed to clarify the effect of RE on muscle adaptation according to sex differences and to determine whether RE protocols should be prescribed differently for older men and women.

In general, men have a greater absolute muscle size and muscle strength than women, but the reduction in muscle size and muscle strength due to aging in men may be almost twice that in women [17]. In studies on older individuals, sex differences in muscle size and strength that accumulate with age suggest that sex can affect the prevalence of and may be a risk factor for sarcopenia. Sex-specific interventions for muscle size, muscle strength, and preventing sarcopenia should be considered when developing exercises to minimize muscle loss due to aging [18-20]. The physiology of sarcopenia is thought to be multifactorial and many explanations have been proposed, including neurodegenerative processes, proteolytic hormone production, decreased sensitivity, dysregulation of cytokine secretion, and modification of inflammatory states [21]. Thus, sex-differences in muscle physiology may affect adaptation to RE. Moreover, the sexes differ in terms of fatigue, inflammatory response, recovery time after exercise, and muscle fiber size and composition [22-24]. In addition, in terms of metabolism during exercise, women oxidize more fat than men, but demonstrate less carbohydrate oxidation and exhibit faster oxygen intake dynamics during moderate intensity exercise [25,26]. Previous studies have shown that post-exercise adenosine triphosphate (ATP) concentration decreases less in women than in men. These results indicate that women's skeletal muscle metabolism is more suitable for the resynthesis of ATP during exercise [27]. However, despite these known sex-specific physiological differences, sex differences in the adaptation of older adults to REs remain unclear. Moreover, evidence of the usefulness of RE in older individuals with sarcopenia is lacking. Such scientific evidence is necessary in order for exercise scientists and field exercise experts to contribute to prevention of sarcopenia among older individuals.

Therefore, in this review, we aimed to analyze sex differences in the effect of RE on older adults with sarcopenia and to provide meaningful information for the direction of future research into or exercise programs for individuals with sarcopenia.

METHODS

PubMed, Science Direct, and Google Scholar databases were searched, for clinical and non-clinical studies on the effects of RE in older individuals with sarcopenia, published between 1980 and 2023. The keywords were "aging muscle and sarcopenia," "sex differences and RE effects," "response to RE in the elderly," "sex differences and sarcopenia in the elderly," and prevalence of sarcopenia and sex differences.

This review included cross-sectional studies, randomized, double-blind studies (randomized controlled trials, RCTs), and retrospective analysis studies. Animal and experimental model studies were excluded from the review. In addition, studies with a small sample size were excluded, as well as studies that did not adequately specify the selection criteria or included groups of subjects receiving medication for another disease that affected bone or muscle metabolism. This review included studies using EWGSOP and IWGS among the criteria for evaluating various sarcopenia.

RESULTS

1. Sex differences in muscle strength and RE adaptation in older individuals

Several studies have shown that sarcopenia strongly affects muscle strength. In cases of sarcopenia, muscle mass decreases at a rate of approximately 1% per year, while the accompanying reduction in muscle strength and function occurs more quickly [28]. One study found that muscle strength decreased by 2-4% per year, while another study found that muscle strength decreased by 8-9% over a 3-year period [29,30]. Decreased muscle strength strongly predicts physical injury in older individuals.

Consequently, maintaining muscle strength, such as through RE, is an important factor in treating sarcopenia, and in preventing reduced muscle function and physical injury [31,32]. RE is an exercise style that

brings about many health benefits, particularly for older individuals, by improving their quality of life by improving muscle strength, muscle mass, body function, and bone density, and preventing chronic diseases [33,34]. The effectiveness of RE in reversing age-related reduction in muscle function has been consistently demonstrated. Conducting REs above intermediate intensity for 8-12 weeks showed a 25-25% increase in lower and upper body strength in older individuals [35,36]. Interestingly, an increase in muscle strength due to RE occurs before muscle hypertrophy develops [29], and are due to physiological stages of neural adaptation that appear early in training [37,38].

When considering RE to prevent and treat sarcopenia, it is necessary to consider the abovementioned timing of sarcopenia development according to sex. It is also necessary to consider the effect of RE on muscle strength and neuromuscular function in older individuals according to sex differences, because absolute values, such as muscle mass and fat content, typically differ between the sexes [39]. Sex differences exist not only in the mass but also in the distribution of skeletal muscle. Women generally have lower muscle mass, higher body fat ratios, and smaller muscle fiber cross-sectional areas than men [40]. Differences in muscle strength and muscle mass between men and women can, at least partially, be ascribed to differences in muscle fiber type. Compared to men, women have a higher distribution of type 1 fibers, with relatively less muscle force and smaller size of the outer vastus lateralis and biceps brachii [41,42]. In addition, reduction in muscle strength and muscle mass occurs faster in women in the early stages of aging than in their male counterparts, due to the reduced estrogen levels in the blood after menopause.

In several studies examining the effect of RE according to sex differences in older individuals, men showed higher muscle strength improvement than did women [14,43-46]. In a s tudy published in 2021-year examined sex differences in response to RE over a 40-week period in 160 older adults (aged 55-74 years). The study showed an upper body strength improvement of 7.2 kg for men and 2.7 kg for women (one repetition maximum: 1RM), and a total strength improvement of 14.5 kg for men and 10.9 kg for women (1RM) after RE [43], Tracy et al., in 1999, studied the effect of performing RE three times a week for 9 weeks in 23 older persons (aged 65-75 years). They showed that knee extension strength (1RM) improved by 13% in men after RE, while women showed no significant increase [44]. In a 2016 study of sex differences in responses to RE training in 23 older persons aged 65 years, isometric knee extensor strength increased by 41.7% in men and 15.8% in women after RE [14]. A study, published in 2021 by Anne et al. [45], of 275 older people (aged 62-70 years) investigated sex differences in responses to gradual RE three times a week for 9 weeks showed an increase in maximal isometric knee extensor strength of 26 Nm in men and 10 Nm in women. A study published in 2000-year investigating the effect of RE on muscle quality according to sex and age in 22 older people (aged 65-75 years) showed that knee extensor strength (1RM) improved by 19.9 kg in men and 12.2 kg in women after RE investigating the effect of RE on muscle quality according to sex and age in 22 older people (aged 65-75 years) showed that knee extensor strength (1RM) improved by 19.9 kg in men and 12.2 kg in women after RE [46]. In five studies, women showed significant improvement as compared to the pre-test or control group, while men showed more improvement than women (Table 1).

On the other hand, in a study published in 2016-year investigating the effect of RE on muscle quality according to sex and age in 22 older people (aged 65-75 years) showed that knee extensor strength (1RM) improved by 19.9 kg in men and 12.2 kg in women after RE investigating the effect of RE twice a week for 20-24 weeks in 103 older persons (aged 60 years or older) showed that maximum bilateral concentric strength (1RM) of the hip and knee extensors and plantar flexors improved by 18.9% in men and by 30% in women [47]. In addition, the study published in 1998-year of 21 older persons (aged 65 years) on the effect of RE, based on electromyography and muscle strength, showed that maximum isometric leg extension force improved by 36% in men and 57% in women, and that leg extension (1RM) increased by 21% in men and 30% in women [48]. According to a study published in 1994 by Häkkinen et al., who investigate the effect of two weekly REs on muscle strength and hormonal development in 21 older persons (aged 64-73 years), isometric leg extension maximal force increased by 484 N in men and by 667 N in women after RE. However, the improvement did not differ statistically significantly between the sexes [49]. A study published in 2014 by Gregory et al. [50] investigated changes in maximum muscle strength in 32 older individuals (aged 74 years) in response to RE. They found improvements in leg press (Male: 9.3 kg, Female: 6.1 kg), leg extension (Male: 2.3 kg, Female: 2 kg), and bicep curl (Male: 1 kg, Female: 1.1 kg) after RE, but found no significant difference in the changes in muscle strength between the sexes. In a study comparing the effect of RE on muscle strength in older individuals by sex, both male and female groups showed improvement over the pre-test or control group (Table 1).

Taken together, sex is a biological factor that should be considered in the differences in the response to and effectiveness of RE. Because the

Table 1. Sex differences in the effect of resistance exercise in the elderly on muscle strength, muscle mass, and muscle function

Factor	Note	Significant difference		Age	Case number	Reference
		Male	Female			
Muscle strength	- Maximal bilateral concentric strength (one repetition maximum, 1RM) of the hip and knee extensors and plantar flexors (Men: 18.9%, Women: 30%)	+	+	60 <	103	[47]
	- Total strength (1RM): (Men: 14.5 kg, Women: 7.3 kg)	+	+	55-74	160	[43]
	- Upper body strength (1RM): (Men: 7.2 kg, Women: 2.7 kg)					
	- Knee extensor strength (1-RM, isometric peak): (Men: 13%, Women: 7%)	+	N.S	65-75	23	[44]
	- Knee extensor isometric strength: (Men: 41.7%, Women: 15.8%)	+	+	65 <	23	[14]
	- Maximal isometric knee extensor strength: (Men: 26 Nm, Women: 10 Nm)	+	+	62-70	275	[45]
	- Isometric leg extension maximal force: (Men: 484 N, Women: 667 N)	+	+	64-73	21	[49]
	- Knee extensors strength (1RM): (Men: 19.9 kg, Women: 12.2 kg)	+	+	65-75	22	[46]
	- Maximal isometric leg-extension force: (Men: 36%, Women: 57%)	+	+	65 <	21	[48]
	- 1 RM leg-extension: (Men: 21%, Women: 30%)					
	- Leg press 1RM: (Men: 9.3 kg, Women: 6.1 kg)	+	+	74.3 ± 5.4	32	[50]
	- Leg extension 1RM: (Men: 2.3 kg, Women: 2 kg)					
	- Bicep curl 1RM: (Men: 1 kg, Women: 1.1 kg)					
Muscle mass	- Only the data of the changes in quadriceps femoris muscle cross-sectional area (CSA); Magnetic resonance imaging (MRI) scanner, vastus lateralis muscle thickness or leg lean mass: dual-energy X-ray absorptiometry (DXA): (Men: 5.1%, Women: 4.2%)	+	+	60 <	103	[47]
	- Rectus femoris muscle CSA; MRI scanner: (Men: 4.3 cm^2, Women: 2.9 cm^2)	+	+	55-74	160	[43]
	- Quadriceps muscle volume CSA: MRI scanner: (Men: 3.6%, Women: 2.0%)	+	+	65 <	23	[14]
	- Vastus lateralis CSA; MRI scanner: (Men: 63 mm^2, Women: 20 mm^2)	+	+	62-70	275	[45]
	- Lean body mass; DXA: (Men: 715 g, Women: 690 g)					
	- Quadriceps muscle volume CSA: (Men: 203.5 cm^3, Women: 135 cm^3)	+	+	65-75	22	[46]
	- Vastus lateralis CSA: (Men: 36%, Women: 7.1%)	+	+	61-77	14	[13]
	- Lean body mass; DXA: (Men: 3.5%, Women: 2.4%)	+	+	70 <	70	[58]
	- Lean leg mass: (Men: 3.4%, Women: 3.7%)					
	- Lean arm mass: (Men: 5.8%, Women: 5.2%)					
	Lean mass: body composition was estimated using bioelectrical impedance analysis: (Men: 1.3 %, Women: 1.4%)	+	+	50-80	764	[59]
Physical function	- A 30s chair-stand test to determine the ability to rise from a chair: (Men: 3.1 reps, Women: 1.8 reps)	+	+	62-70	275	[45]
	- Short performance physical battery test (SPBB): Tests of balance, walk speed, and timed chair standing (Men: 10.0%, Women: 13.9%)	+	+	65 <	23	[14]
	- SPBB: tests of balance, walk speed, and timed chair standing 4-m walk time, sec: (Male: - 6.2%, Female: -4.8%), Sit-to-stand, sec: (Men: -16.3%, Women: -4.7%), Times up and go, sec: (Men: -17.6%, Women: -10%)	-	-	70 <	70	[58]
	- Push-ups in 30 sec: (Men: 1.5 reps, Women: 2 reps)	+	+	50-80	764	[59]
	- Chair-stand in 30 sec: (Men: 1.5 reps, Women: 1.7 reps)					
	- Sit-ups in 30 sec: (Men: 1.1 reps, Women: 1.6 reps)					
	- Sit-and-reach: (Men: 3 cm, Women: 2.8 cm)					

+: increase, -: decrease.
N.S, not significant; Ref., reference.

proportion of studies in which men showed more improvement than women was high, the effect of RE may differ depending on sex in older individuals. However, some studies have reported a greater increase or no difference among women. Many studies have examined the effectiveness of RE in older individuals, but few studies have directly compared the differences in the effectiveness of RE between men and women. Thus, the differences in RE according to sex in older individuals remain unclear because there are many individual factors that could affect changes in response to RE [51,52]. For effective treatment and prevention of sarcopenia, sex differences should be investigated, and differences in RE methods between men and women should be presented. Further studies are needed to prove the differences in muscle strength changes after RE in older individuals according to sex, and a comprehensive review of studies directly comparing sex differences is needed.

2. Sex differences in muscle mass and RE adaptation in older individuals

Skeletal muscle is used as a source of energy by the body when other energy sources are depleted; therefore, a decrease in muscle mass can significantly increase mortality [53]. In addition, a decrease in skeletal muscle mass increases the prevalence of metabolic diseases, such as insulin resistance, diabetes, dyslipidemia, and hypertension, and is closely associated with cardiovascular disease, cancer, and mortality [54,55]. Muscle mass is related to sarcopenia caused by aging and is a major factor in the evaluation of sarcopenia. Therefore, maintaining or improving muscle mass in older individuals is important for healthy aging. RE has proven to be a particularly effective means for maintaining and improving muscle mass [56]. However, the effects of RE vary depending on factors such as sex, age, and race. Nevertheless, few studies have investigated RE prescriptions considering these individual differences. In addition, in the case of older individuals, muscle strength and function decrease faster due to sarcopenia in women than in men, and studies have shown differences in muscle aging according to sex [29,57].

In several studies that investigated the effect of RE according to sex differences in older individuals, men showed a greater increase in muscle mass than women [13,14,43,45,46,48]. In 2021, a study of 160 people aged 55-74 years surveyed changes in muscle mass in response to RE training. After RE, the rectus femoris muscle cross-sectional area improved by 4.3 cm^2 in men and 2.9 cm^2 in women. The study found a significant improvement in muscle mass in both men and women, with men showing a greater increase in muscle mass than women [43]. A study published in 2016-year of 23 older persons (aged 65 years or older) investigated sex differences in muscle mass changes due to RE. They found that the quadriceps muscle cross-sectional area increased by 3.6% in men and 2.9% in women [14]. In 2021, a study of 275 older persons aged 62-70 years showed that the vastus lateralis cross-sectional area increased by 63 mm^2 in men and 20 mm^2 in women after three gradual REs per week for 9 weeks. In addition, lean body mass increased by 715 g in men and 690 g in women [45]. In 2000, a study of the effect of RE on muscle mass in 22 older persons aged 65-75 years showed that quadriceps muscle cross-sectional area increased by 203.5 cm^3 in men and 135 cm^3 in women [46]. According to a study, published in 2013 by Bamman et al., on the effect of RE on muscle hypertrophy in 14 older individuals (aged 61-77 years) who performed RE three times a week, the vastus lateralis cross-sectional area increased by 36% in men and 7.1% in women (Table 1) [13].

In six studies that showed increased muscle mass in older men in response to RE, the older women also showed significant improvement over the pre-test or control group, although men showed a greater improvement than women. However, in other studies, women showed greater muscle mass increase than did men. According to a 1998 study on sex differences in the effect of RE, as assessed by electromyography, muscle mass, and muscle strength, in 21 older persons (aged 65 years or older), the quadriceps femoris cross-sectional area increased by 6% in women, whereas no significant increase in muscle mass was observed in men [48]. In a study published in 2019 by Sanna et al., the effect of RE (three times a week for 4 weeks) on muscle mass was investigated in 70 older persons (aged 70 years or older) with sarcopenia. The study found significant increases in lean body mass (men, 3.5%; women, 2.4%), lean leg mass (men, 3.4%; women, 3.7%), and lean arm mass (men, 5.8%; women, 5.2%), but the sexes did not differ significantly [58]. A 2022 study of the acute response of muscle mass to RE in 764 older persons (aged 65-80 years) showed that lean mass improved by 1.3% in men and 1.4% in women, which was not significantly different between the sexes (Table 1) [59].

Taken together, when comparing the effect of RE on muscle mass in older individuals by sex, many studies found that men showed a greater increase in muscle mass than did women, but other studies found the opposite, or found no differences between the sexes. Thus, although older men who perform RE tend to show more muscle mass increase than older women, few studies have directly compared the effect of RE on muscle mass in older individuals according to sex. As with muscle strength, many individual factors can affect muscle mass changes caused by RE. In addition, the results of these studies may be inconsistent due to differences in exercise protocols and muscle mass measurement methods used [52,60]. Therefore, further studies are needed to prove this difference by directly comparing the changes in muscle mass after RE in older individuals according to sex, using standardized approaches.

3. Sex differences in physical function changes in response to RE in older individuals

The main problem associated with sarcopenia is the reduction in physical ability due to loss of muscle function, which increases the likelihood of falls and reduces the quality of life of older individuals. Sarcopenia has been reported to cause physical disability and even death [61,62]. Although opinions are divided on the diagnosis of sarcopenia, muscle strength, muscle mass, and physical function are key diagnostic criteria for sarcopenia [63]. Studies have shown that muscle power decreases at a

faster rate than muscle strength during aging and that muscle power has a higher correlation with physical function than does muscle strength or mass [64,65]. Various physical functions, such as walking speed, stride, flexibility, and balance ability can be improved through RE.

The main cause of deterioration in physical function due to aging is sarcopenia, characterized by reduced muscle strength and mass, which can be improved by RE [14,45,58,59], although individual factors, such as sex, age, and race, modulate the effects of RE [29,66]. Studies have examined sex differences in the effect of RE on physical function in older individuals; however, the differences in the effects of RE on physical function according to sex remain unclear because very few studies have directly compared the effects in men and women [38,48,67]. Thus, to maintain and improve physical function effectively in older individuals, it is necessary to study the effects of RE according to sex.

In 2021, Anne et al. published a study sex differences in the effect of gradual RE (three times a week for 9 weeks) on the physical function of 275 older persons (aged 62-70 years). After the RE intervention, a 30-s chair-stand test was used to determine the ability to rise from a chair. The study showed that this ability increased by 3.1 repetitions in men and 1.8 repetitions in women [45]. A study published in 2019-year investigating the effect of RE on functional muscle strength in older individuals (aged 70 years or older) showed that RE, conducted three times a week for 10 weeks [58], resulted in overall improvements in SPBB: 4-m walk time, sec (male: -6.2%, female: -4.8%), sit-to-stand time test, sec (male: -16.3%, female: -4.7%), timed up-and-go, sec (male: -17.6%, female: -10%) (Table 1) [58].

Other studies have shown that, after RE, the physical function improved more in older women than in older men, or that these improvements did not differ by sex. In a study published in 2016 by Da Boit et al., sex differences in changes in muscle function in response to RE were investigated in 23 older individuals (aged 65 years or older). They showed that, after RE twice a week for 18 weeks, tests for balance, walking speed, and timed chair standing increased by 10% in men and by 13.9% in women. While both men and women showed improved physical function after RE, women showed a higher rate of improvement than did men [14]. According to a study of 764 older persons (aged 50-80 years) that researched differences in the effects of RE according to sex and age, physical function improved after three sessions of RE per week for 4 weeks in terms of push-ups in 30s (men: 1.5 repetitions, women: 2 repetitions), chair-stand in 30s (men: 1.5 repetitions, women: 1.7 repetitions), sit-ups in 30s (men: 1.1 repetitions, women: 1.6 repetitions), sit-and-reach (men: 3 cm, women: 2.8 cm) (Table 1) [59].

Thus, in studies of the effect of RE on the physical function of older adults by sex, both male and female groups showed greater improvement in physical function than did the pre-test or control groups. Many studies found that men showed a greater increase than women, while other studies found the opposite results or did not discover sex differences. Few studies have directly compared the effect of RE on physical function in older individuals according to sex, so that the effect of RE in the sexes is unclear, partly due to differences across studies in terms of exercise method and exercise period. Therefore, further research is needed to investigate sex differences in the effects of RE, in order to maintain and improve physical function, which is directly related to quality of life, in older individuals.

4. Sex differences in physiological characteristics and adaptation to RE in older individuals

Sex differences in the effect of RE intervention in older individuals, while unclear, may be due to sex-differences in physiological characteristics, such as skeletal muscle type, protein synthesis, hormones, and muscle fatigue [67,68]. Examining the physiological characteristics of skeletal muscles clarifies that sex differences can affect responses to exercise. Sex differences in gene expression causes differences in phenotypic expression and significant differences in the morphological composition of skeletal muscle. Men possess more skeletal muscle than women, which contributes to greater maximal muscle strength [68,69]. Women have more type I muscle fibers, which are relatively small in size and power but are more resistant to fatigue, than do men, while men have more type II muscle fibers, which are relatively large in size and strong in power, but show weak resistance to fatigue. These sex-related differences in muscle fiber types according to the sexes also affect responses to RE intervention.

In a study in which RE was conducted for 9 weeks, muscle hypertrophy was seen in both type I and II muscle fibers in older men [70]. In contrast, older women showed less muscle hypertrophy than men after RE. Another study investigated the effect of 12-week RE on muscle hypertrophy in older women and showed a significant increase in type II muscle fibers, but not in type I muscle fibers [71]. In yet another study, only type I fibers, but not type II fibers, showed an increase in cross-sectional area (10%). The physiological characteristics of these skeletal muscles, according to sex, can cause differences in the effects of RE in older men and women [72].

Another physiological property that can affect sex differences in re-

sponses to RE intervention involves the hormones that are related to protein synthesis. With aging, muscle health can be affected by the whole-body environment, including changes in the hormonal environment. Several circulating (insulin-like growth factor 1 [IGF-1] and testosterone) and locally expressed factors are thought to be important in the regulation of muscle mass based on their involvement in muscle protein synthesis [73]. IGF-1 is upregulated in overloaded muscles and is associated with increased expression of myogenic regulatory factors, such as myogenin. In a previous study an increase in IGF1 mRNA expression in young adults after a single RE session in young adults an increase in IGF1 mRNA expression in young adults after a single RE session in young adults [74]. When stimulated by loading or myotoxicity, the expected increase in myogenic expression in older muscles, as compared with younger muscles, is reduced or delayed [75,76]. Based on these data, possible sex differences in RE-induced hypertrophy among older adults may be related to sex differences in muscle IGF-1 or myogenin expression.

Additionally, evidence suggests that decreased muscle mass during aging is associated with decreased testosterone levels [77]. Testosterone treatment in men increases muscle protein synthesis and IGF-1 expression, suggesting that testosterone regulates muscle growth by activating IGF-1 expression. In this case, a higher level of protein synthesis and regulation can be expected in men than in women, due to the 35-40-fold difference in their testosterone levels [78]. These hormonal differences between men and women may provide insights into increased mortality associated with sarcopenia in older women [79].

Muscle fatigue can define the limitations of male and female performance, ergonomic work, and performance during rehabilitation. It also serves as the basis for defining neuromuscular overload and the adaptation needed to improve skeletal muscle training and rehabilitation [80]. The details of the task determine the neuromuscular areas that would be most stressed, which reduces the muscle power or strength required during the task. Thus, muscle fatigue and contribution mechanisms are specific not only to the needs of the task but also to the physical characteristics of the individuals being evaluated, including their sex [81]. A study on muscle fatigue associated with isometric contraction performed in a single-limb muscle group showed that women had lower fatigue levels than men [22]. Sex-specific differences within the neuromuscular system can cause differences in the stress rate of an area between men and women for a given contraction fatigue, resulting in differences in muscle fatigue between the sexes. These factors that affect muscle fatigue according to sex are due to differences in the prevalent fiber type of skeletal muscle [82]. Types I and II muscle fibers have different calcium dynamics, and differences in muscle contraction and relaxation speeds, which lead to differences in muscle fatigue according to sex [83]. In addition, women have a greater vasodilatory response during exercise than men, indicating that there is a sex difference in muscle metabolism due to differences in muscle perfusion [84]. Overall, these studies suggest differences in muscle metabolism and muscle fatigue according to sex, but few studies have investigated these sex differences in terms of RE intervention in older individuals. Therefore, our understanding of the relationship of muscle metabolism to the responses to RE in older individuals is limited.

CONCLUSION

Muscle function may deteriorate with age, resulting in the development of sarcopenia. RE is one of the most effective methods of preventing and improving sarcopenia. This review showed that sex-specific differences are present in terms of both sarcopenia and the effects of RE interventions on muscle strength, muscle mass, and physical function in older adults. Both men and women show greater improvements in muscle strength, muscle mass, and physical function than a pre-test or control group after RE. In addition, when analyzing sex-related differences, a greater increase in muscle strength, mass, and physical function was observed in men than in women. Differences are likely due to differences in physiological characteristics, such as skeletal muscle type, hormones, and muscle fatigue proclivity. Because there are sex differences in the response to RE and physiological characteristics of older individuals, it is necessary to consider RE protocols according to sex. However, few studies have directly compared sex differences in this regard in older individuals, and there are limitations in understanding of sex differences in terms of the effect of RE in older people, due to the confounding effects of individual characteristics. Therefore, to improve and prevent sarcopenia effectively, future studies need to investigate sex differences in the effects of RE interventions in older individuals comprehensively, to prove and present effective RE methods appropriate for each sex.

CONFLICT OF INTEREST

These authors have no support or funding to report, and the authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: KW Noh, S Park; Data curation: KW Noh; Formal analysis: KW Noh, S Park; Methodology: KW Noh, S Park; Project administration: KW Noh, S Park; Visualization: KW Noh; Writing - original draft: KW Noh; Writing - review & editing: S Park.

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