Management of Sarcopenia to Improve Quality of Life in Geriatric Populations

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ABSTRACT: Sarcopenia, characterized by a progressive loss of skeletal muscle mass and strength that occurs with advancing age, has been associated with falls, fracture, disability, and mortality. Depending on the definitions used, the prevalence in 60- to 80-year old population is reported as 0.9%–35.9%, while the prevalence ranges from 7%–70.0% in people older than 80 years. Sarcopenia has been associated with lower quality of life. Well-designed exercise interventions, particularly resistance training as well as nutritional supplementation, have been proved to improve muscle strength and performance in geriatric populations. Resistance training may also enhance quality of life. However, there are limited data on the effects of nutritional supplementation as an intervention on quality of life among individuals with sarcopenia. This review briefly summarizes the relationship between sarcopenia and quality of life and presents the potential of interventions to improve muscle quality, physical performance, and quality of life.

KEYWORDS: sarcopenia, skeletal muscle mass, quality of life, health-related quality of life, interventions

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Sarcopenia

Sarcopenia, defined as a geriatric syndrome characterized by a progressive loss of skeletal muscle mass and strength that occurs with advancing age, was first introduced by Rosenberg in 1989.[1,2] The decline in muscle mass occurs after the age of 30 years.[3,4] After the age of 50 years, muscle mass is reported to decline at an annual rate of approximately 0.2%;[5] after 70 years, the decline may accelerate to 0.6%–1% per year.[6–8] Over the past few decades, refining the definition of sarcopenia has led to significant variation in the meaning. Initially, the definition consists of the measurement of appendicular mass divided by height in meter squared.[9] However, some use body weight as the denominator.[10] More recently, there is a consensus that the definition should include a measurement of muscle power and/or physical performance measures. Three infusive organizations, namely, the European Working Group on Sarcopenia in Older People (EWGSOP), the International Working Group on Sarcopenia, and Asia Working Group on Sarcopenia, share their consensus on the definition and diagnosis of sarcopenia, which defined it as a progressive and generalized loss of muscle mass and low muscle function (muscle strength or physical performance).[11–13] In addition to the loss of muscle mass and strength, sarcopenia is often characterized by an increase in fat mass and fat infiltration into the muscle tissues, which has recently been defined as sarcopenic obesity.[14] However, a consensus definition of sarcopenic obesity does not presently exist. While sarcopenic obesity was defined as ASM/h^2 less than 2 standard deviation below the sex-specific mean of a younger reference group and a percentage of body fat greater than 27% in men and 38% in women (approximately a BMI of 27 kg/m^2),[14,15] an alternative definition was subsequently suggested, which is primarily based on anthropometric and bioelectrical impedance.[16]

The Prevalence, Risk Factors, and Consequences of Sarcopenia

Depending on the definitions used for defining sarcopenia, the prevalence in 60- to 80-year old population is reported as 0.9%–35.9%,[9,17–20] while the prevalence ranges from 7% to 70.0% in people older than 80 years.[9,21–28] The prevalence of sarcopenic obesity varies. A recent review comparing eight different definitions reported that the rate ranged from 4.4% to 84.0% in men and 3.6% to 94.0% in women.[29]

The causes of sarcopenia are multifactorial, where age-related changes in hormonal regulation (eg, impaired growth hormone/insulin-like growth factor-I secretion)[30,31] and body composition (eg, increase in fat mass, particularly intramyocellular fat mass, which is associated with an increased risk of insulin resistance[32,33] and mitochondrial dysfunction)[34,35] may have an important role in the process of protein metabolism,[36,37] leading to sarcopenia.[38,39] The increase in fat mass may also contribute to sarcopenia via inflammation. Several studies have suggested that visceral fat produces proinflammatory cytokines (eg, TNF-α and IL-6)[40,41] and adipokines (eg, leptin and adiponectin),[40,42] which stimulate muscle catabolism that in turn has been associated with lower muscle mass and

strength.[43,44] The age-related decline in central motor system alpha motor neurons may also contribute to sarcopenia.[45] Other mechanisms contributing to the etiology of sarcopenia include oxidative stress, muscle damages by free radicals, and mitochondrial mutations.[46,47] Lifestyle behaviors such as physical inactivity, smoking, and poor diet are also important risk factors of sarcopenia.[48–51] Genetic factors also play a role in the etiology of sarcopenia.[52–54]

Similar to osteopenia that predicts risk of fracture, sarcopenia is a predictor of falls,[55] fracture,[56] disability,[57–59] and mortality,[26,60] Sarcopenia also plays a predominant role in the development of frailty,[61] which is predictive of adverse events such as hospitalization, morbidity, disability, and mortality.[62] Like sarcopenia, sarcopenic obesity has been associated with functional and mobility limitations.[63–65] Sarcopenia obesity has also been associated with decreased resting metabolic rate,[66] insulin resistance,[67,68] and metabolic impairments.[69,70] The association of sarcopenic obesity and all-cause mortality has also been reported.[71] Further studies have documented the potential association between sarcopenia and cognitive impairment.[72,73]

Quality of Life

Given the detrimental impact of sarcopenia on health and functional status, which are important determinants of quality of life, quality of life of those with sarcopenia is likely to be deteriorated. Thus, targeted interventions are needed for individuals with sarcopenia to improve muscle quality, functional status, and quality of life. Although there is no consensual definition of quality of life,[74,75] there is considerable agreement among quality of life researchers about some of the characteristics of the quality of life construct. The World Health Organization (WHO) defines quality of life as an individual's perceptions of his/her position in life in the context of the culture and value systems in which he/she lives in relation to his/her goals, expectations, standards, and concerns.[76] Rosenberg[77] described that the term quality of life encompasses several constructs including physical, functional, emotional, social, and cognitive domains. Farquhar[78] described the taxonomy of definitions of quality of life and that the term *health-related quality of life* refers only to the components of health or functional ability.

In general, quality of life can be assessed by standardized questionnaires, being classified into generic and disease-specific questionnaires. Generic quality of life questionnaires post general questions on health status and can be used in different disease states. Among the generic quality of life questionnaires, Medical Outcomes Study 36-item Short-Form Health Survey (SF-36)[79] is the most widely used measurement among sarcopenic subjects. It covers domains of physical functioning, physical roles, bodily pain, general health mental health, emotional roles, social functioning, and vitality. Other questionnaires like European Quality of Life Questionnaire (EQ)-5D,[80] Older People's Quality of Life questionnaire,[81,82] World Health Organization Quality of Life (WHOQOL)-BREF,[76,83] and Quality of Life Systemic Inventory Questionnaire[84] have also been applied in sarcopenia assessment. Recently, Beaudart et al[85] developed the first self-administrated quality of life questionnaire for sarcopenia in elderly subjects named the Sarcopenia-specific Quality of Life Questionnaire, which consists of 55 sarcopenic-related items organized into seven domains of dysfunction: physical and mental health, locomotion, body composition, functionality, activities of daily living (ADLs), leisure activities, and fears.

Quality of Life and its Relationship with Sarcopenia

The impact of multiple chronic diseases on quality of life has been well established.[86] However, few studies have reported the impact of sarcopenia, as listed in Table 1, although its adverse outcomes such as impaired mobility are an important element of quality of life. Using SF-36, Patel et al[87] reported a reduced quality of life in the domain of physical function and general health for sarcopenic subjects in the Hertfordshire Cohort Study (HCS) in the UK. In a study in Nishinomiya, Japan, sarcopenia was common in patients before allogeneic hematopoietic stem cell transplantation and related to low muscle mass, fatigue, and and health-related quality of life.[88] Similarly, in a population-based cohort in Lääne-Viru County in northern Estonia, quality of life (in terms of role-physical, vitality, role-emotional, and mental health) was significantly lower in sarco-osteopenic individuals compared with their counterparts.[89]

The Sarcopenia and Physical impairment with advancing Age (SarcoPhAge) study in Liège, Belgium, incorporated the SF-36, the EQ visual analogue scale (EQ-VAS), and the EQ-5D into its study. Quality of life was assessed in 534 community-dwelling subjects aged 65 years or older. At baseline, 73 subjects had sarcopenia and 461 subjects did not. Highly significant differences were observed between the two groups for the domain of physical functioning. However, other domains of the SF-36 questionnaire were not different between the two groups. No difference was found between sarcopenic and nonsarcopenic subjects regarding the EQ-VAS and the EQ-5D scores.[90] Using data obtained from the Korea National Health and Nutrition Examination Survey, Go et al[91] and Koo et al[92] reported that the EQ-5D scores were significantly lower in those with sarcopenia than in those without. However, Messier et al[93] found no difference in quality of life between sarcopenic and nonsarcopenic postmenopausal women using Medical Outcomes Study General Health Survey questionnaire in Canada.

Relationship Between Quality of Life and Components of Sarcopenia

While few studies evaluated the quality of life in populations of older individuals with a diagnosis of sarcopenia, a number of studies have evaluated the independent contributions of

Table 1. Quality of life and its relationships with sarcopenia.

REFERENCE	SAMPLE CHARACTERISTICS	DEFINITION OF SARCOPENIA	SARCOPENIA PREVALENCE (%)	QUALITY OF LIFE ASSESSMENT	MEAN ± SD			KEY FINDINGS
					SARCOPENIA	NO SARCOPENIA	*P*-VALUE	
Patel HP et al[87] England	N = 1787 Mean age = 67 yr Women (57.2%)	Simple anthropometry, grip strength and physical performance (EWGSOP)	Men (4.6%) Women (7.9%)	SF-36	Men[a] GH: 60 (45–77) PF: 85 (55–90) Women[a] GH: 67 (57–77) PF: 75 (55–90)	 72 (62–85) 90 (80–95) 75 (62–87) 85 (65–95)	 <0.001 <0.001 <0.001 0.002	Quality of life in domains of PF and general health were reduced for sarcopenic subjects
Morishita S et al[88] Japan	N = 164 Age range = 16–68 yr Women (39%)	SM/h^2	Men (55%) Women (43.75%)	SF-36	PF: 66.9 ± 24.4 BD: 58.4 ± 28.0 VT: 49.8 ± 24.8	74.7 ± 18.5 68.9 ± 27.5 58.5 ± 18.7	0.022 0.016 0.012	Patient with sarcopenia had significantly lower scores in PF, BD, and VT in health-related quality of life that those without sarcopenia
Kull M et al[89] Esontia	N = 227 Age range = 40–70 yr Women (57.3%)	ALM/h^2, or grip strength	Men (Sarcopenia: 6.2%, Sarcopenia 3.1%) Women (Sarcopenia: 20.0%, Sarcopenia: 9.2%)	SF-36	–	–	<0.05	Quality of life in domains of RP, VT and MH were significantly lower in sarco-osteopenic individuals compared to their counterparts
Beaudart C et al[90] Belgium	N = 534 Mean age = 73.5 ± 6.16 yr Women (60.3%)	ALM/h^2, grip strength and physical performance (EWGSOP)	Men (11.8%) Women (14.9%)	SF-36	PH: 52.0 ± 29.2	65.2 ± 25.9	0.001	Significant differences were observed for the domain of PF between those with sarcopenia and those without
Go SW et al[91] Korea	N = 1397 Mean age = 67.4 ± 0.87 yr (w sarcoepnia), 60.4 ± 0.26 yr (w/o sarcopenia) Women (0%)	ALM/h^2	Men (15.7%)	EQ-5D	0.88 ± 0.015	0.94 ± 0.003	<0.001	The EQ-5D scores were significantly lower in those with sarcopenia than in those without
Koo HK et al[92] Korea	N = 574 Mean age = 64.0 ± 0.6 yr Women (0%)	ASM/w	Men (29.3%)	EQ-5D EQ-VAS	0.89 ± 0.02 67.2 ± 2.0	0.93 ± 0.01 72.4 ± 1.5	0.03 0.03	Sarcopenia was associated with more subjective activity limitation and poorer quality of life
Messier V et al[93] Canada	N = 136 Mean age = 58.5 ± 4.0 yr (w sarcopenia), 57.6 ± 4.9 yr (w/o sarcoepnia) Women (100%)	ALBM/h^2	Women (6.62%)	MOSGHS	77.8 ± 14.7	79.0 ± 13.9	NS	There is no significance difference between two groups (Class-I sarcopenic overweight and obese postmenopausal women) for quality of life

Notes: SF-36: Short-Form 36 Questionnaire composes of eight health-related qualities of health domains: Physical functioning (PF), role limitation due to physical problems (RP), bodily pain (BD), general health (GH), vitality (VT), social functioning (SF), role limitation due to emotional problem (RE) and mental health (MH). EQ-5D: EuroQoL 5-Dimension Questionnaire composes of five dimensions: Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. MOSGHS: Medical Outcomes Study General Health Survey composes of six subscales: Physical functioning, pain, social functioning, role functioning, mental health and health perceptions. [a]Median (interquartile range).

Abbreviations: EWGSOP, European Working Group on Sarcopenia in Older People; SM/h^2, Skeletal muscle mass divided by height squared; ALM/h^2, Appendicular lean mass divided by height squared; ASM/w, Appendicular skeletal mass divided by weight; ALBM/h^2, Appendicular lean body mass divided by height squared.

declines in muscle mass, muscle strength, and physical performance to decreased quality of life. For example, in the HCS, Sayer et al[94] reported a significant association between lower handgrip strength and poor quality of life in a sample of nearly 3000 community-dwelling men and women aged 59–73 years living in Hertfordshire, UK. In a small sample of 84 older adults aged 60–88 years living in Scotland, both lower extremity strength and biomechanical functional moments were significantly associated with SF-36 scores.[95] Similarly, in the Integrated Systematic Care for Older People study of 570 older adults (with follow-up data) aged 75 years and over, living in the Netherlands, baseline handgrip strength was independently associated with quality of life after 12 months in longitudinal analysis.[96] In a recent longitudinal study in Boston, US, decreased muscle mass (as measured by muscle cross-sectional area) and physical performance (as measured by Short Physical Performance Battery score and 400 m walk time) were independently associated with declining SF-36 physical component summary score in a sample of 26 community-dwelling older adults aged 70–85 years; however, neither lower extremity muscle strength nor muscle power were associated with SF-36 physical component summary score.[97] These findings suggest that declines in muscle mass, low muscle strength, and poor physical performance affect the physical tasks in the physical function domain of quality of life and underline the importance of preserving muscle quality with advancing age to improve quality of life.

Potential Links Between Sarcopenia and Reduced Quality of Life

The possibility that quality of life may be deteriorated in individuals with sarcopenia and/or declined muscle quality has not been extensively investigated. However, sarcopenia and/or its components may influence quality of life through physical, psychological, and/or social mechanisms. There is evidence suggesting that individuals who have knowledge of sarcopenia or a low value of muscle mass/strength were associated with fear of falls; their perception of health may be altered due to concerns that their conditions may predispose them to fracture,[56,98] which impact negatively upon quality of life.[97,99] Furthermore, those with sarcopenia were more likely to report having chronic diseases such as chronic obstructive pulmonary disease, stroke, and chronic kidney disease,[51,92,100] which have been associated with poor quality of life.[101,102] As mentioned earlier, sarcopenia and obesity often coexist and that a loss of muscle mass could be related to impaired metabolism (such as insulin resistance and metabolic syndrome),[68,70] both of which may have negative effects on quality of life.[103,104] Sarcopenia is also significantly associated with ADL/instrumental activities of daily living (IADL) impairments,[51,105,106] which have been demonstrated to be strong predisposing factors of poor quality of life.[107] There is also evidence that ADL impairments are associated depression, loneliness, and social isolation,[108,109] which are also risk factors of poor quality of life.[110,111]

Management of Sarcopenia to Improve Quality of Life

Considerable evidence suggests that sarcopenia is a reversible cause of adverse outcomes;[51] therefore, by targeting sarcopenia and its components, therapeutic and preventive interventions have the potential to improve physical function, maintain independence, and improve quality of life.

Resistance training. Physical activity and exercise, in particular resistance training, remain the most preferable intervention for increasing muscle mass and muscle strength that are important for improving physical performance and maintaining independence. The American College of Sports Medicine and the American Heart Association suggested that strength training (8–10 exercises, 10–15 repetitions for each exercise, with the level of effort for muscle-strengthening activities being moderate to high) targeting the major muscle groups on two or three nonconsecutive days per week was the appropriate training intensity to produce gains in muscle size and strength, even in frail elderly.[112–114] A meta-analysis suggested that resistance exercise among aging adults demonstrated significant positive effects in improving muscle mass.[115] Cruz-Jentoft et al[116] also summarized the effects of four resistance training interventions on sarcopenia. The findings from these studies demonstrated that resistance training interventions improved muscle mass, muscle strength, and physical performance. There is also evidence that improvements in muscle quality index (a novel evidence-based assessment of functional status calculating muscle power from anthropometric measures and timed chair rises), gait time, and sit-to-stand performance can be achieved with a short base training period of six weeks.[117] More recent studies suggested that resistance training interventions have the potential to improve muscle power, a critical determinant of physical functioning in older adults.[118] For example, Reid et al[119] demonstrated significant improvements in muscle power and physical performance after a 16-week period of progressive high-velocity resistance training in a sample of 52 mobility-limited elderly over 70 years old.

The beneficial effect of resistance training has also been extended to well-being. Increasing evidence suggested that resistance training is a viable intervention for increasing or maintaining quality of life among older adults. Levinger et al[120] demonstrated that a 10-week resistance training increased muscle strength and the capacity to perform ADLs as well as quality of life in a small sample of men and women aged 40–69 years. The positive effect of resistance training on quality of life is further supported in other elderly populations.[121–123]

Nutritional supplementation in combination with resistance training. There is also evidence that optimal nutritional supplementation improves muscle quality. Several studies have demonstrated the beneficial effects of essential amino acid (EAA),[124] β-hydroxy-β-methylbutyric acid (HMB),[125] as well as vitamin D and leucine-enriched whey protein nutritional supplement[126] in muscle mass and physical

performance. Optimal nutritional supplementation may also enhance the anabolic effect of resistance training. A number of clinical trials have demonstrated the beneficial effects of EAA or HMB supplementation in combination with resistance training on muscle parameters.[127,128] A recent review found evidence of additional benefits of exercise training when combined with nutritional supplementation in older adults.[129] Several studies have also highlighted the importance of timing of nutritional supplementation and resistance exercise training. For example, Esmarck et al[130] reported that 12 weeks of resistance training, combined with a protein and carbohydrate supplement consumed immediately after each training session, significantly increased muscle parameters including fiber cross-sectional area and isokinetic knee extensor strength, whereas resistant training with supplement consumption 2 hours post training did not lead to the same increases. Taken together, these studies indicate that resistance training combined with timed nutritional supplementation results in an improvement in muscle quality. However, there are limited data on the effects of nutritional supplementation, with or without a combination with resistance training, as an intervention on the quality of life among individuals with sarcopenia. At present, one recent trial has demonstrated the possible effects of a combined physical training and nutrition intervention on physical performance and quality of life. The authors found that the intervention improved several domains of SF-36 (role-physical, bodily pain, and role-emotional) significantly, but the positive effects were not maintained at six-month follow-up.[131]

Pharmacological interventions. In terms of pharmacological interventions, there are very few treatments that have been proven to be effective. A trial of hormone treatments has shown a significant increase in muscle strength, but was failed to improve gait speed. Furthermore, the authors reported complications of cardiovascular events during the trial.[132] Trials of myostatin or angiotensin II converting enzyme inhibitors also failed to demonstrate a beneficial effect on muscle strength or functional capacity.[133,134] Other pharmacological therapies (eg, growth hormone replacement and insulin-like growth factor 1 therapy) have also been attempted, but no clear evidence was found.[135,136]

Conclusion

The major potential threats to a high quality of life in older people are chronic physical illness and declined functioning. Sarcopenia, characterized by low extremity muscle mass, strength, and physical performance, is a critical determinant of independent functioning in later life. Therefore, it is both intuitive and widely accepted that sarcopenia and its components may be detrimental to quality of life. While few studies evaluated quality of life in older individuals with a diagnosis of sarcopenia, the link between declined muscle mass, muscle strength, and/or physical performance and declined quality of life has been established. A number of interventions are being investigated for sarcopenia. Physical activity and exercise interventions, especially those based on resistance training may have a role in improving muscle strength, physical performance, and quality of life. Some nutrition interventions such as vitamin D and whey protein, EAAs, or HMB supplementations alone and those in combination with resistance training may also improve muscle parameters and quality of life. These findings suggest that preventive approaches targeting muscle strength and physical performance have the potential to enhance quality of life in geriatric populations.

Author Contributions

Conceived and designed the experiments: RY, L-YZ, RC, and JW. Analyzed the data: RY and L-YZ. Wrote the first draft of the manuscript: RY and L-YZ. Contributed to the writing of the manuscript: RY, L-YZ, RC, and JW. Agreed with manuscript results and conclusions: RY, L-YZ, RC, and JW. Jointly developed the structure and arguments for the paper: RY, L-YZ, RC, and JW. Made critical revisions and approved the final version: RY, L-YZ, RC, and JW. All the authors reviewed and approved the final manuscript.

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