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An Overview of Frailty and Sarcopenia in Older People

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Abstract

Physical frailty and sarcopenia are two closely associated conditions commonly observed in older people, which are often precursors to disabilities. These two conditions are also associated with adverse health outcomes. Therefore, strategies are needed to identify, prevent and treat physical frailty and sarcopenia with the aim of improving clinical outcomes. Treatments to reverse physical frailty and sarcopenia or improve clinical outcomes should be multicomponent which integrates physical activity and nutritional care. Further research is needed to develop effective multicomponent interventions for the treatment of frailty and sarcopenia.

Keywords

Aging; Frailty; Sarcopenia; Outcomes; Treatment

Introduction

Globally, the proportion of older people aged 65 years and above are growing, from 461 million people in 2004 to a projected 2 billion by 2050 [1]. One of the serious challenges of an aging population is the manifestation of physical frailty and the closely associated sarcopenia. Both of these conditions are features of 'Unhealthy Ageing' and are associated with adverse health-related outcomes [2,3].

Several definitions of frailty and sarcopenia have been proposed (Table 1) [4-12]. However, no consensus has been reached on these definitions. In 2013, six societies involved in geriatric medicine have published a consensus statement on frailty definition, in an attempt to reconcile the two model of frailty definition. It defines frailty as "a medical syndrome with multiple causes and contributors that is characterised by diminished strength, endurance and reduced physiological function that increases an individual's vulnerability for developing increased dependency and/or death" [13].

Similarly, there have been six operational definitions of sarcopenia (Table 1) [6-12]. Whilst there has been no agreement on the operational definition, there is general agreement that sarcopenia is marked by loss of skeletal muscle mass, strength and function [6]. Furthermore, sarcopenia is considered a key aspect of frailty [6,14]. The close relationship between sarcopenia and frailty has led many to believe that sarcopenia plays an important part in the development of frailty and a mechanism in which poor health outcome of frailty manifest clinically [14]. The high quality of research into sarcopenia has led to its recognition as a clinical condition entity with the awarding of an ICD-10-CM (M62.84) code in September 2016 (www.prweb.com-prweb13376057) [15]. This represents a major step forward in recognizing sarcopenia as a clinical condition. This should lead to an increase in research into diagnostic tools and drug development for sarcopenia.

Despite the differences in the diagnostic approach and the screening strategies of frailty and sarcopenia, it is interesting to note that they are not mutually exclusive. Both conditions share very similar health outcomes and treatment strategies. The final endpoint of untreated physical frailty and sarcopenia are characterised by a decline in physical functioning, which is usually assessed objectively by gait speed and muscle strength. Such impairment can be responsible for the development of disability. In general, both frailty and sarcopenia are amendable to treatment. This review article provides an overview of prevalence, diagnostic and screening strategies, health outcomes and potential treatment or preventive strategies for frailty and sarcopenia.

Prevalence

The prevalence of frailty can vary and has been reported to range from 4.0% in the community to as high as 85% in those living in residential care setting [16,17]. Several factors impact on these varying reports of prevalence, including the use of different operational definitions for frailty, settings of studies and the varying inclusion or exclusion criteria between studies. For example, three studies reported on the prevalence of frailty in residential care, that ranged from 34.9% to 85% [17-19]. It was noted that one of the reason for the differences in the reported prevalence was the use of different operational definitions.

The prevalence of sarcopenia differs in clinical studies depending on the definitions or cut-offs used, applied settings (community-dwelling, hospital or residential facility) and age of cohorts [20]. In the community, the prevalence of sarcopenia has been reported to be between 5 and 13% [21-24]. In a study of patients aged 80-88 years admitted to a hospital geriatric ward in Germany, sarcopenia was diagnosed in 25.3% using the European Working Group on Sarcopenia in Older People (EWGSOP) diagnostic algorithm [25]. In another study involving residents in a nursing home in Italy, the prevalence of sarcopenia was 33% [s].

Screening for Frailty and Sarcopenia

Identification of frailty and sarcopenia in its early stages is important for implementing early treatment and intervention. Simple screening test have been developed and validated for frailty and sarcopenia [13,27]. The Royal College of Physicians (UK) and the French Society of Geriatrics and Gerontology advocated for screening for frailty in older peoples [28,29]. A consensus paper in 2013 from world authorities similarly supported screening for frailty in those 70 years and over [13]. Table 2 summarises currently available screening methods for frailty and sarcopenia [4,13,30-39].

Overlap between physical frailty and sarcopenia

The overlapping relationship between frailty and sarcopenia was shown in a cross-sectional Maastricht Sarcopenia Study (MaSS) [40].

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Table 1: Definition and diagnostic criteria of frailty and sarcopenia.

Study group	Definition	Criteria/Cut-off points
Frailty definition		
Fried's Phenotypic Model [4]	Characterized by a constellation of five possible components, which reflects an underlying state of multisystem dysregulation and subsequently loss of physiologic reserve.	Three or more of the five frailty phenotype: 1. Weight Loss – unintentional weight loss of ≥ 10 pounds in prior year or at follow up, of ≥5% of body weight in prior year. 2. Weakness – Grip strength in the lowest 20% at baseline, adjusted for gender and body mass index. 3. Poor endurance and energy – self reported exhaustion, identified by two questions from the CES-D* scale. 4. Slowness of speed – based on time to walk 15 feet, adjusting for gender and standing height. 5. Low activity (reduced energy consumption) – a weighted score of kilocalories expended per week, calculated at baseline. The lowest quintile of physical activity was identified for each gender.
Minitski et al. [5]	An accumulation of deficits model, which counted the number of impairments and conditions to create a frailty index. Frailty index score is calculated as the number of deficits divided by the total number of deficits that were considered.	No specific cutoff score for frailty index. Increasing values of the frailty index reflects greater deficits and are highly associated with adverse health outcome. With more deficit, the more risk and so are more frail.
Sarcopenia definition†		
European Working Group on Sarcopenia in Older People [6]	Sarcopenia is a syndrome characterized by progressive loss of skeletal muscle mass and strength with a risk of adverse outcomes such physical disability and mortality.	Low muscle mass Dual-energy X-ray absorptiometry (DXA) >2 SD below mean of the younger adults : • Men <7.26 kg/m^2 • Women <5.5 kg/m^2 Lowest 20% of the distribution of appendicular skeletal mass (ASM) in a normative population (aged 65 years and older) : • Men <7.23 kg/m^2 • Women <5.67 kg/m^2 Lowest 20% distribution of the residual of ASM adjusting for height and fat mass • Men <2.29 • Women <1.73 Bioimpedance analysis (BIA) >2 SD below mean (SMI) of the younger adults : • Men <8.87 kg/m^2 • Women <6.42 kg/m^2
		Low grip strength • Men <30 kg • Women <20 kg
		Low physical function • **SPPB ≤8 • Gait speed <0.8 m/s
		Diagnosis based on presence of criteria 1 plus criteria 2 or 3
ESPEN special interest group [7]	Loss of muscle mass and strength	Low muscle mass >2 SD below mean of the younger adults
		Low gait speed <0.8 m/s in 4 m
		Diagnosis based on presence of both criteria
International Working Group on Sarcopenia [8]	Age-associated loss of skeletal muscle mass and function	***Criteria 1:*** If patient unable to walk – consider sarcopenia and need DXA to confirm low muscle mass
		Criteria 2: Walk Speed <1.0 m/s than DXA
		Criteria 3: Low muscle mass: Appendicular fat free mass (AFFM) to height squared or whole body fat free mass to height. Recommended AFFM cut-offs for sarcopenia: • Men <7.23 kg/m^2 • Women <5.67 kg/m^2
		Diagnosis based on presence of either criteria 1 or 2 plus criteria 3.
Society of Sarcopenia, Cachexia and Wasting Disorders [9]	Sarcopenia with limited mobility – loss of muscle mass whose walking speed is ≤1 m/s or who walks <400 m during 6-minute walk test	Slow walk speed ≤1 m/s or <400 m during 6-minute walk test
		Low muscle mass >2 SD below younger people between 20-30 years.

Asian Working Group for Sarcopenia [10]	Low muscle mass and low muscle strength or low physical performance (walk speed). Sarcopenia with limited mobility – loss of muscle mass whose walking speed is ≤1 m/s or who walks <400 m during 6-minute walk test	***Criteria 1*:** Low muscle mass: Appendicular skeletal muscle mass/height^2 >2 SD below mean of the younger adults DXA • Men <7.0 kg/m^2 • Women <5.4 kg/m^2 BIA • Men <7.0 kg/m^2 • Women <5.7 kg/m^2 ***Criteria 2*:** Low grip strength: lowest 20th percentile of the study population • Men <26 kg • Women <18 kg ***Criteria 3*:** Low physical performance • Gait speed ≤0.8 m/s **Diagnosis based on presence of criteria 1 plus criteria 2 or 3**
Foundation for the National Institutes of Health (FNIH) Sarcopenia Project [11,12]	Two possible FNIH definitions: (i) clinically relevant weakness and low lean mass (low grip strength + low ALM_{BMI}) or; ii) clinically relevant slowness with weakness and low lean mass (slow gait speed + low grip strength + low ALM_{BMI}).	Appendicular lean body mass (ALM) Recommended: ALM_{BMI} • Men: <0.789 • Women: <0.512 Weakness Recommended: grip strength • Men: <26 kg • Women: <16 kg Low gait speed • Gait speed ≤0.8 m/s
Note: *CES-D: Centre for Epidemiological Studies Depression **SPPB: Short Performance Battery † Adapted from Yu *et al* [20]		

Table 2: Reported screening tools for frailty and sarcopenia.

Screening tools for frailty
Simple "FRAIL" Questionnaire Screening Tool [13] The tool evaluates Fatigue, Resistance, Aerobic capacity, Illnesses, Loss of weight. A score of 3 or greater indicates frailty and 1 or 2 indicates prefrail. The FRAIL scale may be used as the first step in a step care approach to detecting frailty in the community, allowing targeted intervention.
FRAIL-NH [30] The FRAIL-NH is designed specifically for long term care patients and it has been validated against common outcome such as risk of falls and mortality. It is easy to administer tool and can be applied without the need for training.
Cardiovascular Health Study Frailty Screening [4] The tool assesses weight loss, exhaustion, low activity, gait speed and grip strength. A score of 3 or greater indicates frailty and 1 or 2 indicates prefrail.
Gérontopôle Frailty Screening [31] This screening tool consist of 6 questions about living alone, involuntary weight loss, fatigue, mobility difficulties, memory impairment and slow gait speed. 'Yes' to one of these variables identifies an individual for further assessment of frailty.
Edmonton Frail Scale [32] A measure across ten domains including cognition, social support, medication use and functional performance. It gives a score from 0 to 17. No specific cut-point was suggested, although previous studies have adopted a cut-point of 8 or more points to define frailty.
PRISMA-7 [33] A simple seven item screening instrument. It consist of a set of "yes" or "no" answers. It has high sensitivity but limited specificity. Three or more "yes" responses suggest presence of frailty.
Groningen Frailty Index [34] This is a multi-domain frailty instrument. It consists of 15 items, that gives a summed score from 0 to 15 across the scale. Frailty is present with a score of 4 or more points.
Screening tools for sarcopenia
SARC-F questionnaire [35] This tool assesses five domains: Strength, independence with walking, rising from a chair, climbing stairs and history of falls. A score of ≥4 out of 10 indicates a risk of sarcopenia
Goodman et al. [36] This tool uses a grid based on age and body mass index to generate a probability of sarcopenia which can be <0.20, 0.20-0.49 and ≥0.50.
Ishii et al. [37] These researchers have estimated the probability of sarcopenia with a score chart using age, handgrip strength and calf circumference.
Yu et al. [38,39] A predictive equation using age and body mass index estimates the appendicular skeletal mass. When used in combination with grip strength, the tool is useful to rule out those not-at-risk of sarcopenia.

This study examined older people living in different community care settings [40]. Using the EWGSOP algorithm, 23.3% of participants were identified to have sarcopenia. Physical frailty was identified in 8.4% (frailty defined by Fried's criteria) and 9.3% (frailty defined by FRAIL scale criteria) of the study cohort. It was further noted that there were higher proportion of prefrail and frail older people in those with sarcopenia than those without sarcopenia (sarcopenic group (n=53): prefrail 71.7%, frail 22.6 vs. non-sarcopenic group (n=174): prefrail 24.7%, frail 4%). Conversely, of the frail older people (n=19), 12 participants had sarcopenia, whereas of the nonfrail older people (n=127), only 3 participants had sarcopenia. Sarcopenia and physical frailty were significantly associated (P=0.022).

Sarcopenia and physical frailty are closely associated and partly overlap, especially on parameters of impaired physical function [40]. The MaSS study has shown some evidence for concurrent validity between the FRAIL scale and Fried criteria was found [40]. More

Table 3: Associated adverse health outcomes of frailty and sarcopenia.

Frailty	
	Falls
	Worsening disability
	Increased risk of hospitalisation
	Increased Mortality
Sarcopenia	
	Falls
	Worsening disability
	Increased risk of hospitalisation
	Increased risk of institutionalisation
	Increased Mortality

research is required to elicit the value of combining sarcopenia and frailty measures in preventing disability and other negative health outcomes.

Frailty and health outcomes

Frailty is associated with adverse clinical outcomes including falls, worsening disability, hospitalization and mortality, as reported in four large prospective studies (Table 3) [4,41-43].

Falls: Frailty is associated with increased risk of falls. These were demonstrated through several large studies. The Cardiovascular Health Study (CHS) assessed the effects of frailty in 5,317 men and women aged 65 years and older over 3 or 7 years [4]. Severe frailty was associated with a hazard ratio (HR) of 1.82 (95% CI 1.50-2.21) for falls. Similarly, the Study of Osteoporotic Fractures (SOF), which involved 6701 participants, over 4.5 years also found severe frailty to be associated with an odds ratio (OR) of 2.44 (95% CI 1.95-3.04) [43] for falls. The study also showed that frailty was associated with increased odds of 2 or more falls in the subsequent year. Compared with non-frail women, women who were intermediately frail had a 1.2- to 1.4-fold age-adjusted increase in risk (P<0.04) of falls and frail women had a 2.4-fold increase in risk (P<0.001) of falls [43].

Worsening disability: Two studies, CHS and SOF, also found that severe frailty was associated with worsening disability [4,43]. In the CHS, the investigators reported HR of 1.79 (95% CI 1.47-2.17) for disability associated with severe frailty. SOF also reported an increased OR of incident disability (≥1 new instrumental ADL impairment) with increasing level of frailty (OR 2.79; 95% CI 2.31-3.37) [43].

Hospitalization: In CHS, participants with severe frailty were more likely to be hospitalized, with a HR of 1.27 (95% CI 1.11-1.46) [4]. However, in the Women's Health and Aging Study (WHAS) found no significant relationship between frailty and hospitalization [42].

Institutionalisation: The Canadian Study of Health and Aging (CSHA) found that moderate or severe frailty is also associated with increased risk of admission to long-term care (OR 2.60, 95% CI 1.36-4.96) [41]. The WHAS also observed a significantly higher risk of institutionalization among older people who were frail (OR 24.0 95% CI 4.45-129.2) [42].

Mortality: CSHA also highlighted that increasing frailty was associated with an increased 5-year risk for death, with an OR of 4.82 (95% CI 3.74-6.21) in mildly frail people and 7.34 (95% CI 4.73-1.38) in severely frail people [41]. Other studies such as CHS, WHAS and SOF also found similar findings [4,42,43].

Sarcopenia and health outcomes

Sarcopenia is also associated with several adverse outcomes (Table 3). The studies described here used either EWGSOP definition [6] or Foundation for the National Institutes of Health (FNIH) criteria [44] to diagnose sarcopenia.

Falls: Two studies have found a significant association between sarcopenia and the incidence of falls [45,46]. One of these studies was undertaken in 260 community-dwelling people with an average age of 86.7 ± 5.4 years who were followed up over 2 years to determine the incidence of falls [45]. This study reported 27.3% of subjects with sarcopenia fell at least once, compared with 9.8% of those without sarcopenia (p<0.001). A crude HR of 3.45 (95% CI 1.68-7.09) for falls in association with sarcopenia was reported. The HR was still significant in an adjusted model, resulting in an HR of 3.23 (95% CI 1.25-8.29).

The second study included 5828 community-dwelling people to assess the relationship between recurrent falls (at least 2 falls per annum) and sarcopenia [46]. Investigators found a higher risk of recurrent falls for subjects with sarcopenia, with an OR of 2.38 (95% CI 1.75-3.23) when adjusted for age.

Worsening disability: A meta-analysis evaluated six studies that reported on the association between sarcopenia and incidence of functional disability [3]. The pooled results revealed an increased risk of functional disability for older people with sarcopenia compared to those without (pooled OR 3.03; 95% CI 1.80-5.12). Five of these studies reported a significant functional decline assessed by the Katz scale, instrumental activities of daily living (IADL)-Lawton scale, Barthel Index and self-reported functional limitations, among subjects with sarcopenia compared to those without the condition. One study found that sarcopenia was associated with functional decline only for men and not for women [47].

Hospitalization: One study evaluated the incidence of hospitalization in subjects with sarcopenia [48]. This study involved 538 community-dwelling subjects aged 77.1 ± 5.5 years who were followed for a median of 55 months. Researchers of this study found that the risk of hospitalization was higher in subjects with sarcopenia (crude HR of 1.57; 95% CI 1.09-2.26).

Institutionalization: In the Concord Health and Ageing in Men Project (CHAMP), 1678 men (mean age 77 years) had assessment of sarcopenia in terms of low appendicular lean mass (ALM), using the FNIH criteria [49]. This study graded the severity of sarcopenia as low ALM alone (sarcopenia I), low ALM with weakness (sarcopenia II), and sarcopenia with weakness and poor gait speed (sarcopenia III). Associations between sarcopenia I, II, and III, and institutionalization were found to be HR of 1.96 (95% CI 1.14-3.35), HR 2.53 (95% CI 1.31-4.90) and HR 2.27 (95% CI 1.08-4.80) respectively. However, data on this association in women is lacking.

Mortality: In a meta-analysis of 12 studies, a higher risk of mortality was found in subjects with sarcopenia compared with those without (OR 3.60; 95% CI 2.96-4.37) [3]. The effect was greater in the cohort between 79 years and above compared with those younger (p=0.02). Another meta-analysis of 10 studies also found a significantly higher risk of mortality in sarcopenia compared to non-sarcopenia (HR 1.87; 95% CI 1.61-2.18) [50].

Treatment and Management Strategies

Preventing and reducing the degree of frailty have benefits for individuals, their families and society. So far, the evidence from published literature show treatments that have potential to manage physical components of frailty are exercise, nutritional support,

Table 4: Management of frailty and sarcopenia.

Physical activity and exercise [57]		
	Frequency and intensity	***Duration***
Aerobics	Minimum 5 days' week of moderate intensity or 3 days/ week of vigorous intensity	At least 30 minutes/day of moderate intensity or at least 20 minutes/day vigorous activity
Resistance	At least 2 days per week or at least low to moderate velocity	8-10 exercise 1-3 sets per exercise 8-12 repetitions
Nutrition [65-67]		
	Amount	*Type of protein*
Protein supplementation	Normal *GFR: At least 1.0-1.2 g/kg/day in people 65 years and over GFR 30-60ml/hour: 0.8g/kg/day GFR <30ml/hour: between 0.6-0.8g/kg/day	Whey based proteins are thought to be more beneficial but evidence are lacking
Vitamin D	Need to replace low vitamin D level and maintain adequate daily requirement (700 to 1000 IU/day) of cholecalciferol.	
Essential amino acid supplementation	Daily leucine in combination of exercise may help improve muscle mass (only shown in small number of studies).	
Beta-hydroxy-beta-methylbutyrate (HMB)	Evidence only shown in small number of studies. Benefit seen in HMB alone or in combination of resistance exercise	
Other treatment strategies		
Medication rationalisations	Reduction of medication load	
Treating contributing factors	Identification of reversible contributing factors of frailty and sarcopenia and optimising the management of each condition.	
Note: *GFR: Glomerular Filtration Rate		

vitamin D and reduction of polypharmacy [13]. As for sarcopenia, there is no current standard treatment and as many risk factors cannot be changed, nutrition and physical exercise seem to be the current cornerstones of intervention. The overlapping nature of sarcopenia and frailty also means similar strategies for both conditions. Table 4 summarises the approach to treating frailty and sarcopenia.

Physical activity and exercise

Physical activity and exercise are not the same. Physical activity is usually defined as any bodily movement produced by skeletal muscles that results in energy expenditure, and can be linked to occupational, sports, household, or other activities [51]. Exercise is a subset of physical activity that is planned, structured and repetitive, and has as a final or an intermediate objective the improvement or maintenance of physical fitness [52]. Exercise and physical activity fall into four basic categories—aerobic, resistance training, balance, and flexibility [52]. Aerobic exercises increase respiratory and pulse rate. Resistance training strengthens skeletal muscles. Balance exercises help prevent falls, a common problem in older adults. Flexibility exercises stretch muscles and help to keep the body limber.

Exercise has been shown to improve outcomes of mobility and functional ability in two systematic reviews of home-based and group-based exercise interventions for frail older people [53,54]. Resistance exercise training increases muscle mass, strength and morphology, and improves protein synthesis in skeletal muscles of older people [55-57]. Aerobic exercise training may also benefit ageing skeletal muscle and improve insulin sensitivity [58]. Exercise may be more effective when started early, but can be useful even in very old and frail people [59,60]. At least in clinical trials, resistance exercise programmes can have a good long-term compliance (24 weeks) [61].

It has been well known that implementing exercise program in older people is challenging. There are barriers such as pain, injury and illnesses that can "demotivate" an older individual to participate in any form of exercise [62,63]. Other factors such as poor health, negative experience, lack of company and non-conducive environment could also deter individuals from continuing with exercise [64]. It is therefore, important to be mindful of the barriers and address the individual concern sensitively and timely. Using the multidisciplinary approach is often necessary to achieve a positive experience with exercises.

Nutritional supplementation

Nutrition is considered one of the key parts of managing sarcopenia and frailty but evidence of the effect of nutrition on skeletal muscle is often derived from short-term studies in selected samples. However, there is a paucity of data from large clinical trials. As a result, there is no robust evidence for nutritional recommendations for people with sarcopenia or frailty.

Protein supplement has been recommended as key nutritional strategies in individuals with weight loss associated frailty and sarcopenia. Protein supplementation could increase muscle mass, reduce complications, improve grip strength and produce weight gain [65]. Bauer et al. recommended increasing protein intake to 1.2 g/kg body weight/day by either diet or by protein supplementation in older people because of blunted muscle protein synthesis and anabolic resistance [65]. Frail older people who have acute or chronic diseases need even higher dietary protein (1.2-1.5 g/kg body weight/day) [65].

β-hydroxy β-methyl butyrate supplements have been found to increase muscle mass but its effects on muscle strength and performance are inconsistent [66,67]. Supplementation with protein and leucine combined with resistance exercises have been reported to improve muscle mass, strength and performance [68].

Vitamin D supplementation for older people who are deficient in this vitamin have reduced the number of falls and mortality but the optimal approach has not been fully defined [69].

Medication rationalization

Polypharmacy is recognized as a possible major contributor to the pathogenesis of frailty [13]. Reducing inappropriate medications could reduce the incidence of frailty in older people [70].

Multidisciplinary approach

Frailty and disability could be successfully treated using an interdisciplinary multifaceted care program [71]. Combination

therapeutic approach using resistive exercises and protein supplementation, as well as psychological management has been supported by some studies [72,73]. A systematic review has found that multidisciplinary interventions improve residents' clinical outcomes in nursing home settings [74]. Despite this, the details of the therapeutic regimen remain controversial. As a result, a large multi-center trial known as the Sarcopenia and Physical frailty in older people: A multi-component treatment strategy (SPRINT-T) is currently underway in Europe [75]. This trial involves multicomponent treatment strategies that combine exercise, nutritional advice and innovative technologies to prevent frail older people from becoming disabled and losing their mobility. The results of this trial are eagerly awaited.

Treating other contributing causes to frailty

Other potential reversible causes for frailty will need to be identified and addressed accordingly [13]. These include but are not limited to visual and hearing problems, diabetes mellitus, cognitive decline, congestive heart failure and depression.

On the horizon

Since the discovery of myostatin, a potent negative regulator of growth that is highly enriched in skeletal muscle, there has been great interest in it as a potential mediator of sarcopenia as well as a therapeutic target. A proof-of-concept, randomized, placebo-controlled, double-blind, parallel, multicenter, phase 2 study has found a myostatin antibody to increase lean mass and might improve functional measures of muscle power [76]. Although additional studies are needed to confirm these results, available data suggest a myostatin antibody should be tested for its potential ability to reduce the risk of falls or physical dependency in older weak fallers. A novel, human anti-activin type II antibody (bimagrumab, or BYM338) has been identified to prevent binding of ligands such as activins to their receptors and thus disinhibit downstream signalling [77]. Bimagrumab enhances differentiation of human skeletal myoblasts and inhibits the differentiation induced by myostatin or activin. Phase 2 and 3 trials (NCT02333331) are currently ongoing to evaluate its effectiveness in sarcopenia. Therefore, further research is needed to identify targeted therapies to reverse sarcopenia in older people.

One of the urgent needs in the research of frailty and sarcopenia is to standardise methods used for screening, diagnosing and grading of severity of these conditions. When there is standardisation research into the outcome of interventional strategies will yield higher quality results. Furthermore, the efficacy of multicomponent interventions to manage frailty and sarcopenia can be better assessed.

Conclusion

Clinically, physical frailty overlaps substantially with that of sarcopenia and both these conditions are reversible. Sarcopenia may be considered the key component of physical frailty, which indicates that interventions specifically targeting the skeletal muscle may offer preventive and therapeutic benefits against these conditions. Physical frailty and sarcopenia are associated increased risk of falls, functional decline, hospital admissions, need for residential facility care and mortality. Treatments to reverse physical frailty and sarcopenia or improve clinical outcomes should be multicomponent which integrates physical activity and nutritional care. Further research is required to better define the appropriate multicomponent interventions that are effective in treating frailty and sarcopenia.

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