



# Frailty and Sarcopenia in Older Adults

## Potential for Nutrition and Exercise Strategies to Counteract Disabling Conditions



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Frailty is a common and important geriatric syndrome characterised by age-associated declines in physiologic reserve and function across multiorgan systems, leading to increased vulnerability for adverse health outcomes including falls, incident disability, hospitalisation and mortality.<sup>1,2</sup> Frailty has been operationally defined by Fried *et al.* as meeting three out of five phenotypic criteria indicating compromised energetics: low handgrip strength, low energy, slowed walking speed, low physical activity, and/or unintentional weight loss.<sup>1</sup> Loss of muscle mass and function (sarcopenia) and malnutrition are key components of the frailty cycle.<sup>1</sup> Many alterations in metabolism and body composition occur as part of normal ageing but can become significant and pathological. It is known that total energy expenditure (TEE) reduces with ageing.<sup>3,4</sup> Specific components of TEE such as basal metabolic rate (BMR), resting metabolic rate (RMR) and activity energy expenditure (AEE) reduce with ageing.<sup>3,4</sup> Indeed, these reductions in energy expenditure (EE) are the hallmarks of physical frailty, and research has shown that individuals with frailty have reduced EE, reduced RMR, measured using indirect calorimetry and reduced TEE and AEE measured by doubly labelled water.<sup>5,6</sup>

The reductions in BMR, RMR, AEE and overall TEE are largely due to alterations in body composition with ageing, i.e., there is a significant reduction in skeletal muscle mass (SMM) and fat free mass (FFM) compartments.<sup>7,8</sup> SMM is critical for physical function and physical activity, and is a metabolically active tissue (increasing EE), with a dual functional role acting as labile source of amino acids that can be partitioned into different pathways during nutrient deprivation (e.g. gluconeogenesis) and immuno-inflammatory stress (e.g. acute phase protein production).<sup>9</sup> A key factor known to influence the loss of lean mass and is a risk factor for the development of malnutrition,

sarcopenia and frailty is a loss of appetite (and reduction in food intake), or the 'anorexia of ageing'.<sup>3,10</sup> This is thought to be due to physiological changes which occur with ageing such as alterations in taste and smell, appetite hormones (e.g. leptin and ghrelin), and a range of other factors such as effects of disease, medications, physical factors and social factors.<sup>3,10</sup> Other factors known to influence the loss of lean mass include age-related changes in hormones (e.g. reduction in sex hormones and growth hormone - insulin-like growth factor (GH-IGF) axis activities), physical inactivity and inflammation (due to effects of illness, ageing, obesity, etc).<sup>11</sup>

Ultimately, the loss of SMM with ageing and chronic disease is intimately linked to poor clinical outcomes, which includes reduced functional performance, falls risk, physical disability, morbidity and mortality.<sup>11, 12</sup> This is termed 'sarcopenia' and is a major component of the physical frailty phenotype. Sarcopenia is now recognised as an independent condition with an International Classification of Diseases (ICD-10) code.<sup>13</sup> It has been currently defined as "A progressive and generalised skeletal muscle disorder that is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality".<sup>12</sup>

The importance of being able to easily screen for sarcopenia in all settings (hospital, care home, community, GP clinic) is a key and current issue. Suggested methods for screening include hand grip strength assessment, which is easy to perform, portable, cheap and non-invasive.<sup>12</sup> Another tool is the SARC-F screening questionnaire developed by Malmstrom and Morley.<sup>14</sup> The SARC-F has recently been used alongside the 'MUST' as a remote screening tool (R-MAPP) for sarcopenia and malnutrition in patients during the COVID-19 pandemic.<sup>15</sup> Other techniques for measuring lean mass and SMM include anthropometry (e.g. calf circumference), bioelectrical impedance assessment (BIA) and scanning techniques such dual-energy x-ray absorptiometry (DEXA), computed tomography (CT) and magnetic resonance imaging (MRI). Each technique has its pros and cons (e.g., accuracy, portability, cost, radiation exposure etc), and as the most important component of sarcopenia is physical function (as it closely relates to disability risk), having simple tools is key to practical screening.<sup>12</sup>

## Nutrition

Nutrition is key to modulating risk of developing frailty and sarcopenia and may play an important role in treatment. As mentioned above one of the main issues with ageing and disease is a reduction in food, energy and protein intake. Higher energy intake has been shown to reduce odds risk of developing frailty in the recent Rotterdam study.<sup>16</sup> Overall diet quality has also been found to affect risk of frailty development.<sup>17</sup> Many recent studies have shown that adherence to a Mediterranean diet may reduce risk of frailty.<sup>18-20</sup> A Spanish study found that overall protein, animal protein and mono-unsaturated fat (MUFA) intake was associated with reduced frailty

in older adults.<sup>21</sup> In particular, protein intake has been highlighted as an important factor in preserving skeletal muscle mass and function in older people. Recommendations have been developed and guided by expert consensus papers from the PROT-AGE study group and ESPEN.<sup>22, 23</sup> Both groups recommend 1.0-1.2 g/kg/body weight (BW)/day for healthy older people and for those with acute and chronic disease, 1.2-1.5 g/kg/BW/day. These updated recommendations were based upon a wealth of research indicating that ageing and disease has a detrimental effect on skeletal muscle. During ageing there is a reduced propensity to stimulate muscle protein synthesis with protein intake, termed 'anabolic resistance'.<sup>24</sup> Evidence shows that it may be possible to overcome this using higher doses of essential amino acids (EAAs).<sup>22-24</sup> These key papers cited also discuss the potential synergy between protein intake and effects of exercise (e.g., resistance training). One key aspect open to debate is the intake pattern of protein throughout the day. For example, protein spread feeding (evenly spreading protein intake throughout the day, e.g. 3-4 meals with ~20-30 g of protein per meal) has been suggested to be more anabolic, whereas protein pulse feeding (consuming ~70% of daily protein in one meal) may lead to greater whole-body anabolism.<sup>25-27</sup> Other recent studies have confirmed that consuming higher amounts of protein in one meal may be more anabolic.<sup>28</sup> More research needs to be performed to confirm which is the best approach. In terms of meal planning for older person it makes more sense to spread protein intake out throughout the day.

Other nutrients that may have a beneficial effect on SMM and function include vitamin D, the leucine metabolite  $\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) and fish oils/omega-3 fatty acids. Older people are at risk of vitamin D deficiency due to reduced UV exposure and skin metabolism, and intake. A recent systematic review and meta-analysis of studies highlighted that low vitamin D (serum 25-hydroxyvitamin D levels) is associated with increased risk of frailty.<sup>29</sup> Papers have also discussed the relationship between vitamin D and risk of development of sarcopenia and treatment.<sup>30</sup> At present, research suggests that vitamin D has a positive effect on muscle, however, there is some controversy in study outcomes. HMB has been shown to have effective anabolic and anti-catabolic properties improving lean mass and function.<sup>31</sup> For example, in a 10-day bed

rest study, HMB supplementation helped to preserve muscle mass in older participants.<sup>32</sup> Omega-3 fatty acids have also been shown to have some beneficial effects, e.g., on muscle mass and function. They have significant anti-inflammatory effects (e.g. reducing catabolic pro-inflammatory cytokines) and may have a positive effect on insulin sensitivity and muscle protein synthesis.<sup>33</sup> A recent systematic review and meta-analysis of studies showed that they have positive effects, although noted that larger trials are needed.<sup>34</sup> These specific nutrients should be considered alongside changes to overall diet, protein and energy intake, and physical activity, as they may have a synergistic effect with other nutrients.

## Physical activity and exercise

It is known that frailty is associated with reduced AEE/physical activity (PA) and increased sedentary behaviour.<sup>5, 35</sup> A recent systematic review and meta-analysis of studies (112 studies; n = 43,796 individual participants) investigated the relationship between PA, sedentary behaviour and skeletal muscle strength and power in older adults.<sup>36</sup> It was found that higher PA and lower sedentary behaviour was associated with better muscle strength, in particular, with lower body strength, e.g., chair stand test. In particular, moderate-to-vigorous PA is highlighted to be of benefit. A recent Swedish study (n = 3,334 older adults of 70 years of age) noticed a significant relationship between the amount of moderate-to-vigorous PA completed and reduced risks of sarcopenia.<sup>37</sup> Landi *et al.* studied PA in the 'Longevity check-up 7+' (Lookup 7+) project in Italy, involving 6,242 participants, mean age 54.4 +/- 15.2 (range 18-98 years).<sup>38</sup> They showed a particular relationship between PA and chair stand performance (time taken to complete 5 repetitions), with sedentary individuals taking significantly longer to complete the test than those who were physically active. In particular, they showed that those who engaged in resistance training and combined resistance training + aerobic exercise, were faster than those who engaged in light PA walking. A recent systematic review and meta-analysis of studies was performed by Talar *et al.* investigating the effects of resistance training in frailty and sarcopenia (25 studies with 2,267 participants).<sup>39</sup> Resistance training was found to be highly effective in both early and late stages of frailty and sarcopenia.

Resistance training significantly improved hand grip strength, lower-limb strength, agility, gait speed, postural stability, functional performance and muscle mass in older adults. Resistance training can be practically undertaken in a safe and effective manner in older adults, for example, using some basic weight bearing and resistance band type activities. However, the inclusion of moderate-to-vigorous PA is noted with some caution as it may be more difficult to perform in individuals with reduced physical function and certain clinical conditions. One alternative being investigated in the field is sedentary behaviour fragmentation, whereby periods of sedentary behaviours (e.g., sitting and watching TV) are broken up with short periods of light PA. A recent study looked at using a sedentary behaviour fragmentation protocol (2 minutes of light PA per every 30 minutes of sedentary behaviour) and comparing it to 45-50 minutes of continuous daily light PA in 28 older women (age 73±5 years).<sup>40</sup> This was very interesting as both protocols had a significant beneficial effect on physical function, however, there was a greater effect using the sedentary behaviour fragmentation for handgrip strength. This paper was written in the context of the COVID-19 pandemic and associated lockdowns. Indeed, research has shown that pandemic had a particular negative impact upon PA levels, reducing overall PA and increasing sedentary behaviour time. This was recently summarised in a systematic review of studies (66 articles and 86,981 participants).<sup>41</sup> In the UK, Public Health England published a survey which showed

that older adults performed less PA and muscle-strengthening activities in early-mid 2020.<sup>42</sup>

In addition to the beneficial effects of exercise alone, there is some suggestion of a potential synergy of exercise (e.g., resistance training) with nutrition.<sup>43</sup> Exercise has a number of beneficial effects on skeletal muscle such as improving blood flow, insulin sensitivity, mitochondrial function, growth factor release and satellite cell activation, stimulation of protein synthesis via mTOR activation and others.<sup>43</sup> This in turn may lead to muscle hypertrophy and enhanced strength and function. This may have potential synergy with protein and energy intake and be beneficial in frailty and sarcopenia. More controlled trials will need to be performed to fully establish this relationship.

## Conclusions

Frailty and sarcopenia are leading causes of disability in older people. The ability to accurately screen for sarcopenia and physical frailty in routine clinical practice is of paramount importance. Use of simple, non-invasive, inexpensive and portable methods is recommended which can be used in all settings (e.g., hospital, care home, GP clinic, community and remote). Nutrition is of particular importance for prevention and treatment with focus on energy and protein intake, and diet quality (and Mediterranean type diets). Physical activity and exercise may also play an important role and may have synergistic effects with nutritional intake, although more research needs to be performed to confirm with certainty.

“Recent studies have shown a significant relationship between the amount of moderate-to-vigorous physical activity completed and reduced risks of sarcopenia.”

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