Prevention and Treatment of Sarcopenia

Dr Tak-kwan KONG

MBBS(HK), FHKAM(Medicine), FHKCP, FRCP(Lond, Edin, Glasg)

Specialist in Geriatric Medicine
Honorary Clinical Associate Professor, Department of Medicine, The University of Hong Kong
Clinical Associate Professor (Honorary), Department of Medicine & Therapeutics, The Chinese University of Hong Kong
Consultant, Division of Geriatrics, Department of Medicine & Therapeutics, Prince of Wales Hospital

Dr Tak-kwan KONG

This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 July 2018.

Sarcopenia is clinically defined as a syndrome characterised by progressive and generalised loss of skeletal muscle mass and muscle function (either low muscle strength or physical performance) with a risk of adverse outcomes such as physical disability, poor quality of life and death.[1-3] Sarcopenia can be viewed from a pathophysiologic perspective as an organ failure ("muscle insufficiency") which can develop chronically or acutely associated with hospitalisation.[4]

Treatment of Chronic Sarcopenia

Why?

Intervening sarcopenia, which is linked to physical frailty in elderly persons, has the potential to slow, stop or reverse progressive decline towards disability and dependency, as well as to improve physical function. We can see treatment of sarcopenia as a means to avoid disability, just like treating hypertension as a means of preventing stroke, or treating osteoporosis to prevent fractures. While osteoporosis is related to the outcome of fractures, a hard clinically relevant outcome for sarcopenia has yet to be identified. Potential outcomes of sarcopenia studied in sarcopenia intervention trials include mobility disability (dysmobility), activities of daily living (ADL) disability, fractures, recurrent falls, injurious falls, mortality, or hospitalisation.[5]

What cut-off to intervene?

There is a need to establish evidence-based cut-off points in assessment of sarcopenia to distinguish it from normal ageing of the skeletal muscle. Both the European and Asian Working Groups on Sarcopenia have proposed cut-off points of measurements two Standard Deviations (SDs) below the mean from a reference population of healthy young people for diagnosis of sarcopenia.[1,3] However, these cut-off points are not outcome-based and do not necessarily represent the threshold for interventions. The choice of a cut-off has to balance sensitivity and specificity according to the needs of the evaluation. Sensitivity is preferred for screening to identity those at risk, while specificity is preferred for targeting intervention to those who may benefit from treatment. In establishing a cut-off for interventions, the most important outcome needs to be identified, but as mentioned above, consensus on such a gold standard has not been reached in sarcopenia research.[5]

How?

Currently, there are no approved drug treatments for sarcopenia. Most sarcopenia intervention studies focused on exercise, nutrition, or their combination. But very few trials enrolled people with sarcopenia and their study designs are diverse in terms of participant inclusion, exercise or nutrition interventions, and quality of the study design. The International Conference on Frailty and Sarcopenia Research Task Force met in April 2017 to reflect and evaluate on past trials in sarcopenia and discussed on strategies to accelerate development of new therapies.[5]

The four categories of exercise (resistance exercise, aerobic exercise, flexibility and balance) have potential benefits in improving independence in elderly people.[6] Exercise has been shown to increase muscle strength, physical function, aerobic capacity, muscle protein synthesis, and muscle mitochondrial enzyme activity in both young and elderly people. Systemic inflammation has been increasingly recognised in the genesis of sarcopenia, and exercise has a beneficial role in sarcopenia through its anti-inflammatory effect.[7] For exercise to slow muscle loss, a minimum of twice to thrice per week is recommended. Resistance exercise (exercise against an increasing external load) is the most studied form of exercise intervention. In a Cochrane review of 121 trials with 6,700 participants with an average age of at least 60 years old, resistance exercise has been shown to be beneficial on muscle strength and physical function.[8]

While some studies have shown that protein supplementation augments the beneficial effect of resistance exercise for younger healthy adults, a meta-analysis of 15 studies failed to show a similar effect in older (mean age 77.4 years) healthy, frail, and sarcopenic adults, though there may be an additional benefit of protein supplementation on resistance exercise programmes in frail older adults who do not regularly consume sufficient protein at baseline, particularly those in institutionalised care.[9] However, another systematic overview of community-dwelling elderly patients (aged 65 years or above) with physical frailty and sarcopenia, majority from China and Japan, showed that exercise interventions (that include resistance and balance training) with or without nutritional supplementation improved muscle strength and physical performance.[10]

The "Sarcopenia and Physical fRailty IN older people: multi-componenT Treatment strategies" (SPRINTT) is an ongoing randomised controlled trial designed to evaluate the efficacy of multicomponent intervention (consisting of structure physical activity, personalised nutritional counselling/dietary intervention, and an informational/communication technology) for preventing mobility disability and other outcomes such as injurious falls in 1,500 frail sarcopenic elderly persons in Europe. This study is expected to promote significant advancements in the management of frail sarcopenic elderly persons at high risk of disability.[11]

Prevention of Chronic Sarcopenia

A key issue in geriatric medicine is whether to focus on treatment or prevention. For sarcopenia, public health interventions should adopt a life-course approach in order to have a positive impact on the earlier phases of the skeletal muscle decline starting after the age of 40 years. It has been suggested that everyone who gets a prescription for a long term condition in a clinic should also get an activity prescription at the end of every consultation.[12]

The British Geriatrics Society recommends that exercise, in particular strength and balance training, improves both mobility and functional ability, though the optimal exercise regimen to minimise frailty and sarcopenia remains uncertain.[13] Nutritional interventions also need to be considered, although evidence remains limited. Nutrition recommendations currently include optimising protein intake and correcting vitamin D insufficiency.[13-15] Testosterone improves muscle strength, but is also associated with adverse effects, particularly on the cardiovascular system.[13,16]

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends that the diet should provide at least 1.0–1.2 g protein/kg body weight/day for healthy elderly persons and up to 1.2–1.5 g protein/kg body weight/day for malnourished/at risk of malnutrition elderly people, with even higher intake for individuals with severe illness or injury. However, this recommendation is based on data from longitudinal epidemiological studies rather than intervention trials. Daily physical activity or exercise (resistive or aerobic) should be undertaken by all elderly people, for as long as possible.[17]

The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) Working Group highlights the importance of 'healthier' dietary patterns of adequate quality in old age for muscle health: to ensure sufficient intakes of protein, vitamin D, antioxidant nutrients and long-chain polyunsaturated fatty acids. However, much of the evidence is observational and from high-income countries.[18]

The most practical means of increasing skeletal muscle protein is to include proteins of high biological value during each meal, e.g. lean cuts of meat, fish, eggs, low fat dairy products, beans, pulses, lentils. It has been suggested that leucine, an essential amino acid, is critical to the maintenance of healthy muscle. However, no consistent results have been shown from studies of leucine supplementation. Dietary omega-3 fatty acid supplementation (e.g. fish oil or flaxseed oil) increases the rate of muscle protein synthesis in elderly persons.[19] A Korean community study of elderly people (aged ≥65 years) showed that dietary intake of vegetables and fruits, which are rich in antioxidant, was associated with a significantly reduced risk of sarcopenia.[20] Low vitamin D levels have been associated with low muscle strength.[21] Vitamin D supplementation in individuals with low levels can help improve muscle mass and function.[22-24]

While lifestyle and behavioural interventions (e.g. nutrition, physical activity) may be promoted on a large scale as a public health preventive measure, the development of drugs to prevent sarcopenia can be targeted at the higher risk sub-population because of a sedentary lifestyle or inadequate energy intake and those with specific sarcopenia conditions characterised by accelerated ageing.[25] The ENRGISE (ENabling Reduction of 10wGrade Inflammation in Seniors) is a prevention trial in Florida that targets age-related inflammation as a risk factor for mobility loss, frailty, and sarcopenia.[26] The anti-inflammatory intervention used in this study combines an angiotensin receptor blocker (losartan) with omega-3 fatty acids. If proven efficacious, this widely available and low-cost combined intervention could be relatively easy to deliver to elderly people at high risk of mobility disability.

Acute Sarcopenia Secondary to Hospitalisation

The term "acute sarcopenia" refers to acute loss of muscle mass and function associated with hospitalisation, arising from a combination of acute inflammatory burden, muscle disuse and endocrine dysregulation.[4] The risk factors associated with acute sarcopenia are:[27-34]

- Cognitive impairment: acute (delirium) or chronic (dementia)
- Immobility: bedrest, disuse, restraint
- Acute medical illness
- Intensive Care Unit admission
- Medications, e.g. steroids
- Surgical procedures
- Malnutrition
- Chronic disease
- Pre-sarcopenia and chronic sarcopenia
- Psychological stress: acute or chronic
- Depression
- Insomnia

Prevention and Treatment of Acute Sarcopenia

Identifying and intervening the risk factors of acute sarcopenia mentioned above are important in preventing or reversing acute sarcopenia and its long-term sequelae of chronic sarcopenia.

Physical activity interventions

Hospitalised elderly patients often have their mobility restricted by reclining beds, bedside rails, restraints, and the use of bed and chair alarms due to perceived risks of falls.[35,36] Bedrest and restraints, which are associated with sarcopenia and other adverse outcomes,[36-38] should

be minimised during hospitalisation. There is increasing evidence that early mobilisation and physical activity regimes can help to improve outcomes.[39,40] The optimum duration and intensity of physical activity to treat or prevent acute sarcopenia has yet to be answered by future research. For in-hospital mobility intervention programmes to be sustainable, such programmes may have to be tailored to specific sites.[41]

Nutrition

Studies have shown that elderly persons have higher protein requirements than younger adults because of anabolic resistance, which means that elderly individuals need to consume a greater amount of protein to stimulate muscle protein synthesis.[42] The protein requirements are further increased during acute illness.[43] A randomised study on protein pulse feeding in an inpatient rehabilitation unit has demonstrated clinically relevant effects on the lean mass in malnourished and at-risk hospitalised elderly patients.[44] A meta-analysis of high protein oral nutritional supplements in patients following hospital discharge showed a reduction in complications and re-admissions as well as improvements in weight and grip strength.[45]

Other potential interventions

Neuromuscular electrical stimulation, the application of electrical currents to stimulate muscular contraction, is a potential strategy to prevent targeted muscle atrophy in situations where mobilisation is not possible, such as in the intensive care unit setting.[46] In patients with advanced cancer undergoing standard-of-care therapy, adjunct testosterone (weekly injections of 100 mg testosterone enanthate for seven weeks) improved the lean body mass and was also associated with increased quality of life, and physical activity compared with placebo.[47] It is thought that testosterone achieves this by both stimulating anabolic and suppressing catabolic skeletal muscle pathways.

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Prevention and Treatment of Sarcopenia" by Dr Tak-kwan KONG and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 July 2018 Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. **Patients with sarcopenia are at risk of mobility disability and treating sarcopenia is a means to avoid disability.**
2. **The proposed cut-off points to diagnose sarcopenia for Asians are outcome-based and can be used as the threshold for interventions.**
3. **The minimum recommended frequency of exercise to slow muscle loss is once a week.**
4. **Current evidence-based treatments for sarcopenia are drugs, exercise, and nutrition.**
5. **Prevention of sarcopenia should start at the age of 40 years when skeletal muscle declines in the life-course.**
6. **Though testosterone improves muscle strength, it is associated with adverse effects on the cardiovascular system.**
7. **Vitamin D supplementation in individuals with low vitamin D levels can help improve muscle mass and function.**
8. **Since inflammation is a risk factor for sarcopenia, anti-inflammatory drugs are being studied in sarcopenia prevention trials.**
9. **Intensive Care Unit admission is a risk factor for acute sarcopenia.**
10. **Anabolic resistance means that younger adults need to consume a greater amount of protein than older adults to stimulate muscle protein synthesis.**

ANSWER SHEET FOR JULY 2018

Please return the completed answer sheet to the Federation Secretariat on or before 31 July 2018 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

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Dr Tak-kwan KONG

MBBS(HK), FHKAM(Medicine), FHKCP, FRCP(Lond, Edin, Glasg)

Specialist in Geriatric Medicine
Honorary Clinical Associate Professor, Department of Medicine, The University of Hong Kong
Clinical Associate Professor (Honorary), Department of Medicine & Therapeutics, The Chinese University of Hong Kong
Consultant, Division of Geriatrics, Department of Medicine & Therapeutics, Prince of Wales Hospital

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Answers to June 2018 Issue

American College of Cardiology, Annual Scientific Congress (ACC 18')
Late-Breaking Clinical Trials Sessions

1. F 2. F 3. F 4. F 5. F 6. T 7. T 8. T 9. T 10. T