Effectiveness and clinical application of multidisciplinary combined exercise and nutrition intervention for sarcopenic older adults with metabolic syndrome: study protocol for a multicentre randomised controlled trial

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ABSTRACT
Introduction Among chronic diseases affecting older adults, metabolic syndrome (MetS) is known to be closely related to sarcopenia. Insulin resistance may play a key role in the increased frequency of sarcopenia associated with metabolic disorders. To date, an exercise–nutrition combined intervention has been the treatment of choice for sarcopenia. However, trials of combined interventions for individuals with sarcopenia and MetS are still lacking. This study aims to develop and conduct a standardised intervention, named the Multidisciplinary combined Exercise and Nutrition inTervention for Sarcopenia (MENTORS), for sarcopenic older patients with MetS.

Methods and analysis This multicentre, randomised controlled trial includes 168 community-dwelling older adults with sarcopenia and MetS. The 12-week MENTORS comprises an exercise intervention consisting of an introductory phase (3 weeks; twice-weekly visits), an expanded phase (3 weeks; twice-weekly visits) and a maintenance phase (6 weeks; once-weekly visits); and a nutrition intervention tailored to the nutritional status of individual subjects. Outcomes will be measured at 0-week, 12-week and 24-week postintervention. The data will be analysed using the intention-to-treat and per-protocol principle.

Ethics and dissemination Before screening, all participants will be provided with oral and written information. Ethical approval has already been obtained from all participating hospitals. The study results will be disseminated in peer-reviewed publications and conference presentations.

Trial registration number NCT04948736

INTRODUCTION
Sarcopenia is a condition in which skeletal muscle mass declines and physical capabilities worsen with age, which increases the risk of senility, disability, falls, fractures and mortality.1 An increasing elderly population is a major public health issue that rapidly increases the costs of medical and long-term care.2 Sarcopenia is also linked to a variety of chronic and geriatric illnesses, such as stress fractures, metabolic diseases, degenerative joint diseases and cancer.3 Among these chronic diseases affecting older adults, metabolic syndrome (MetS) is closely related to sarcopenia. Chronic degenerative/geriatric disease-related sarcopenia has a positive prognosis when the appropriate interventions and management of the underlying disease are implemented.4 Targeted treatment not only improves physical function, but also reduces symptoms of the underlying disease.5 Insulin resistance, which is the main pathogenesis of MetS, worsens as sarcopenia


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progresses because muscle tissue is the principal site for glucose absorption and storage.6 Furthermore, cytokines generated by muscle tissue, such as myokine, interact with adipokine secreted by adipose tissue and help prevent insulin resistance.7 As a result, sarcopenia is linked to MetS.8 Increased muscle mass is known to enhance insulin sensitivity, whereas sarcopenia induces primary hypertension by stiffening arteries.9 Kim et al evaluated the appendicular skeletal muscle mass (ASM) in 414 older adults (144 in a diabetic group and 270 in the control group) in a study investigating the correlation between diabetes and sarcopenia, and found a high prevalence of sarcopenia in the diabetic group.10

Insulin resistance may play a key role in the increased frequency of sarcopenia associated with metabolic disorders. Sarcopenia increased the incidence of glucose metabolic diseases, such as insulin resistance and elevated glycated haemoglobin, in the US National Health and Nutrition Examination Survey III.11 It has also been noted that, as people age, their body composition changes; decreased muscle and increased fat may be seen. Furthermore, lipid deposition in muscle cells, and/or adipose tissue between muscle tissue, is linked to insulin resistance.3

To date, an exercise–nutrition combined intervention has been the treatment of choice for sarcopenia.12 The majority of exercise–nutrition combined intervention trials found that elderly subjects with sarcopenia exhibited improved muscular function.13 This type of intervention combines nutrition with resistance exercise and protein supplementation, and is the most effective therapeutic strategy for improving muscle mass, muscle strength and physical function in elderly patients with sarcopenia.14 15 Studies using this combined method found it was superior to a single intervention in an elderly group, and in men with sarcopenia.16 17

However, no trials using combined intervention for individuals with both sarcopenia and MetS have been published. Furthermore, evidence supporting an integrated management plan targeting all phases of sarcopenia (ie, the acute, recovery/transition and maintenance phases) is lacking. Therefore, we designed a multidisciplinary programme combining exercise and nutrition for older adults with both sarcopenia and MetS, tailored according to their functional and nutritional status. Multicentre clinical trials are well suited to the investigation and validation of standardised, complex interventions, and can also be used to determine ideal clinical outcome indicators for sarcopenia.

Objectives
1. To develop the standardised Multidisciplinary combined Exercise and Nutrition Intervention for Sarcopenia (MENTORS).
2. To conduct a multicentre, controlled clinical trial comparing the effectiveness of MENTORS with conventional medical care for sarcopenic older patients with MetS.

METHOD AND ANALYSIS
Study design
This is a single-blind, multicentre, randomised controlled trial in five tertiary hospitals with a 24-week follow-up period. The trial was registered prospectively at Clinicaltrials.gov (NCT04948736) prior to participant recruitment. Significant protocol modifications will be communicated to the trial registry. Sarcopenia will be assessed before, and immediately and 12 weeks after, completion of the intervention (24-week total study duration) (figure 1).

Provisional study schedule
- Start of study: January 2022.
- Recruitment period: January 2022 to December 2023.
- Follow-up period: 24 weeks.
- Total duration of the study: 30 months

Open access
Estimated end of study (last visit of the last patient): June 2024.

Participants and eligibility criteria
Community-dwelling older adults (aged ≥65 years) with sarcopenia and MetS will be included. The study subjects will be recruited from five hospitals. After confirming eligibility among the subjects who voluntarily consent through the subject recruitment poster in each hospital, the screening step will proceed (see online supplemental material 1). Sarcopenia will be diagnosed according to the criteria proposed by the Asian Working Group for Sarcopenia 2019. It can be defined as low ASM (<7.0 kg/m² for male patients and <5.4 kg/m² for female patients according to dual-energy X-ray absorptiometry, or ASM <7.0 kg/m² for male patients and <5.7 kg/m² for female patients using bioimpedance analysis) with low muscle strength (handgrip strength <28 kg for male patients and <18 kg for female patients) or low physical performance (6-metre walking speed <1 m/s, 5-time chair stand test ≥12s or Short Physical Performance Battery ≤9s). MetS will be defined as the presence of at least three of the following five risk factors: increased waist circumference (male patients ≥90 cm, female patients ≥85 cm (Asian cut-off points)); elevated blood pressure (BP) (systolic BP ≥130 mm Hg and/or diastolic BP ≥85 mm Hg, or receiving treatment for hypertension); fasting blood glucose ≥5.6 mmol/L (100 mg/dL) or receiving treatment for elevated glucose; triglycerides ≥1.7 mmol/L (150 mg/dL) or receiving treatment for hypertriglyceridaemia; and increased high-density lipoprotein cholesterol (HDL-C) (male patients <1.0 mmol/L (40 mg/dL), female patients <1.3 mmol/L (50 mg/dL) or receiving treatment for HDL-C). Participants will be excluded if any of the following conditions were met: estimated glomerular filtration rate ≤30 mL/min per 1.73 m²; vitamin D intake ≥1000 IU per day; controlled diet for the purpose of disease management; disorder of the central nervous system (such as stroke, Parkinson’s disease or spinal cord injury); cognitive dysfunction (Mini Mental Status Examination score <24); difficulty communicating (due for example to severe hearing loss); musculoskeletal conditions affecting physical function (such as limb amputation); long-term use of corticosteroids due to inflammatory disease; malignancy requiring treatment within the previous 5 years; and other medical conditions requiring active treatment. Subjects who refused to participate in the study will be also excluded.

Randomisation
Participants will be randomly assigned to a control group receiving standard care or the MENTORS experimental group according to a table of random numbers. The probability of being assigned to each group will be 1:1. Because it is impossible to blind the subjects due to the nature of the exercise–nutrition intervention, a single blind trial will be conducted in which only the outcome evaluator was blinded. The trial will be conducted over a 12-week period, and the two groups will be compared before the intervention (baseline), immediately after the intervention (12 weeks) and 12 weeks after the intervention (24 weeks).

Combined exercise and nutritional intervention (MENTORS)
The 12-week exercise intervention will consist of three phases: an introductory phase (3 weeks, twice-weekly visits), an expanded phase (3 weeks, twice-weekly visits) and a maintenance phase (6 weeks, once-weekly visits) (table 1). Each 60-minute session will include stretching, resistance exercise and aerobic exercise. In the introductory phase, conventional resistance training will focus mainly on concentric contractions; thereafter, eccentrically biased strengthening and power exercises were applied. Resistance exercises will focus on the upper extremities (biceps curl, dips, front raise, chest press).

Table 1: Exercise intervention part of MENTORS

<table>
<thead>
<tr>
<th>Phase</th>
<th>Introductory (3 weeks, 2 visits/week)</th>
<th>Expanded (3 weeks, 2 visits/week)</th>
<th>Maintenance (6 weeks, 1 visit/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stretching</td>
<td>Warm up/cool down</td>
<td>Warm up/cool down</td>
<td>Warm up/cool down</td>
</tr>
<tr>
<td>Aerobic</td>
<td>Stationary bicycle (RPE 9–11 or HR\text{max} 60) 10 min</td>
<td>Stationary bicycle (RPE 11–13 or HR\text{max} 70) 15 min</td>
<td>Stationary bicycle (RPE 11–13 or HR\text{max} 70) 20 min</td>
</tr>
<tr>
<td>Resistance</td>
<td>Conventional concentric resistance training (chair/bed-based elastic band exercise)</td>
<td>Eccentric exercise (chair/bed-based elastic band exercise)</td>
<td>*Power/eccentric exercise (standing position with chair)</td>
</tr>
<tr>
<td>Intensity</td>
<td>8–10 reps, 3 sets</td>
<td>10–12 reps, 3–4 sets</td>
<td>15 reps, 3–4 sets</td>
</tr>
<tr>
<td></td>
<td>Upper TheraBand yellow (F) red (M)</td>
<td>Upper TheraBand yellow−red (F) red−green (M)</td>
<td>Upper TheraBand red (F) green (M)</td>
</tr>
<tr>
<td></td>
<td>Lower loop band, red (F) green (M)</td>
<td>Lower loop band red−green (F) green−blue (M)</td>
<td>Lower loop band green (F) blue (M)</td>
</tr>
</tbody>
</table>

*Make the movement as fast as possible (power exercise) and slowly return while feeling the resistance of the band (eccentric contraction). HR\text{max}, maximal heart rate; MENTORS, Multidisciplinary combined Exercise and Nutrition Intervention for Sarcopenia; RPE, rating of perceived exertion.
lower extremities (lateral leg rotation, leg extension, hip abduction, squat, heel raise) and trunk (back extension, curl up, bridge). In the second stage (expanded phase), the strengthening exercises will consist of task-oriented eccentric exercises. The third stage (maintenance phase) will be conducted over 6 weeks and added power/eccentric exercises. In each subsequent stage, the number of repetitions and sets will be increased by 20%. Participants will be encouraged to perform the exercise programme at home on non-visiting days. To improve exercise compliance, we will provide an exercise diary and encouraged study subjects to keep track of their progress, and contacted the study subjects via video call every week to check compliance.

The nutritional intervention will be tailored to the nutritional status and individual eating patterns of the study subjects. The goal of this food intake strategy will be to allow the subjects to achieve optimal nutrition and high protein intake. After each subject's nutritional status will be evaluated with the Mini Nutritional Assessment (MNA) and Korean Protein Assessment Tool (KPAT), which is composed of food type, serving size and eating frequency questionnaires. After achieving questionnaires, we will record and calculate the daily protein intake of all participants using Microsoft Excel (Redmond, Washington, USA). The daily protein intake goal will be determined: MNA 24–30 (well nourished), 1.2 g/kg/day; MNA 17–23.5 (at risk), 1.5 g/kg/day; or MNA <17 (maltreated), 1.5 g/kg/day. Individual dietary counselling was provided by a clinical nutritionist. For protein consumption, we will provide an individualised, protein-rich diet tailored to the preferences of the participants, and/or a protein powder supplement (PROMAX, Korea Medical Foods, Seoul, South Korea; protein: 24 g, cholesterol: 35 mg, sodium: 120 mg, total carbohydrate: 3 g, dietary fibre: 0 g, sugars: 2 g per 1 scoop (30 g) serve) corresponding to the subjects’ daily protein intake goals. Dietary compliance and adherence will be monitored using a food diary (figures 2 and 3). As the subjects are patients with MetS, their daily caloric intake has been individually assessed during nutritional counselling, with an aim to increase protein intake and to achieve eucaloric diet while simultaneously reducing carbohydrate consumption.

The control group will participate in a rehabilitation programme based on general good practice medical care and follow-up. They will be given a brochure about exercise and protein-rich foods at their first visit. Exercises such as walking, exercise training, muscle strengthening and aerobic exercise will be tailored to the subjects’ individual abilities and preferences. Medical management, such as inpatient or outpatient treatment of osteoporosis, will be provided. The control group will be instructed to maintain their usual amount of activity and diet during the 6-month evaluation period. To prevent drop-out and check for medical issues, we will contact the subjects every month.

**Outcomes measures**

The following outcomes will be measured before and immediately after the 12-week intervention, as well as 12 weeks after its completion, for an overall study period of 24 weeks (table 2).

The 5-time chair stand test, conducted immediately after the intervention (12 weeks), are the primary outcome measures. The secondary outcome measures before the intervention (baseline), immediately after the intervention (12 weeks) and 12 weeks after the intervention (24 weeks) are as follows: conventional sarcopenic indices (an ASM assessment using dual-energy X-ray absorptiometry and bio-impedance analysis, the Short Physical Performance Battery, 6-metre walking speed, handgrip strength and the SARC-F Questionnaire); nutritional status assessment (MNA and KPAT); psychiatric assessment (Delirium Rating Scale, Korean Mini Mental Status Examination, 2nd edition (score range: 0–30; lower scores indicate a worse outcome) and Korean version of the Geriatric Depression Scale21 (score range: 0–30; lower scores indicate a worse outcome)); and other comprehensive geriatric assessments (Korean version of the Physical Activity Scale for the Elderly, Standardised Swallowing Assessment, Korean version of the Health

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**Nutritional status evaluation**

- Mini-nutritional assessment (MNA)
- Korean Protein Assessment Tool (KPAT)

**Set a daily protein intake goal**

- MNA 24-30 (well nourished): 1.2 g/kg/day
- MNA 17-23.5 (at risk): 1.5 g/kg/day
- MNA <17 (maltreated): 1.5 g/kg/day

**Nutritional management**

Figure 2  Nutrition intervention tailored according to nutritional status.
Empowerment Scale, Korean Activity Daily Life Questionnaire, Korean Instrumental Activities of Daily Living questionnaire (score range: 0–3; higher scores indicates worse outcomes) and the EuroQol-5D (EQ-5D; score range: 0–1; lower scores indicate worse outcomes)).

**Data analysis**

Data will be collected using a standardised data entry form and entered into the data management system. The intention-to-treat and per-protocol principles will be followed for data analysis. Participants undergoing baseline measurements and the first-week intervention will be included in the intention-to-treat analysis; missing data were handled by using the last recorded observation carried forward and multiple imputation methods.

Participant characteristics will be described as means and SDs for continuous data and frequencies and percentages for categorical data. To compare paired data between two different points, we will use repeated-measures analysis of variance and the Friedman test for continuous and non-parametric data, respectively. Statistical significance will be defined as p<0.05. All statistical analyses will be performed using SPSS software (V.19.0 for Windows; IBM, Armonk, New York, USA).

**Sample size**

Based on a previous study, the study power will be set at 90% and alpha was set at 0.05, with p<0.05 indicating statistical significance. Using PASS 2020 statistical software (NCSS Statistical Software, Kaysville, Utah, USA), we

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**Table 2** Overview of the outcome measures and assessment time points

<table>
<thead>
<tr>
<th>Measure</th>
<th>Visit 0 (Screening)</th>
<th>Visit 1 (Week 0, start point)</th>
<th>Visit 2 (Week 12, end point)</th>
<th>Visit 3 (Week 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Informed consent</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Demographic information</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Medical history</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Conventional sarcopenic indices</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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<tr>
<td>Nutritional assessment</td>
<td>O</td>
<td>O</td>
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<td>O</td>
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<tr>
<td>Comprehensive geriatric assessment</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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<tr>
<td>Exercise and nutritional intervention</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

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*Figure 3* Overall flow chart of the MENTORS programme. MENTORS, Multidisciplinary combined Exercise and Nutrition inTervention fOR Sarcopenia.
will determine that, to measure a difference of 2.5 s on the 5-repetition chair test between groups, 50 participants per group will be required. A total of 168 participants will be recruited based on an estimated 80% compliance and 25% dropout rate for the two groups.

**Patient and public involvement**

While participants will not be involved in the development of the research question and the selection of outcome measures, their needs and preferences will be considered throughout the process. Feedback to the participants regarding scientific results, will be organised on each study site.

**ETHICS AND DISSEMINATION**

This study protocol received approval from the institutional review board of Seoul National University Bundang Hospital (B-2010/645-005), SMG-SNU Boramae Medical Center (10-2021-107), Seoul National University Hospital (J-2108-192-1249), Jeju National University Hospital (2022-01-017) and Kyung Hee University Medical Center (2022-02-057). The study will be performed in accordance with the relevant guidelines of the Declaration of Helsinki, 1964, as amended in Tokyo, 1975; Venice, 1983; Hong Kong, 1989; and Somerset West, 1996. Written informed consent for all interventions and examinations will be obtained at subject participation. The Ethics Board will be informed of all serious adverse events and any unanticipated adverse effects that occur during the study. The study protocol has been registered at Clinicaltrials.gov and will be updated. Direct access to the source data will be provided for monitoring, audits, Research Ethics Committee (REC)/Institutional Review Board (IRB) review and regulatory authority inspections during and after the study. All patient information will be coded anonymously, with only the study team having access to the original data. The study results will be disseminated in peer-reviewed publications and conference presentations.

**DISCUSSION**

Complex interactions among inflammation, fat deposition and insulin resistance play a role in the relationship between MetS and sarcopenia. Insulin resistance is the main cause of MetS and mediates the association between MetS and sarcopenia. Because skeletal muscle is a major site of insulin-induced glucose metabolism, reduced skeletal muscle mass causes insulin resistance. This promotes skeletal muscle protein synthesis by increasing lipolysis, which releases free fatty acids from adipose tissue and inhibits the insulin-like growth factor 1 axis. Recently, it was reported that sarcopenia is closely related to MetS, type 2 diabetes mellitus and cardiovascular disease. Because MetS causes excessive accumulation of visceral fat, elevated BP, fasting hyperglycaemia and abnormal lipid levels, it can increase the risk of diabetes mellitus, cardiovascular disease and even cancer. Sarcopenia is also linked to persistent inflammation, which plays a role in the pathophysiology of MetS. IL-6 is an inflammatory cytokine that is increased in a variety of inflammatory illnesses, and its effects on skeletal muscle have previously been investigated.

Several studies have reported a positive correlation between MetS and sarcopenia. One meta-analysis of 13 cross-sectional studies including 35,581 non-obese adults reported that the prevalence of MetS in those with sarcopenia was 36.45%. A large cross-sectional study including 13,620 subjects found a strong correlation between sarcopenia and the frequency of MetS, with a 56% reduction in the risk of MetS for every 1-quarter increase in the limb skeletal muscle index. Lower grip strength, which is one of the main diagnostic tools for sarcopenia, is also closely related to the development of MetS.

Patients who have both MetS and sarcopenia have a higher risk of many health problems than those who have neither condition. Therefore, clinical interventions for MetS and sarcopenia should be applied simultaneously. Higher levels of physical activity have been reported to improve MetS and sarcopenia. Regular exercise can increase brown adipose tissue, which regulates myostatin secretion and is involved in the regulation of skeletal muscle mass and function. A protein-enriched diet and regular exercise can help prevent MetS-related sarcopenia.

**STRENGTHS**

To our knowledge, this is the first study investigating an exercise and nutrition interventional programme for older adults with both MetS and sarcopenia. Furthermore, no study has investigated whether such a programme can increase muscle mass, muscle strength and muscle function in the same population. For future studies, we intend to develop a standardised, multidisciplinary interventional programme and conduct multicentre clinical trials to compare its effectiveness with conventional medical care for sarcopenic older patients with MetS. To prevent unnecessary use of resources, we have carefully designed our study to be efficient and effective in its use of resources. For instance, we plan to conduct a two-arm design, which will allow us to focus on a specific intervention and reduce the resources needed for a larger, more complex study. Additionally, we plan to conduct this study based on the literature review and expert opinions, which will reduce the need for additional studies and ensure rigorous validation of our results.

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REFERENCES


본 연구는 한국보건산업진흥원의 연구비를 지원 받아 수행하는 연구로 기저 질환(대사중후군, 고관절 골절)이 있는 근간소중 환자를 대상으로 운동-영양 복합 중재를 시행하였을 때 근간소중 지표, 기능 및 삶의 질에 미치는 영향을 확인하고자 하는 임상시험입니다. 기저 질환 및 기능 상태 별 맞춤 운동-영양 복합 중재를 12주간 시행하는 환자군과 일반적 의학적 관리와 경과 관찰에 해당하는 통상적 관리 (usual care)를 받는 환자군을 비교하여 환자의 근간소중 지표의 개선 정도와 기능적 호전, 환자만족도 정도를 보고자 하는 비교 대조군 연구이며 대상자를 모집하고 데이터 분석을 통하여 문제점을 발견하고 개선점을 찾아 해결방안을 알아보고자 하는 목 적의 임상시험입니다.

4. 임상연구 참여대상자 수 및 참여기간

<참여 대상자 수>

- 본 연구에서는 기저 질환 및 기능 상태 별 맞춤 운동-영양 복합 중재를 12주간 시행하는 환 자군과 일반적 의학적 관리와 경과 관찰에 해당하는 통상적 관리 (usual care)를 받는 환자군 으로 무작위 배정을 통해 진행 할 계획입니다. 연구에 참여하기라도 맞춤형 운동-영양 복합 중재를 적용 받지 않는 군으로 배정될 수도 있습니다. (무작위 배정 확률 1:1)

- 대사중후군 근간소중 환자

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<thead>
<tr>
<th>기관명</th>
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<참여 기간> (1회 방문시 1시간 정도 소요, 총 참여 기간 6개월)

<대사증후군 근갑소증 환자>
- 방문 1: 동의서 작성 및 스크리닝
- 방문 2: 평가 시행 - 증후 시작 시 (Baseline)
- 방문 3: 평가 시행 - 증후 시작 후 12주 후
- 방문 4: 평가 시행 - 증후 시작 후 24주 후

<고관절 골절 근갑소증 환자>
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- 방문 4: 평가 시행 - 증후 시작 후 24주 후

5. 연구의 절차 및 방법
- 대조군에 배정된 대상자들은 근갑소증 환자를 대상으로 본원에서 현재 시행되고 있는 일반적 의학적 관리와 경과 관찰에 해당하는 통상적 관리 (usual care)를 12주 받게 됩니다. 평가 및 치료 등의 의학적 관리와 환자 개개인의 상태에 맞춘 근력, 유산소 운동과 식이 및 영양소 보충에 관한 편장이 포함됩니다. 웰수 아미노산 중심의 단백질 섭취를 강화하고 유연성 운동과 근력강화운동치료를 병행하는 치료가 시행됩니다. 이후 6개월의 증후 및 추적 관찰 기간 동안 평상시의 활동량 및 식이 습관을 유지하면서 방문 시기별 평가를 받습니다.

Version 2.3

- 실험군에 배정된 대상자들은 두 가지의 복합 중재를 받습니다. 첫번째로는 운동중재로 동안 주 2회, 이후 6주 동안은 주 1회 병원 방문하여 운동 프로그램을 따라 운동 중재를 받습니다. 두번째로는 영양 중재로 첫 번째 방문시 영양상태 파악을 위해 PIAT, MNA 측정을 하여 이를 토대로 1일 목표단백질 및 부족 단백질량을 산출합니다. 이후 운동중재를 위해 병원을 방문하면서 영양사를 통해 상담이 진행됩니다. 이후 2주마다 모니터링을 통해 연구 참여에 어려움이 있다고 판단되는 경우에 중재 후 6주 시점에 다시 한번 영양상담을 진행할 수 있습니다.

<실험군 연구 참여 과정>

<table>
<thead>
<tr>
<th>순번</th>
<th>내용</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>동의서 작성 및 스크린닝 검사</td>
</tr>
<tr>
<td>2</td>
<td>신체 기능 평가 (스크린닝 검사 후 2주 후)</td>
</tr>
<tr>
<td>3</td>
<td>영양상담 1회</td>
</tr>
<tr>
<td></td>
<td>운동 프로그램 참여 I (6주 동안 주 2회 방문)</td>
</tr>
<tr>
<td></td>
<td>운동 프로그램 참여 II (6주 동안 주 1회 방문)</td>
</tr>
<tr>
<td>4</td>
<td>신체 기능 평가 (프로그램 시작 후 12주 후)</td>
</tr>
<tr>
<td>5</td>
<td>신체 기능 평가 (프로그램 시작 후 24주 후)</td>
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</tbody>
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<대조군 연구 참여 과정>

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<td>운동/영양 교육 자료 제공</td>
</tr>
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<td></td>
<td>전화 모니터링 (2주에 1회)</td>
</tr>
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</tr>
</tbody>
</table>

6. 연구대상자가 준수하여야 할 사항

안타깝게도 본 임상연구에 참여하시기로 결정한다면 다음 사항을 준수해야 합니다.
- 임상연구 방문 일정 준수해야 합니다. 본 연구에 참여하게 되면 선별평가와 기능평가 배정군에 따른 중재를 위해 6개월 동안 총 4회의 방문을 하셔야 합니다. 또한 운동중재 프로그램 참여를 위해 주 2회 방문을 하여 운동 중재 및 영양 중재 프로그램에 참여하고 나머지 날에는 가정운동을 시행합니다.
- 귀하의 건강에 변화가 있거나, 임상연구에 대해 어떠한 우려가 있다면 즉시 연구자에게 알려야 합니다.

7. 연구대상자에게 예견되는 부작용, 위험과 불편함
8. 연구대상자에게 예절되는 이득

본 연구에 참여함으로써 얻게 되는 직접적인 이득은 없습니다. 하지만 본 연구의 대상은 임상적, 과학적, 사회적, 도덕적 이익을 제공할 수 있습니다. 또한 연구에 참여하셔서 받게 되는 각종 재활 평가에 대한 결과 정보를 받으실 수 있습니다.

9. 대안 치료 (임상시험 이외의 다른 대체 가능한 치료법)

본 연구는 무작위 배정을 통하여 실험군과 대조군으로 나누게 됩니다. 실험군은 기저 질환과 기능 상태 양쪽의 동등한 경우를 선택하고, 대조군은 현재 본원에서 시행되고 있는 일반적 의학적 관리와 경과 관찰에 해당하는 통상적 관리 (usual care)를 받게 됩니다. 귀하가 본 연구에 참여하기를 원하지 않는다면 대조군에 준하는 의학적 관리와 운동치료와 교육, 식이상담을 받을 수 있습니다.

10. 연구 참여 비용 및 손실에 대한 보상

본 연구에 참여하시는 분께는 보상이 드릴 예정입니다. 연구 참여를 중도에 포기하시는 경우에는 보상이 드릴 예정입니다. 연구에 참여하면서 발생하는 모든 비용은 연구자가 부담할 것이며, 연구대상자가 지불해야 하는 비용은 없습니다. 본 연구 참여로 인해 발생하는 피해는 거의 없을 것으로 보이나, 만에 하나 발생하는 부작용이 있다면 이에 대한 모든 치료의 경비뿐 아니라 보상에 대해서 연구 책임자인 임제영 교수에서 책임을 지고 피해보상에 관한 규약에 의거하여 피해 보상할 것이며, 이상반응 및 장래 악화의 경우에는 가능한 한 최선의 치료방법으로 치료할 것입니다.

11. 자발적 참여 및 동의 철회

본 연구의 참여 여부는 자발적으로 결정하실 수 있으며, 언제든지 연구 참여를 중도에 포기하실 수 있습니다. 또한 연구자가 연구의 지속이 어렵다고 판단할 경우에는 연구가
<연구 참여 도중 대상자의 연구 참여가 중지되는 경우 및 그 사유>
- 우발적인 병발 현상으로 연구의 진행이 불가능하다고 판단되는 경우
- 실험담당자의 판단에 의해 연구 참여 지속이 적합하지 못하다고 판단되는 경우
- 본 과제에서 제공되는 기기 사용이 어려워지는 상황이 발생하거나 평가를 위한 방문이 어렵게 된 경우
- 그 외 시험자의 의결에 따라 임상시험을 진행하는 것이 대상자에게 유익성을 제공하는 것이 아니라고 생각되는 모든 임상적 이상반응 발생시 중도 퇴락

12. 개인정보보호 및 개인정보 제공에 관한 사항
본 연구는 개인정보보호를 수집하지 않으며, 본 연구 결과가 출판될 경우 대상자의 신상은 비밀로 보호될 것입니다. 진행 및 종료 후에도 임상연구의 모니터링, 점검을 실시하는 사찰, IRB 및 보건복지부장관이 관계 법률에 따라 연구의 절차와 자료의 품질을 검증하기 위하여 연구참여자의 신상에 관한 비밀이 보호되는 범위에서 대상자의 연구 기록을 열람할 수 있으며, 연구 참여자가 서명한 동의서에 의하여 이러한 자료의 열람이 허용됩니다. 본 연구의 결과는 연구 참여자가 서명한 동의서에 의하여 익명화한 후 데이터 생산을 위한 기초데이터로 제3자에게 제공될 수 있습니다. 본 데이터는 후속 연구, 기록, 축적 등을 위해 3년간 보관할 계획으로 암호가 걸린 외장하드를 이용하여 데이터를 저장합니다.

13. 연구 관련 새로운 정보의 지속적 제공
이 연구가 진행되는 동안에 귀하가 연구 참여 지속 여부를 생각하게 될 만한 새로운 사실이나 정보를 시험자가 알게 되면 언제든지 연구자는 귀하 또는 귀하의 대리인에게 이 사실이나 정보를 알려드릴 것입니다.

14. 담당자 연락처
본 연구에서 발생한 문제, 우려, 질문에 대하여 상의할 담당자의 연락처
- 책임연구자: 임재영 교수, 본당 서울대병원 재활의학과
  전화번호: 031-787-7732
Version 2.3

- 연구담당자: 김은혜, 백윤정 연구원, 분당 서울대병원 재활의학과
  전화번호: 031-787-6896, 010-4658-0376

연구대상자의 권익에 대한 문제, 우려, 질문이 있을 때 상의할 IRB(생명윤리심의위원회) 또는
임상연구윤리센터 연락처

- IRB(생명윤리심의위원회)지원실 ☏ 031-787-8801~8806
- 임상연구윤리센터 ☏ 031-787-8811~8813
연구대상자 동의서

1. 본인은 임상연구에 대해 구두로 설명을 받고 상기 연구 설명문을 읽었으며 담당 연구원과 이 연구에 대하여 충분히 의논하였습니다.

2. 본인은 연구의 위험과 이득에 관하여 들었으며 나의 질문에 만족할 만한 답변을 얻었습니다.

3. 본인은 이 연구에 참여하는 것에 대하여 자발적으로 동의합니다.

4. 본인은 이후의 치료에 영향을 받지 않고 언제든지 연구의 참여를 거부하거나 연구의 참여를 중도에 철회할 수 있고 이러한 결정이 나에게 어떠한 해가 되지 않을 것이라는 것을 알고 있습니다.

5. 본인은 이 설명서 및 동의서에 서명함으로써 의학 연구 목적으로 나의 개인정보가 현행 법률과 규정이 허용하는 범위 내에서 연구자가 수집하고 처리하는데 동의합니다.

6. 본인은 연구 설명문 및 동의서의 사본을 받을 것을 알고 있습니다.

이에 나의 자유로운 의사에 따라 본 연구에 참여할 것을 동의합니다.

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<thead>
<tr>
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<td>년 월 일</td>
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<tr>
<td>대상자의 대리인 (해당되는 경우)</td>
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