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Sarcopenia of Spine (SarcoSpine): A Prospective Cohort Study Protocol

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ABSTRACT

Introduction: Sarcopenia in the lumbar paraspinal muscles is receiving renewed attention as a cause of spinal degeneration. However, there are few studies on the precise concept and diagnostic criteria for spinal sarcopenia. Here, we develop the concept of spinal sarcopenia in community-dwelling healthy, elderly people. In addition, we aim to observe the natural aging process of paraspinal and back muscle strength and investigate the association between conventional sarcopenic indices and spinal sarcopenia.

Methods and analysis: This is a prospective observational cohort study with 120 healthy community-dwelling, elderly people over 4 years. All subjects will be recruited in no sarcopenia, possible sarcopenia, or sarcopenia groups. The primary outcomes of this study are isokinetic back muscle strength and lumbar paraspinal muscle quantity and quality evaluated using lumbar spine magnetic resonance imaging. Conventional sarcopenic indices and spine specific outcomes such as spinal sagittal balance, back performance scale, and Sorenson test will also be assessed. The data will be analysed using the intention-to-treat 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: NCT03962530

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study is a prospective cohort study in healthy community-dwelling elderly people, to develop the concept of spinal sarcopenia, by observing the natural aging process of paraspinal muscle and back muscle strength and investigating the association between conventional sarcopenic indices and spinal sarcopenia.
- Standardised data evaluation for sarcopenia and the function of spinal extensor muscles will be used for the analysis with an application of relevant statistical methods.
- Sample size was evaluated based on calculation of feasibility study due to the absence of previous literature concerning isokinetic back muscle strength or lumbar paraspinal muscle quantity.

INTRODUCTION

Sarcopenia is the age-related loss of skeletal muscle mass and function. It is a problem of not only muscle mass, but also muscle strength and performance.[1,2] It can also be defined as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life, and death.[3] The loss of muscle mass plays an important role in the frailty process of elderly people, being a key player of its latent phase and explaining many aspects of the frailty status itself.[4]

Does Sarcopenia affect the spine? It is not difficult to answer the question if we think about the anatomy of the spine. While skeletal bone is the frame, and there are neural tissues inside the spinal canal, almost all surrounding tissues are skeletal muscles. There are huge extensor muscles at the posterior part of the spine and iliopsoas muscles also exist bilaterally around the spine. Thus, it is inevitable for sarcopenia to impact the spine. Receiving renewed attention is sarcopenia of the lumbar paraspinal muscles as a cause of spinal degeneration. Both the atrophy and fatty change of paraspinal muscles originating from sarcopenia on lumbar paraspinal, are also known to be associated with functional disorders and chronic back pain.[5] We want to suggest classifying this phenomenon as “spinal sarcopenia”. However, there are few studies on the precise concept and diagnostic criteria for spinal sarcopenia and no clinical trials to determine whether it can be treated or

prevented by strengthening exercise or nutritional support.

Classical sarcopenia indices proposed by several sarcopenia working groups[6,7] to date cannot be used to diagnose spinal sarcopenia. While feasible, inexpensive, and less radiation-exposed tools such as dual energy X-ray absorptiometry have been used to measure appendicular skeletal muscle mass, paraspinal muscle assessment still requires the use of spinal computed tomography (CT) or magnetic resonance imaging (MRI). In addition, spinal extensor strength measurement is necessary to confirm the function of the lumbar paraspinal muscle, but isokinetic strength measuring equipment for accurate measurement is not as feasible as a dynamometer of hand-grip strength to evaluate sarcopenia. Furthermore, many elderly people may experience pain during the measurement of spinal extension strength.

Therefore, it is necessary to develop a simple, accessible, and clinically meaningful measurement index to confirm the function of spinal extensor muscles. In this prospective cohort study, we will investigate the basic data of sarcopenia and physical function as well as spine imaging (MRI and X-ray), back performance, spinal sagittal balance, and back extensor strength in 120 healthy elderly people. Based on this, we will analyse the correlation between baseline sarcopenia, spinal functional index, spinal sagittal balance index, and physical function. Furthermore, we will observe the natural aging process of these indicators through long-term

follow-up over 4 years.

Objectives

1. To develop the concept of spinal sarcopenia in community-dwelling healthy elderly people.
2. In addition, we aim to observe the natural aging process of paraspinal muscle and back extensor strength and investigate the association between conventional sarcopenic indices and spinal sarcopenia.

METHOD AND ANALYSIS

Study design

This is a prospective observational cohort study with 120 healthy community-dwelling elderly people in a single center (SMG-SNU Boramae Medical Center). Individual follow-up will last 4 years.

Participants and eligibility criteria

Elderly people (≥ 65 years old) who are community-dwellers and able to walk with or

without assistive devices will be included. Participants who have experienced the following will be excluded: 1) low back pain with moderate severity (numeric rating scale 5 and over); 2) history of any types of lumbar spine surgery; 3) history of hip fracture surgery and arthroplasty of hip or knee; 4) contraindications for MRI (such as cardiac pacemaker, implanted metallic objects, and claustrophobia); 5) disorders in central nervous system (such as stroke, parkinsonism, spinal cord injury); 6) cognitive dysfunction (Mini Mental State Examination score < 24); 7) communication disorder (such as severe hearing loss); 8) severe cardiopulmonary disease (such as heart failure with New York Heart Association Class III or IV); 9) uncontrolled chronic disease (such as hypertension with systolic blood pressure >165 and diastolic blood pressure >95); 10) musculoskeletal condition affecting physical function (such as amputation of limb); 11) long-term use of corticosteroids due to inflammatory disease; 12) malignancy requiring treatment within 5 years; and 13) other medical conditions which need active treatment; patients who refuse to participate in a study will also be excluded.

Sarcopenia can be divided by two stages: 1) possible sarcopenia (PS) defined by low handgrip strength and/or low gait speed and 2) sarcopenia (SA) confirmed by low handgrip strength and/or low gait speed and low muscle mass defined by the consensus report of the Asian working group for sarcopenia.[6] A no sarcopenia (NS) group is added to this classification, and the study participants are classified into three groups (NS, PS, and SA) after the screening tests (Figure 1).

Outcomes measures

Primary outcome measures

1. *Isokinetic back muscle strength*

   The investigators will use the isokinetic dynamometer (Biodex multi-joint system, Biodex Corporation, Shirley, NY, USA) to measure the torque of the back extensors. Briefly, the examination will be performed by seating the patient comfortably in the device, fixing both the thighs and the back to the chair using a strap, and asking the patient to hold the handle placed near the front, at the chest, to measure upper limb and hip joint motions. The dynamometer axis will be located on the anterior superior iliac spine of the patient's pelvis. All patients will be instructed to flex and extend the back five times at an angular velocity of 60°/sec as a warm-up before the examination. During the examination, patients will be instructed to execute flexion and extension of the back, with a maximum effort, 10 times at an angular velocity of 60°/sec. The device will measure the peak torque (PT) (Nm) and the peak torque per body weight (PT/Bwt) (Nm/kg).[8]

2. *Lumbar paraspinal muscle quantity and quality*

   Lumbar spine MRI will be performed using a 1.5-T scanner (Achieva 1.5 T; Philips Healthcare, Netherlands). Subjects will be placed in the supine position with the lumbar spine in a neutral position and a pillow under their head and knees. The imaging protocol will include sagittal T2-weighted fast spin echo imaging (repetition time, 3,200 ms/echo; echo time, 100 ms; echo-train length, 20; section thickness, 4 mm; and field of view, 300 × 300 mm)

and axial T2-weighted fast spin echo imaging (repetition time, 3,500 ms/echo; echo time, 100 ms; echo-train length, 20; section thickness, 4 mm; and field of view, 200 × 200 mm). Axial images will be obtained for each lumbar intervertebral level (T12/L1-L5/S1) parallel to the vertebral endplates with five slices at each intervertebral level.

The measurement of the cross sectional area (CSA) and fatty infiltration ratio (FI %) of the paraspinal muscles (erector spinae [ES], multifidus [MF], and psoas major [PM]) will be performed with axial T2-weighted images using a radiological workstation (MEDIP; Medical IP, Seoul, South Korea) specially designed for such purposes. The measurement of ES and MF will be performed from the level of L1/L2 to L5/S1 and that of PM will be performed at the level of L4/5. The CSA will be measured by manually constructing free-draw points around the outer margins of the individual muscles using touch screen LCD monitor (XPS 15 9570, Dell, Round Rock, TX, USA) and digital touch screen pen (PN556W Dell Active Pen, Dell, Round Rock, TX, USA). The FI % is defined as the percentage of fatty infiltration area, which is obtained by dividing the fatty infiltration area by the total area. The CSA and FI % of paraspinal muscles will be separately measured on the bilateral sides, and mean values will be calculated.[9]

Secondary outcome measures

1. *Conventional sarcopenic indices*

   A. Appendicular skeletal muscle mass (ASM): Both dual-energy X-ray

absorptiometry (Lunar iDXA for Bone Health; GE Healthcare, Schenectady, NY, USA) and bio-impedance analysis (InBody 720; Biospace, Seoul, South Korea) will be used to analyse body composition including lean body and fat masses. ASM will be calculated by obtaining the sum of the lean mass in bilateral upper and lower extremities[10] and standardized by being divided by the squared height value (ASM/Ht^2, kg/m^2).

B. Handgrip strength: It will be measured using a hand-grip dynamometer (T.K.K.5401; Takei Scientific Instruments, Tokyo, Japan) [11], as described previously [12]. Briefly, while sitting in a straight-backed chair with their feet flat on the floor, patients will be asked to adduct and neutrally rotate the shoulder, flex the elbow to 90°, and place the forearm in a neutral position, with the wrist between 0° and 30° extension and between 0° and 15° ulnar deviation. Subjects will be instructed to squeeze the handle as hard as possible for 3 seconds, and the maximum contraction force (Kg) will be recorded.

C. Short physical performance battery (SPPB): Functional examination using SPPB derived from three objective physical function tests (i.e., the time taken to cover 4 m at a comfortable walking speed, time taken to stand from sitting in a chair 5 times without stopping, and ability to maintain balance for 10 s in three different foot positions at progressively more challenging levels).[13] A score from 0 to 4 will be assigned to performance on each task, with higher scores indicating better lower

body function.

2. *Spine specific outcomes*

A. Isometric back muscle strength: Similarly, with the isokinetic back muscle strength test, we will perform the isometric back muscle strength test using a handheld dynamometer (PowerTrack II; JTECH Medical, Salt Lake City, UT, USA). This will involve the participant standing in full extension with their back to a wall, midway between two vertically oriented anchor rails, and feet flat on the floor with heels touching the wall. An inelastic belt will be looped through the anchor rails, and secured firmly around the participant, 1 cm below the anterior superior iliac spines, in order to restrain movement and maintain participant contact with the wall during the test. To standardise posture, arms will be crossed over the chest, with fingertips level with the contralateral shoulders. The participant will be instructed to flex forward approximately 15° at the hips so the handheld dynamometer can be positioned posterior to the spinous process of the seventh thoracic vertebrae. In this way, counter pressure will be provided by the fixed wall behind the participants' back so that variations in resistance by an examiner will be avoided.[14]

B. Spinal sagittal balance (SSB): For each participant, one lateral radiograph of the whole spine will be made and digitized. All measurements will be performed by means of imaging software (INFINITT PACS M6; INFINITT Healthcare, Seoul, South Korea), as previously described.[15,16] Briefly, the following spinopelvic radiographic

parameters will be analysed: sacral slope (SS), pelvic incidence (PI), pelvic tilt (PT), lumbar lordosis (LL), thoracic kyphosis (TK), the ratio of LL to PI (LL/PI), PI-LL mismatch (PI-LL; the difference between the pelvic incidence and lumbar lordosis), and sagittal vertical axis (SVA). PI-LL will be used as the primary outcomes of SSB.[17]

C. Back performance scale (BPS): BPS consists of five tests: Sock Test, the Pick-up Test, the Roll-up Test, the Fingertip-to-Floor Test, and the Lift Test. The 5 tests comprising the BPS demonstrate associations with each other, and each test contributes to high internal consistency, implying that the tests share a common characteristic in measuring physical performance.[18] The BPS sum score (0-15) is calculated by adding the individual scores of the 5 tests.

D. Sorensen test: It is the most widely used test in published studies evaluating the isometric endurance of the trunk extensor muscles. The test consists of measuring the amount of time a person can hold the unsupported upper body in a horizontal prone position with the lower body fixed to the examining table.[19]

3. Other functional outcomes

A. Berg balance scale (BBS): Balance and fall risk will be assessed using BBS (range: 0–56; a lower score indicates a worse outcome).[20]

B. Quality of life (QOL): It will be evaluated using the Euro Quality of Life Questionnaire five-dimensional classification (EQ-5D; range: 0–1; a lower score indicates a worse outcome).[21]

C. Activities of daily living (ADLs): ADLs will be determined using the Korean version of the modified Barthel index[22] (K-MBI; range: 0–100; a lower score indicates a worse outcome) and the Korean version of the Instrumental ADL (K-IADL; range: 0–3; a higher score indicates a worse outcome). [23]

D. Frailty: It will be assessed based on fatigue, resistance, ambulation, illnesses, and loss of weight (FRAIL) using the Korean version of the FRAIL scale (K-FRAIL; range: 0–5; a lower score indicates a worse outcome). [24]

4. Serum examination

A. Serum chemistry, complete blood counts (CBC), blood urea nitrogen and creatinine will be obtained.

B. Interleukin-6 (IL-6) level will be quantified by Green-Cross laboratory (GC lab, Seoul, Korea) using standard procedures.

All outcome variables will be collected at baseline, 2 and 4 years. However, L-S spine MRI for lumbar paraspinal muscle quantity and quality will be performed only at baseline (Table 1).

Table 1. Overview of the outcome measures and time points of assessment

	Screening	Baseline	2 years	4 years
Eligibility	X			
Eligibility confirmation		X		
Informed consent		X		
Demographic information		X		
Medical History		X	X	X
Body composition (image study)				
Wholebody DEXA and BIA	BIA	DEXA	X	X
Whole spine X-ray (lateral)		X	X	X
L-S spine MRI		X		
Function and performance				
Handgrip strength	X	X	X	X
Gait function	X	X	X	X
SPPB		X	X	X
Physical activity		X	X	X
Balance function		X	X	X
Spine performance				
Isokinetic back muscle strength		X	X	X
Isometric back muscle strength		X	X	X
Sorenson test		X	X	X
Back performance scale		X	X	X
Others				
Fear for fall		X	X	X
Nutritional status		X	X	X
Frailty		X	X	X
QoL questionnaire		X	X	X
Activity daily living		X	X	X
Laboratory test with biomarker		X	X	X

DEXA, Dual-energy X-ray absorptiometry; BIA, Bio-impedance analysis; MRI, Magnetic resonance imaging; SPPB, Short Physical Performance Battery, QoL, Quality of life.

Data analysis

Data will be collected using a standardised data entry form and entered into the data management system. The intention-to-treat principle will be used for data analysis. Participant characteristics will be described using means and standard deviations for continuous data and frequencies and percentages for categorical data. The three groups will be compared using an analysis of variance (ANOVA) or the non-parametric equivalence, a Kruskal–Wallis test, if required. To compare paired data (intra-group) between two different points, we will use repeated-measures ANOVA and Friedman tests for continuous and non-parametric data, respectively. Statistical significance will be defined as a P value < 0.05. All statistical analyses will be performed using SPSS version 19.0 for Windows (IBM Corp., Chicago, IL, USA).

Sample size

We intended to perform the sample size calculation based on the difference in mean of isokinetic back muscle strength or lumbar paraspinal muscle quantity among groups. However, there was no literature available concerning isokinetic back muscle strength or lumbar paraspinal muscle quantity in general practices or hospitals, let alone effect sizes. Therefore, we based our sample size calculation on feasibility. A total of 120 subjects will be recruited in order to ensure 20 male and 20 female participants per group, in three groups (NS, PS, and SA groups) based on sarcopenia.

Patient and public involvement

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

ETHICS AND DISSEMINATION

This protocol is approved by the institutional review board of Seoul Metropolitan Government Seoul National University (SMG-SNU) Boramae Medical Center (IRB No. 20-2019-19). 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.[25] Written informed consent for all interventions and examinations will be obtained at patient admission. 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. The study methods are in accordance with the SPIRIT guidelines for reporting randomised trials.[26] 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

Skeletal muscle mass measurement to define sarcopenia has mainly been based on the sum of muscle mass in the limbs (appendicular limb muscle mass). However the question remains whether this sum of limb muscle mass is associated with muscle function throughout the whole body. Lee et al. reported that degenerative arthritis of the knee joint was associated with only lower limb muscle mass, but not with upper limb muscle mass.[27] Recently, Jeon et al. also suggested that the sum of limb muscle mass was not correlated with the radiological degenerative changes of the lumbar spine and hip joint.[28] Therefore, site-specific muscle mass investigation is necessary to evaluate the effect of skeletal muscle on specific regions.

Currently, SSB is an important indicator of outcomes of lumbar spine surgery,[29] and even non-operative treatment of spinal stenosis.[30] While SSB can be affected by sex[31] and ethnicity,[32] aging is the most important cause of spinal sagittal imbalance.[33] Decreased lumbar lordosis is an important cause of spinal sagittal imbalance, and it is known to originate from the wedging or decreased height of the intervertebral discs in the absence of vertebral compression fractures.[34,35] However, spinal sagittal imbalance is difficult to explain only by the height of the intervertebral discs or vertebral bodies. Therefore, we can hypothesize that spinal sarcopenia is

one of the causes of spinal sagittal imbalance which the current cohort study will prove.

Several specific assessments such as cross-sectional area of paraspinal muscles, back muscle strength, and back performance test are required to evaluate spinal sarcopenia. However, unlike limb skeletal muscles, the functional evaluation of the spine corresponding to the center of the body is not practical. Thus, this cohort study will investigate the value of SSB as a substitute for back muscle strength and performance measurement. In other words, if back muscle strength and functional impairment are directly related to the spinal sagittal imbalance, a simple measurable SSB may be a useful index to represent spinal muscle function.

Authors' contributions

SYL conceived the study and is the principal investigator. JCK, SUL, SHJ, JYL, and DHL contributed to the development of the study. All authors approved the version to be published and are responsible for its accuracy.

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Competing interests

None declared

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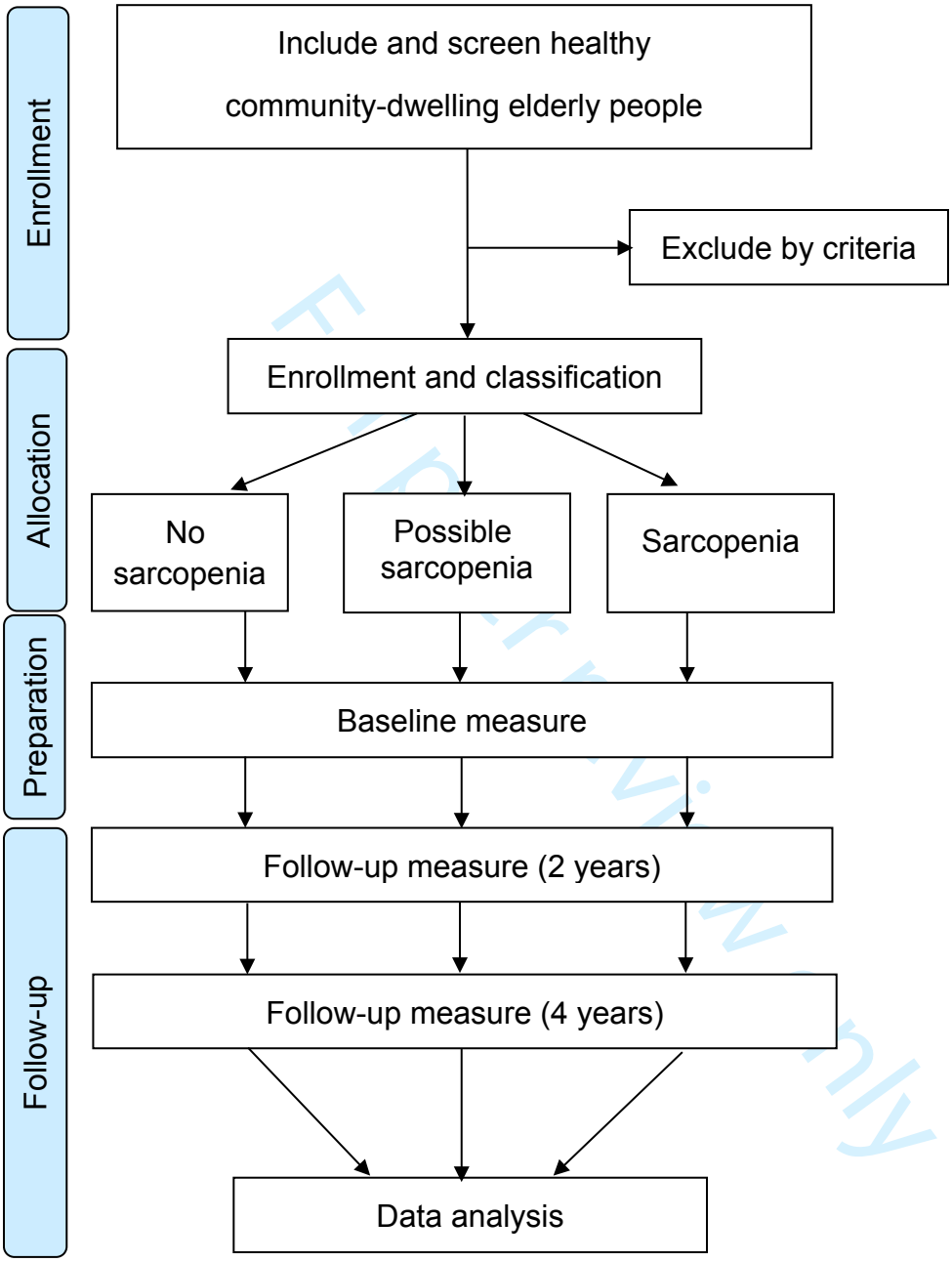
FIGURE LEGEND

Figure 1. Flow diagram of the cohort study

Figure 1.



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Natural Aging Course of Paraspinal Muscle and Back Extensor Strength in Community-dwelling Older Adults (Sarcopenia of Spine, SarcoSpine): A Prospective Cohort Study Protocol

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ABSTRACT

Introduction: Sarcopenia in the lumbar paraspinal muscles is receiving renewed attention as a cause of spinal degeneration. However, there are few studies on the precise concept and diagnostic criteria for spinal sarcopenia. Here, we develop the concept of spinal sarcopenia in community-dwelling older adults. In addition, we aim to observe the natural aging process of paraspinal and back muscle strength and investigate the association between conventional sarcopenic indices and spinal sarcopenia.

Methods and analysis: This is a prospective observational cohort study with 120 healthy community-dwelling older adults over 4 years. All subjects will be recruited in no sarcopenia, possible sarcopenia, or sarcopenia groups. The primary outcomes of this study are isokinetic back muscle strength and lumbar paraspinal muscle quantity and quality evaluated using lumbar spine magnetic resonance imaging. Conventional sarcopenic indices and spine specific outcomes such as spinal sagittal balance, back performance scale, and Sorenson test will also be assessed.

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: NCT03962530

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study is a prospective cohort study in healthy community-dwelling older adults, to develop the concept of spinal sarcopenia, by observing the natural aging process of paraspinal muscle and back muscle strength and investigating the association between conventional sarcopenic indices and spinal sarcopenia.
- Standardised data evaluation for sarcopenia and the function of spinal extensor muscles will be used for the analysis with an application of relevant statistical methods.
- Sample size was evaluated based on calculation of feasibility study due to the absence of previous literature concerning isokinetic back muscle strength or lumbar paraspinal muscle quantity.

INTRODUCTION

Sarcopenia is the age-related loss of skeletal muscle mass and function. It is a problem of not only muscle mass, but also muscle strength and performance.[1,2] It can also be defined as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life, and death.[3] The loss of muscle mass plays an important role in the frailty process of older adults, being a key player of its latent phase and explaining many aspects of the frailty status itself.[4]

Does Sarcopenia affect the spine? It is not difficult to answer the question if we think about the anatomy of the spine. While skeletal bone is the frame, and there are neural tissues inside the spinal canal, almost all surrounding tissues are skeletal muscles. There are huge extensor muscles at the posterior part of the spine and iliopsoas muscles also exist bilaterally around the spine. Thus, it is inevitable for sarcopenia to impact the spine. Receiving renewed attention is sarcopenia of the lumbar paraspinal muscles as a cause of spinal degeneration. Both the atrophy and fatty change of paraspinal muscles originating from sarcopenia are also known to be associated with functional disorders and chronic back pain.[5] We want to suggest classifying this phenomenon as “spinal sarcopenia”. However, there are few studies on the precise concept and diagnostic criteria for spinal sarcopenia and no clinical trials to determine whether it can be treated or prevented by strengthening exercise

or nutritional support.

Classical sarcopenia indices proposed by several sarcopenia working groups[6,7] to date cannot be used to diagnose spinal sarcopenia. While feasible, inexpensive, and less radiation-exposed tools such as dual energy X-ray absorptiometry have been used to measure appendicular skeletal muscle mass, paraspinal muscle assessment still requires the use of spinal computed tomography (CT) or magnetic resonance imaging (MRI). In addition, spinal extensor strength measurement is necessary to confirm the function of the lumbar paraspinal muscle, but isokinetic strength measuring equipment for accurate measurement is not as feasible as a hand-grip strength dynamometer to evaluate sarcopenia. Furthermore, many older adults may experience pain during the measurement of spinal extension strength.

Therefore, it is necessary to develop a simple, accessible, and clinically meaningful measurement index to confirm the function of spinal extensor muscles. In this prospective cohort study, we will investigate the basic data of sarcopenia and physical function as well as spine imaging (MRI and X-ray), back performance, spinal sagittal balance, and back extensor strength in 120 healthy older adults. Based on this, we will analyse the correlation between baseline sarcopenia, spinal functional index, spinal sagittal balance index, and physical function. Furthermore, we will observe the natural aging process of these indicators through long-term follow-up over 4 years.

Objectives

1. To develop the concept of spinal sarcopenia in community-dwelling older adults.
2. In addition, we aim to observe the natural aging process of paraspinal muscle and back extensor strength and investigate the association between conventional sarcopenic indices and spinal sarcopenia.

METHOD AND ANALYSIS

Study design

This is a prospective observational cohort study with 120 healthy community-dwelling older adults in a single center (SMG-SNU Boramae Medical Center). Individual follow-up will last 4 years.

Participants and eligibility criteria

Older adults (≥ 65 years old) who are community-dwellers and able to walk with or without assistive devices will be included. Participants who have experienced the

following will be excluded: 1) low back pain with moderate severity (numeric rating scale[8] 5 and over); 2) history of any types of lumbar spine surgery; 3) history of hip fracture surgery and arthroplasty of hip or knee; 4) contraindications for MRI (such as cardiac pacemaker, implanted metallic objects, and claustrophobia); 5) disorders in central nervous system (such as stroke, parkinsonism, spinal cord injury); 6) cognitive dysfunction (Mini Mental State Examination score < 24); 7) communication disorder (such as severe hearing loss); 8) musculoskeletal condition affecting physical function (such as amputation of limb); 9) long-term use of corticosteroids due to inflammatory disease; 10) malignancy requiring treatment within 5 years; and 11) other medical conditions which need active treatment; patients who refuse to participate in a study will also be excluded.

Sarcopenia can be divided by two stages: 1) possible sarcopenia (PS) defined by low handgrip strength and/or low gait speed and 2) sarcopenia (SA) confirmed by low handgrip strength and/or low gait speed and low muscle mass defined by the consensus report of the Asian working group for sarcopenia.[6] A no sarcopenia (NS) group is added to this classification, and the study participants are classified into three groups (NS, PS, and SA) after the screening tests (Figure 1).

Outcomes measures

Primary outcome measures

1. *Isokinetic back muscle strength*

   The investigators will use the isokinetic dynamometer (Biodex multi-joint

system, Biodex Corporation, Shirley, NY, USA) to measure the torque of the back extensors. Briefly, the examination will be performed by seating the patient comfortably in the device, fixing both the thighs and the back to the chair using a strap, and asking the patient to hold the handle placed near the front, at the chest, to measure upper limb and hip joint motions. The dynamometer axis will be located on the anterior superior iliac spine of the patient's pelvis. All patients will be instructed to flex and extend the back five times at an angular velocity of 60°/sec as a warm-up before the examination. During the examination, patients will be instructed to execute flexion and extension of the back, with a maximum effort, 10 times at an angular velocity of 60°/sec. The back range of movement was 22 limited at 50°, with 30° (−30°) of trunk flexion and 20° (+20°) of trunk extension, relative to the anatomical reference position (0°).[9] The device will measure the peak torque (PT) (Nm) and the peak torque per body weight (PT/Bwt) (Nm/kg).[10]

2. *Lumbar paraspinal muscle quantity and quality*

Lumbar spine MRI will be performed using a 1.5-T scanner (Achieva 1.5 T; Philips Healthcare, Netherlands). Subjects will be placed in the supine position with the lumbar spine in a neutral position and a pillow under their head and knees. The imaging protocol will include sagittal T2-weighted fast spin echo imaging (repetition time, 3,200 ms/echo; echo time, 100 ms; echo-train length, 20; section thickness, 4 mm; and field of view, 300 × 300 mm) and axial T2-weighted fast spin echo imaging (repetition time, 3,500 ms/echo; echo time, 100 ms; echo-train length, 20; section thickness, 4 mm; and field

of view, 200 × 200 mm). Axial images will be obtained for each lumbar intervertebral level (T12/L1-L5/S1) parallel to the vertebral endplates with five slices at each intervertebral level.

The measurement of the cross sectional area (CSA) and fatty infiltration ratio (FI %) of the paraspinal muscles (erector spinae [ES], multifidus [MF], and psoas major [PM]) will be performed with axial T2-weighted images using a radiological workstation (MEDIP; Medical IP, Seoul, South Korea) specially designed for such purposes. The measurement of ES and MF will be performed from the level of L1/L2 to L5/S1 and that of PM will be performed at the level of L4/5. The CSA will be measured by manually constructing free-draw points around the outer margins of the individual muscles using touch screen LCD monitor (XPS 15 9570, Dell, Round Rock, TX, USA) and digital touch screen pen (PN556W Dell Active Pen, Dell, Round Rock, TX, USA). The FI % is defined as the percentage of fatty infiltration area, which is obtained by dividing the fatty infiltration area by the total area. The CSA and FI % of paraspinal muscles will be separately measured on the bilateral sides, and mean values will be calculated.[11]

Secondary outcome measures

1. *Conventional sarcopenic indices*

   A. Appendicular skeletal muscle mass (ASM): Both dual-energy X-ray absorptiometry (Lunar iDXA for Bone Health; GE Healthcare, Schenectady, NY, USA) and bio-impedance analysis (InBody 720;

Biospace, Seoul, South Korea) will be used to analyse body composition including lean body and fat masses. ASM will be calculated by obtaining the sum of the lean mass in bilateral upper and lower extremities[12] and standardized by being divided by the squared height value (ASM/Ht^2, kg/m^2).

B. Handgrip strength: It will be measured using a hand-grip dynamometer (T.K.K.5401; Takei Scientific Instruments, Tokyo, Japan) [13], as described previously [14]. Briefly, while sitting in a straight-backed chair with their feet flat on the floor, patients will be asked to adduct and neutrally rotate the shoulder, flex the elbow to 90°, and place the forearm in a neutral position, with the wrist between 0° and 30° extension and between 0° and 15° ulnar deviation. Subjects will be instructed to squeeze the handle as hard as possible for 3 seconds, and the maximum contraction force (Kg) will be recorded.

C. Short physical performance battery (SPPB): Functional examination using SPPB derived from three objective physical function tests (i.e., the time taken to cover 4 m at a comfortable walking speed, time taken to stand from sitting in a chair 5 times without stopping, and ability to maintain balance for 10 s in three different foot positions at progressively more challenging levels).[15] A score from 0 to 4 will be assigned to performance on each task, with higher scores indicating better lower body function.

2. *Spine specific outcomes*

A. Isometric back muscle strength: In addition to the isokinetic back muscle strength test, we will perform the isometric back muscle strength test using a handheld dynamometer (PowerTrack II; JTECH Medical, Salt Lake City, UT, USA). This will involve the participant standing in full extension with their back to a wall, midway between two vertically oriented anchor rails, and feet flat on the floor with heels touching the wall. An inelastic belt will be looped through the anchor rails, and secured firmly around the participant, 1 cm below the anterior superior iliac spines, in order to restrain movement and maintain participant contact with the wall during the test. To standardise posture, arms will be crossed over the chest, with fingertips level with the contralateral shoulders. The participant will be instructed to flex forward approximately 15° at the hips so the handheld dynamometer can be positioned posterior to the spinous process of the seventh thoracic vertebrae. In this way, counter pressure will be provided by the fixed wall behind the participants' back so that variations in resistance by an examiner will be avoided.[16]

B. Spinal sagittal balance (SSB): For each participant, one lateral radiograph of the whole spine will be made and digitized. All measurements will be performed by means of imaging software (INFINITT PACS M6; INFINITT Healthcare, Seoul, South Korea), as previously described.[17,18] Briefly, the following spinopelvic radiographic parameters will be analysed: sacral slope (SS), pelvic incidence (PI), pelvic tilt (PT), lumbar lordosis (LL), thoracic kyphosis (TK), the ratio of LL

to PI (LL/PI), PI-LL mismatch (PI-LL; the difference between the pelvic incidence and lumbar lordosis), and sagittal vertical axis (SVA). PI-LL will be used as the primary outcomes of SSB.[19]

C. Back performance scale (BPS): BPS consists of five tests: Sock Test, the Pick-up Test, the Roll-up Test, the Fingertip-to-Floor Test, and the Lift Test. The 5 tests comprising the BPS demonstrate associations with each other, and each test contributes to high internal consistency, implying that the tests share a common characteristic in measuring physical performance.[20] The BPS sum score (0-15) is calculated by adding the individual scores of the 5 tests.

D. Sorensen test: It is the most widely used test in published studies evaluating the isometric endurance of the trunk extensor muscles. The test consists of measuring the amount of time a person can hold the unsupported upper body in a horizontal prone position with the lower body fixed to the examining table.[21]

3. Other functional outcomes

A. Berg balance scale (BBS): Balance and fall risk will be assessed using BBS (range: 0–56; a lower score indicates a worse outcome).[22]

B. Quality of life (QOL): It will be evaluated using the Euro Quality of Life Questionnaire five-dimensional classification (EQ-5D; range: 0–1; a lower score indicates a worse outcome).[23]

C. Activities of daily living (ADLs): ADLs will be determined using the Korean version of the modified Barthel index[24] (K-MBI; range: 0–100; a lower

score indicates a worse outcome) and the Korean version of the Instrumental ADL (K-IADL; range: 0–3; a higher score indicates a worse outcome). [25]

D. Frailty: It will be assessed based on fatigue, resistance, ambulation, illnesses, and loss of weight (FRAIL) using the Korean version of the FRAIL scale (K-FRAIL; range: 0–5; a lower score indicates a worse outcome). [26]

4. Serum examination

A. Serum chemistry, complete blood counts (CBC), blood urea nitrogen and creatinine will be obtained.

B. Interleukin-6 (IL-6) level will be quantified by Green-Cross laboratory (GC lab, Seoul, Korea) using standard procedures.

All outcome variables will be collected at baseline, 2 and 4 years. However, L-S spine MRI for lumbar paraspinal muscle quantity and quality will be performed only at baseline (Table 1).

Table 1. Overview of the outcome measures and time points of assessment

	Screening	Baseline	2 years	4 years
Eligibility	X			
Eligibility confirmation		X		
Informed consent		X		
Demographic information		X		
Medical History		X	X	X
Body composition (image study)				
Wholebody DEXA and BIA	BIA	DEXA	X	X
Whole spine X-ray (lateral)		X	X	X
L-S spine MRI		X		
Function and performance				
Handgrip strength	X	X	X	X
Gait function	X	X	X	X
SPPB		X	X	X
Physical activity		X	X	X
Balance function		X	X	X
Spine performance				
Isokinetic back muscle strength		X	X	X
Isometric back muscle strength		X	X	X
Sorenson test		X	X	X
Back performance scale		X	X	X
Others				
Frailty		X	X	X
QoL questionnaire		X	X	X
Activity daily living		X	X	X
Laboratory test with biomarker		X	X	X

DEXA, Dual-energy X-ray absorptiometry; BIA, Bio-impedance analysis; MRI, Magnetic resonance imaging; SPPB, Short Physical Performance Battery, QoL,

Quality of life.

Data analysis

Data will be collected using a standardised data entry form and entered into the data management system. Participant characteristics will be described using means and standard deviations for continuous data and frequencies and percentages for categorical data. The three groups will be compared using an analysis of variance (ANOVA) or the non-parametric equivalence, a Kruskal–Wallis test, if required. To compare paired data (intra-group) between two different points, we will use repeated-measures ANOVA and Friedman tests for continuous and non-parametric data, respectively. Statistical significance will be defined as a P value < 0.05. All statistical analyses will be performed using SPSS version 19.0 for Windows (IBM Corp., Chicago, IL, USA).

Sample size

We intended to perform the sample size calculation based on the difference in mean of isokinetic back muscle strength or lumbar paraspinal muscle quantity among groups. However, there was no literature available concerning isokinetic back muscle strength or lumbar paraspinal muscle quantity in general practices or hospitals, let alone effect sizes. Therefore, we based our sample size calculation on feasibility. A total of 120 subjects will be recruited in order to ensure 20 male and 20 female participants per group, in three groups (NS, PS, and SA groups) based on sarcopenia.

Patient and public involvement

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

ETHICS AND DISSEMINATION

This protocol is approved by the institutional review board of Seoul Metropolitan Government Seoul National University (SMG-SNU) Boramae Medical Center (IRB No. 20-2019-19). 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.[27] Written informed consent for all interventions and examinations will be obtained at patient admission. 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

Skeletal muscle mass measurement to define sarcopenia has mainly been based on the sum of muscle mass in the limbs (appendicular limb muscle mass). However the question remains whether this sum of limb muscle mass is associated with muscle function throughout the whole body. Lee et al. reported that degenerative arthritis of the knee joint was associated with only lower limb muscle mass, but not with upper limb muscle mass.[28] Recently, Jeon et al. also suggested that the sum of limb muscle mass was not correlated with the radiological degenerative changes of the lumbar spine and hip joint.[29] Therefore, site-specific muscle mass investigation is necessary to evaluate the effect of skeletal muscle on specific regions.

Currently, SSB is an important indicator of outcomes of lumbar spine surgery,[30] and even non-operative treatment of spinal stenosis.[31] While SSB can be affected by sex[32] and ethnicity,[33] aging is the most important cause of spinal sagittal imbalance.[34] Decreased lumbar lordosis is an important cause of spinal sagittal imbalance, and it is known to originate from the wedging or decreased height of the intervertebral discs in the absence of vertebral compression fractures.[35,36] However, spinal sagittal imbalance is difficult to explain only by the height of the intervertebral discs or vertebral bodies. Therefore, we can hypothesize that spinal sarcopenia is one of the causes of spinal sagittal imbalance which the current cohort study will prove.

Several specific assessments such as cross-sectional area of paraspinal muscles, back muscle strength, and back performance test are required to evaluate spinal sarcopenia. However, unlike limb skeletal muscles, the functional evaluation of the spine corresponding to the center of the body is not practical. Thus, this cohort study will investigate the value of SSB as a substitute for back muscle strength and performance measurement. In other words, if back muscle strength and functional impairment are directly related to the spinal sagittal imbalance, a simple measurable SSB may be a useful index to represent spinal muscle function.

Authors' contributions

SYL conceived the study and is the principal investigator. JCK, SUL, SHJ, JYL, and DHK contributed to the development of the study. All authors approved the version to be published and are responsible for its accuracy.

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Competing interests

None declared

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FIGURE LEGEND

Figure 1. Flow diagram of the cohort study

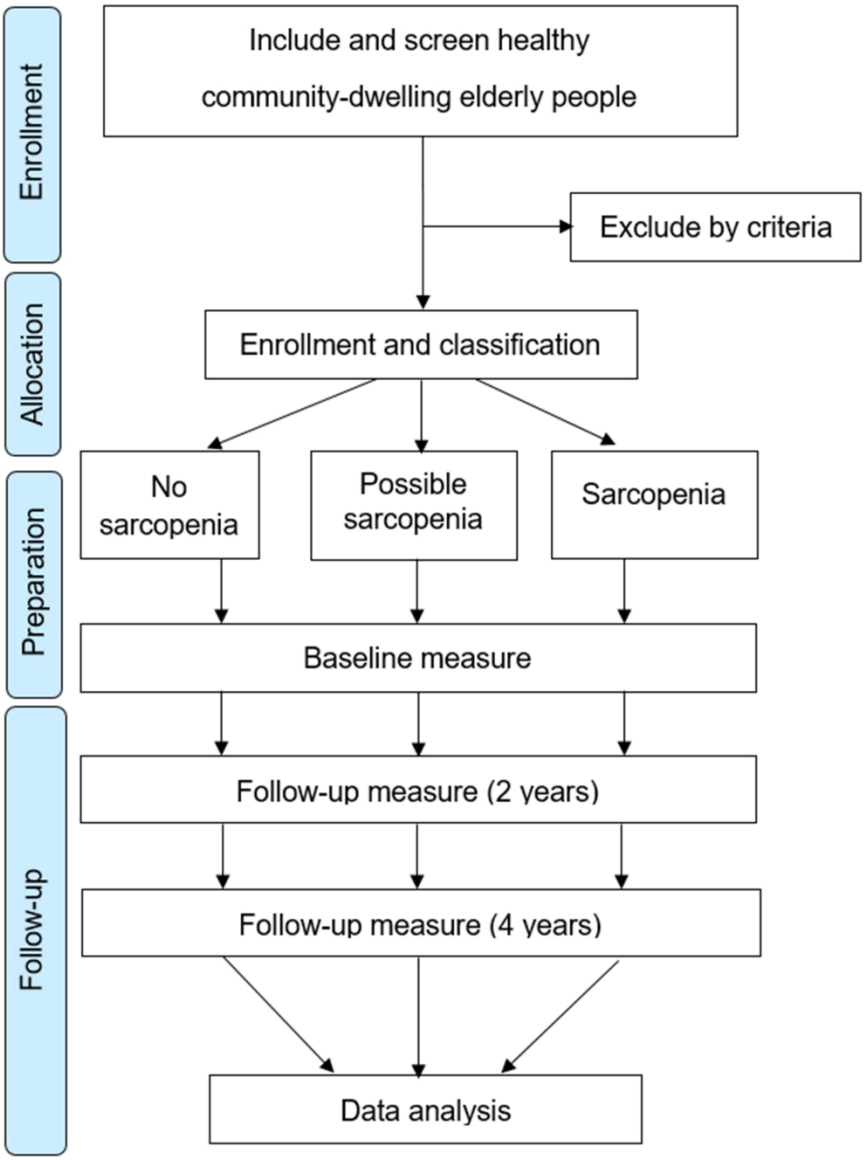

Figure 1. Flow diagram of the cohort study

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