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

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Manuscripts

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

2 Protocol

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23 **ABSTRACT**

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

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

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

43 **Trial registration number:** NCT03962530

44 STRENGTHS AND LIMITATIONS OF THIS STUDY

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

57 INTRODUCTION

58
59 Sarcopenia is the age-related loss of skeletal muscle mass and function. It is a
60 problem of not only muscle mass, but also muscle strength and performance.^{1,2} It
61 can also be defined as a syndrome characterized by progressive and generalized
62 loss of skeletal muscle mass and strength with a risk of adverse outcomes such as
63 physical disability, poor quality of life, and death.³ The loss of muscle mass plays an
64 important role in the frailty process of elderly people, being a key player of its latent
65 phase and explaining many aspects of the frailty status itself.⁴

66
67 Does Sarcopenia affect the spine? It is not difficult to answer the question if we think
68 about the anatomy of the spine. While skeletal bone is the frame, and there are
69 neural tissues inside the spinal canal, almost all surrounding tissues are skeletal
70 muscles. There are huge extensor muscles at the posterior part of the spine and
71 iliopsoas muscles also exist bilaterally around the spine. Thus, it is inevitable for
72 sarcopenia to impact the spine. Receiving renewed attention is sarcopenia of the
73 lumbar paraspinal muscles as a cause of spinal degeneration. Both the atrophy and
74 fatty change of paraspinal muscles originating from sarcopenia on lumbar
75 paraspinal, are also known to be associated with functional disorders and chronic
76 back pain.⁵ We want to suggest classifying this phenomenon as “spinal sarcopenia”.
77 However, there are few studies on the precise concept and diagnostic criteria for
78 spinal sarcopenia and no clinical trials to determine whether it can be treated or

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4 79 prevented by strengthening exercise or nutritional support.
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10 81 Classical sarcopenia indices proposed by several sarcopenia working groups^{6,7} to
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12 82 date cannot be used to diagnose spinal sarcopenia. While feasible, inexpensive, and
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14 83 less radiation-exposed tools such as dual energy X-ray absorptiometry have been
15
16 84 used to measure appendicular skeletal muscle mass, paraspinal muscle assessment
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18 85 still requires the use of spinal computed tomography (CT) or magnetic resonance
19
20 86 imaging (MRI). In addition, spinal extensor strength measurement is necessary to
21
22 87 confirm the function of the lumbar paraspinal muscle, but isokinetic strength
23
24 88 measuring equipment for accurate measurement is not as feasible as a
25
26 89 dynamometer of hand-grip strength to evaluate sarcopenia. Furthermore, many
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28 90 elderly people may experience pain during the measurement of spinal extension
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30 91 strength.
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41 93 Therefore, it is necessary to develop a simple, accessible, and clinically meaningful
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43 94 measurement index to confirm the function of spinal extensor muscles. In this
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45 95 prospective cohort study, we will investigate the basic data of sarcopenia and
46
47 96 physical function as well as spine imaging (MRI and X-ray), back performance,
48
49 97 spinal sagittal balance, and back extensor strength in 120 healthy elderly people.
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51 98 Based on this, we will analyse the correlation between baseline sarcopenia, spinal
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53 99 functional index, spinal sagittal balance index, and physical function. Furthermore,
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55 100 we will observe the natural aging process of these indicators through long-term
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4 101 follow-up over 4 years.
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10 103 **Objectives**

- 13 104 1. To develop the concept of spinal sarcopenia in community-dwelling healthy
15 105 elderly people.
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18 106 2. In addition, we aim to observe the natural aging process of paraspinal muscle
20 107 and back extensor strength and investigate the association between
22 108 conventional sarcopenic indices and spinal sarcopenia.
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33 111 **METHOD AND ANALYSIS**

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39 113 **Study design**

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42 114 This is a prospective observational cohort study with 120 healthy community-
44 115 dwelling elderly people in a single center (SMG-SNU Boramae Medical Center).
46 116 Individual follow-up will last 4 years.
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53 118 **Participants and eligibility criteria**

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56 119 Elderly people (≥ 65 years old) who are community-dwellers and able to walk with or
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4 120 without assistive devices will be included. Participants who have experienced the
5
6 121 following will be excluded: 1) low back pain with moderate severity (numeric rating
7
8 122 scale 5 and over); 2) history of any types of lumbar spine surgery; 3) history of hip
9
10 123 fracture surgery and arthroplasty of hip or knee; 4) contraindications for MRI (such
11
12 124 as cardiac pacemaker, implanted metallic objects, and claustrophobia); 5) disorders
13
14 125 in central nervous system (such as stroke, parkinsonism, spinal cord injury); 6)
15
16 126 cognitive dysfunction (Mini Mental State Examination score < 24); 7) communication
17
18 127 disorder (such as severe hearing loss); 8) severe cardiopulmonary disease (such as
19
20 128 heart failure with New York Heart Association Class III or IV); 9) uncontrolled chronic
21
22 129 disease (such as hypertension with systolic blood pressure >165 and diastolic blood
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24 130 pressure >95); 10) musculoskeletal condition affecting physical function (such as
25
26 131 amputation of limb); 11) long-term use of corticosteroids due to inflammatory
27
28 132 disease; 12) malignancy requiring treatment within 5 years; and 13) other medical
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30 133 conditions which need active treatment; patients who refuse to participate in a study
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32 134 will also be excluded.
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39 135 Sarcopenia can be divided by two stages: 1) possible sarcopenia (PS) defined by
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41 136 low handgrip strength and/or low gait speed and 2) sarcopenia (SA) confirmed by
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43 137 low handgrip strength and/or low gait speed and low muscle mass defined by the
44
45 138 consensus report of the Asian working group for sarcopenia.⁶ A no sarcopenia (NS)
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47 139 group is added to this classification, and the study participants are classified into
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49 140 three groups (NS, PS, and SA) after the screening tests (Figure 1).
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142 **Outcomes measures**

143 Primary outcome measures

144 *1. Isokinetic back muscle strength*

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

158 *2. Lumbar paraspinal muscle quantity and quality*

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

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4 165 and axial T2-weighted fast spin echo imaging (repetition time, 3,500 ms/echo;
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6 166 echo time, 100 ms; echo-train length, 20; section thickness, 4 mm; and field
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9 167 of view, 200 × 200 mm). Axial images will be obtained for each lumbar
10
11 168 intervertebral level (T12/L1-L5/S1) parallel to the vertebral endplates with five
12
13 169 slices at each intervertebral level.

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15 170 The measurement of the cross sectional area (CSA) and fatty infiltration ratio
16
17 171 (FI %) of the paraspinal muscles (erector spinae [ES], multifidus [MF], and
18
19 172 psoas major [PM]) will be performed with axial T2-weighted images using a
20
21 173 radiological workstation (MEDIP; Medical IP, Seoul, South Korea) specially
22
23 174 designed for such purposes. The measurement of ES and MF will be
24
25 175 performed from the level of L1/L2 to L5/S1 and that of PM will be performed
26
27 176 at the level of L4/5. The CSA will be measured by manually constructing free-
28
29 177 draw points around the outer margins of the individual muscles using touch
30
31 178 screen LCD monitor (XPS 15 9570, Dell, Round Rock, TX, USA) and digital
32
33 179 touch screen pen (PN556W Dell Active Pen, Dell, Round Rock, TX, USA).
34
35 180 The FI % is defined as the percentage of fatty infiltration area, which is
36
37 181 obtained by dividing the fatty infiltration area by the total area. The CSA and
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39 182 FI % of paraspinal muscles will be separately measured on the bilateral sides,
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41 183 and mean values will be calculated.⁹

42 43 44 45 46 47 48 49 50 185 Secondary outcome measures

51 52 186 1. *Conventional sarcopenic indices*

53 54 55 187 A. Appendicular skeletal muscle mass (ASM): Both dual-energy X-ray

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4 188 absorptiometry (Lunar iDXA for Bone Health; GE Healthcare,
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6 189 Schenectady, NY, USA) and bio-impedance analysis (InBody 720;
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9 190 Biospace, Seoul, South Korea) will be used to analyse body composition
10
11 191 including lean body and fat masses. ASM will be calculated by obtaining
12
13 192 the sum of the lean mass in bilateral upper and lower extremities¹⁰ and
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15 193 standardized by being divided by the squared height value (ASM/Ht^2 ,
16
17 kg/m^2).
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20 195 B. Handgrip strength: It will be measured using a hand-grip dynamometer
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22 196 (T.K.K.5401; Takei Scientific Instruments, Tokyo, Japan)¹¹, as described
23
24 197 previously¹². Briefly, while sitting in a straight-backed chair with their feet
25
26 198 flat on the floor, patients will be asked to adduct and neutrally rotate the
27
28 199 shoulder, flex the elbow to 90°, and place the forearm in a neutral
29
30 200 position, with the wrist between 0° and 30° extension and between 0° and
31
32 201 15° ulnar deviation. Subjects will be instructed to squeeze the handle as
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34 202 hard as possible for 3 seconds, and the maximum contraction force (Kg)
35
36 203 will be recorded.
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41 204 C. Short physical performance battery (SPPB): Functional examination
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43 205 using SPPB derived from three objective physical function tests (i.e., the
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45 206 time taken to cover 4 m at a comfortable walking speed, time taken to
46
47 207 stand from sitting in a chair 5 times without stopping, and ability to
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49 208 maintain balance for 10 s in three different foot positions at progressively
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51 209 more challenging levels).¹³ A score from 0 to 4 will be assigned to
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53 210 performance on each task, with higher scores indicating better lower
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4 211 body function.
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6 212 2. *Spine specific outcomes*
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9 213 A. Isometric back muscle strength: Similarly, with the isokinetic back muscle
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11 214 strength test, we will perform the isometric back muscle strength test
12
13 215 using a handheld dynamometer (PowerTrack II; JTECH Medical, Salt
14
15 216 Lake City, UT, USA). This will involve the participant standing in full
16
17 217 extension with their back to a wall, midway between two vertically
18
19 218 oriented anchor rails, and feet flat on the floor with heels touching the
20
21 219 wall. An inelastic belt will be looped through the anchor rails, and secured
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23 220 firmly around the participant, 1 cm below the anterior superior iliac
24
25 221 spines, in order to restrain movement and maintain participant contact
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27 222 with the wall during the test. To standardise posture, arms will be crossed
28
29 223 over the chest, with fingertips level with the contralateral shoulders. The
30
31 224 participant will be instructed to flex forward approximately 15° at the hips
32
33 225 so the handheld dynamometer can be positioned posterior to the spinous
34
35 226 process of the seventh thoracic vertebrae. In this way, counter pressure
36
37 227 will be provided by the fixed wall behind the participants' back so that
38
39 228 variations in resistance by an examiner will be avoided.¹⁴
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45 229 B. Spinal sagittal balance (SSB): For each participant, one lateral
46
47 230 radiograph of the whole spine will be made and digitized. All
48
49 231 measurements will be performed by means of imaging software
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51 232 (INFINITT PACS M6; INFINITT Healthcare, Seoul, South Korea), as
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53 233 previously described.^{15,16} Briefly, the following spinopelvic radiographic
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4 234 parameters will be analysed: sacral slope (SS), pelvic incidence (PI),
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6 235 pelvic tilt (PT), lumbar lordosis (LL), thoracic kyphosis (TK), the ratio of LL
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9 236 to PI (LL/PI), PI-LL mismatch (PI-LL; the difference between the pelvic
10
11 237 incidence and lumbar lordosis), and sagittal vertical axis (SVA). PI-LL will
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13 238 be used as the primary outcomes of SSB.¹⁷

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16 239 C. Back performance scale (BPS): BPS consists of five tests: Sock Test, the
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18 240 Pick-up Test, the Roll-up Test, the Fingertip-to-Floor Test, and the Lift
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20 241 Test. The 5 tests comprising the BPS demonstrate associations with
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22 242 each other, and each test contributes to high internal consistency,
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24 243 implying that the tests share a common characteristic in measuring
25
26 244 physical performance.¹⁸ The BPS sum score (0-15) is calculated by
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28 245 adding the individual scores of the 5 tests.

31
32 246 D. Sorensen test: It is the most widely used test in published studies
33
34 247 evaluating the isometric endurance of the trunk extensor muscles. The
35
36 248 test consists of measuring the amount of time a person can hold the
37
38 249 unsupported upper body in a horizontal prone position with the lower
39
40 250 body fixed to the examining table.¹⁹

43 251 3. *Other functional outcomes*

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46 252 A. Berg balance scale (BBS): Balance and fall risk will be assessed using
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48 253 BBS (range: 0–56; a lower score indicates a worse outcome).²⁰

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51 254 B. Quality of life (QOL): It will be evaluated using the Euro Quality of Life
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53 255 Questionnaire five-dimensional classification (EQ-5D; range: 0–1; a lower
54
55 256 score indicates a worse outcome).²¹

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4 257 C. Activities of daily living (ADLs): ADLs will be determined using the Korean
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6 258 version of the modified Barthel index²² (K-MBI; range: 0–100; a lower
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8 score indicates a worse outcome) and the Korean version of the
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10 Instrumental ADL (K-IADL; range: 0–3; a higher score indicates a worse
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12 outcome).²³
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15 262 D. Frailty: It will be assessed based on fatigue, resistance, ambulation,
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17 illnesses, and loss of weight (FRAIL) using the Korean version of the
18 263
19 FRAIL scale (K-FRAIL; range: 0–5; a lower score indicates a worse
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21 outcome).²⁴
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25 266 4. Serum examination

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27 267 A. Serum chemistry, complete blood counts (CBC), blood urea nitrogen and
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29 creatinine will be obtained.
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31 269 B. Interleukin-6 (IL-6) level will be quantified by Green-Cross laboratory (GC
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33 lab, Seoul, Korea) using standard procedures.
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38 272 All outcome variables will be collected at baseline, 2 and 4 years. However, L-S
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40 spine MRI for lumbar paraspinal muscle quantity and quality will be performed only
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42 at baseline (Table 1).
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279 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

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4 280 DEXA, Dual-energy X-ray absorptiometry; BIA, Bio-impedance analysis; MRI,
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6 281 Magnetic resonance imaging; SPPB, Short Physical Performance Battery, QoL,
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9 282 Quality of life.

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284 **Data analysis**

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

296 **Sample size**

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

306 **Patient and public involvement**

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

311

312 **ETHICS AND DISSEMINATION**

313 This protocol is approved by the institutional review board of Seoul Metropolitan
314 Government Seoul National University (SMG-SNU) Boramae Medical Center (IRB
315 No. 20-2019-19). The study will be performed in accordance with the relevant
316 guidelines of the Declaration of Helsinki, 1964, as amended in Tokyo, 1975; Venice,
317 1983; Hong Kong, 1989; and Somerset West, 1996.²⁵ Written informed consent for
318 all interventions and examinations will be obtained at patient admission. The Ethics
319 Board will be informed of all serious adverse events and any unanticipated adverse
320 effects that occur during the study. The study protocol has been registered at
321 Clinicaltrials.gov and will be updated. The study methods are in accordance with the
322 SPIRIT guidelines for reporting randomised trials.²⁶ Direct access to the source data
323 will be provided for monitoring, audits, Research Ethics Committee
324 (REC)/Institutional Review Board (IRB) review, and regulatory authority inspections
325 during and after the study. All patient information will be coded anonymously, with
326 only the study team having access to the original data. The study results will be
327 disseminated in peer-reviewed publications and conference presentations.

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DISCUSSION

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

341 Currently, SSB is an important indicator of outcomes of lumbar spine surgery,²⁹ and
342 even non-operative treatment of spinal stenosis.³⁰ While SSB can be affected by
343 sex³¹ and ethnicity,³² aging is the most important cause of spinal sagittal
344 imbalance.³³ Decreased lumbar lordosis is an important cause of spinal sagittal
345 imbalance, and it is known to originate from the wedging or decreased height of the
346 intervertebral discs in the absence of vertebral compression fractures.^{34,35} However,
347 spinal sagittal imbalance is difficult to explain only by the height of the intervertebral
348 discs or vertebral bodies. Therefore, we can hypothesize that spinal sarcopenia is

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4 349 one of the causes of spinal sagittal imbalance which the current cohort study will
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6 350 prove.
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10 351 Several specific assessments such as cross-sectional area of paraspinal muscles,
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12 352 back muscle strength, and back performance test are required to evaluate spinal
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14 353 sarcopenia. However, unlike limb skeletal muscles, the functional evaluation of the
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16 354 spine corresponding to the center of the body is not practical. Thus, this cohort study
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18 355 will investigate the value of SSB as a substitute for back muscle strength and
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20 356 performance measurement. In other words, if back muscle strength and functional
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22 357 impairment are directly related to the spinal sagittal imbalance, a simple measurable
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24 358 SSB may be a useful index to represent spinal muscle function.
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30 31 32 360 **Authors' contributions**

33
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35 361 SYL conceived the study and is the principal investigator. JCK, SUL, SHJ, JYL, and
36
37 362 DHL contributed to the development of the study. All authors approved the version to
38
39 363 be published and are responsible for its accuracy.
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369 **Competing interests**

370 None declared

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4 372 **REFERENCES**
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- 8 373 1. Doherty TJ. Invited review: Aging and sarcopenia. *J Appl Physiol* (1985)
9
10 374 2003;95:1717-27.
11
12 375 2. Morley JE. Sarcopenia: diagnosis and treatment. *J Nutr Health Aging*
13
14 376 2008;12:452-6.
15
16 377 3. Delmonico MJ, Harris TB, Lee JS, et al. Alternative definitions of sarcopenia,
17
18 378 lower extremity performance, and functional impairment with aging in older men and
19
20 379 women. *J Am Geriatr Soc* 2007;55:769-74.
21
22 380 4. Pedone C, Costanzo L, Cesari M, Bandinelli S, Ferrucci L, Antonelli Incalzi R.
23
24 381 Are Performance Measures Necessary to Predict Loss of Independence in Elderly
25
26 382 People? *J Gerontol A Biol Sci Med Sci* 2016;71:84-9.
27
28 383 5. Masaki M, Ikezoe T, Fukumoto Y, et al. Association of sagittal spinal
29
30 384 alignment with thickness and echo intensity of lumbar back muscles in middle-aged
31
32 385 and elderly women. *Archives of gerontology and geriatrics* 2015;61:197-201.
33
34 386 6. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the
35
36 387 Asian Working Group for Sarcopenia. *J Am Med Dir Assoc* 2014;15:95-101.
37
38 388 7. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European
39
40 389 consensus on definition and diagnosis: Report of the European Working Group on
41
42 390 Sarcopenia in Older People. *Age Ageing* 2010;39:412-23.
43
44 391 8. Lee HJ, Lim WH, Park JW, et al. The Relationship between Cross Sectional
45
46 392 Area and Strength of Back Muscles in Patients with Chronic Low Back Pain. *Annals*
47
48 393 *of rehabilitation medicine* 2012;36:173-81.
49
50 394 9. Sasaki T, Yoshimura N, Hashizume H, et al. MRI-defined paraspinal muscle
51
52
53
54
55
56
57
58
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60

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2
3
4 395 morphology in Japanese population: The Wakayama Spine Study. PLoS One
5
6 396 2017;12:e0187765.
7
8
9 397 10. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of
10
11 398 sarcopenia among the elderly in New Mexico. American journal of epidemiology
12
13 399 1998;147:755-63.
14
15 400 11. Pedrero-Chamizo R, Albers U, Tobaruela JL, Melendez A, Castillo MJ,
16
17 401 Gonzalez-Gross M. Physical strength is associated with Mini-Mental State
18
19 402 Examination scores in Spanish institutionalized elderly. Geriatrics & gerontology
20
21 403 international 2013;13:1026-34.
22
23
24 404 12. Ro HJ, Kim DK, Lee SY, Seo KM, Kang SH, Suh HC. Relationship Between
25
26 405 Respiratory Muscle Strength and Conventional Sarcopenic Indices in Young Adults:
27
28 406 A Preliminary Study. Annals of rehabilitation medicine 2015;39:880-7.
29
30
31 407 13. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-
32
33 408 extremity function in persons over the age of 70 years as a predictor of subsequent
34
35 409 disability. N Engl J Med 1995;332:556-61.
36
37
38 410 14. Harding AT, Weeks BK, Horan SA, Little A, Watson SL, Beck BR. Validity
39
40 411 and test-retest reliability of a novel simple back extensor muscle strength test. SAGE
41
42 412 Open Med 2017;5:2050312116688842.
43
44
45 413 15. Vialle R, Levassor N, Rillardon L, Templier A, Skalli W, Guigui P.
46
47 414 Radiographic analysis of the sagittal alignment and balance of the spine in
48
49 415 asymptomatic subjects. The Journal of bone and joint surgery American volume
50
51 416 2005;87:260-7.
52
53
54 417 16. Buckland AJ, Ramchandran S, Day L, et al. Radiological lumbar stenosis
55
56
57
58
59
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2
3
4 418 severity predicts worsening sagittal malalignment on full-body standing
5
6 419 stereoradiographs. *The spine journal : official journal of the North American Spine*
7
8
9 420 *Society* 2017.
- 10
11 421 17. Koller H, Pfanz C, Meier O, et al. Factors influencing radiographic and clinical
12
13 422 outcomes in adult scoliosis surgery: a study of 448 European patients. *European*
14
15 423 *spine journal : official publication of the European Spine Society, the European*
16
17 424 *Spinal Deformity Society, and the European Section of the Cervical Spine Research*
18
19 425 *Society* 2016;25:532-48.
- 20
21
22 426 18. Strand LI, Moe-Nilssen R, Ljunggren AE. Back Performance Scale for the
23
24 427 assessment of mobility-related activities in people with back pain. *Phys Ther*
25
26 428 2002;82:1213-23.
- 27
28
29 429 19. Demoulin C, Vanderthommen M, Duysens C, Crielaard JM. Spinal muscle
30
31 430 evaluation using the Sorensen test: a critical appraisal of the literature. *Joint Bone*
32
33 431 *Spine* 2006;73:43-50.
- 34
35
36 432 20. Berg K, Wood-Dauphinee S, Williams JI. The Balance Scale: reliability
37
38 433 assessment with elderly residents and patients with an acute stroke. *Scand J*
39
40 434 *Rehabil Med* 1995;27:27-36.
- 41
42
43 435 21. Group TE. EuroQol-a new facility for the measurement of health-related
44
45 436 quality of life. *Health policy* 1990;16:199-208.
- 46
47
48 437 22. Jung HY, Park BK, Shin HS, et al. Development of the Korean version of
49
50 438 Modified Barthel Index (K-MBI): multi-center study for subjects with stroke. *Journal of*
51
52 439 *Korean Academy of Rehabilitation Medicine* 2007;31:283-97.
- 53
54
55 440 23. Won CW, Yang KY, Rho YG, et al. The development of Korean activities of
56
57
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59
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2
3
4 441 daily living (K-ADL) and Korean instrumental activities of daily living (K-IADL) scale.
5
6 442 Journal of the Korean Geriatrics Society 2002;6:107-20.
7
8
9 443 24. Jung HW, Yoo HJ, Park SY, et al. The Korean version of the FRAIL scale:
10
11 444 clinical feasibility and validity of assessing the frailty status of Korean elderly. Korean
12
13 445 J Intern Med 2016;31:594-600.
14
15 446 25. Dale O, Salo M. The Helsinki Declaration, research guidelines and
16
17 447 regulations: present and future editorial aspects. Acta anaesthesiologica
18
19 448 Scandinavica 1996;40:771-2.
20
21
22 449 26. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and
23
24 450 elaboration: updated guidelines for reporting parallel group randomised trials.
25
26 451 International journal of surgery 2012;10:28-55.
27
28
29 452 27. Lee SY, Ro HJ, Chung SG, Kang SH, Seo KM, Kim DK. Low Skeletal Muscle
30
31 453 Mass in the Lower Limbs Is Independently Associated to Knee Osteoarthritis. PLoS
32
33 454 One 2016;11:e0166385.
34
35
36 455 28. Jeon H, Lee SU, Lim JY, Chung SG, Lee SJ, Lee SY. Low skeletal muscle
37
38 456 mass and radiographic osteoarthritis in knee, hip, and lumbar spine: a cross-
39
40 457 sectional study. Aging Clin Exp Res 2019.
41
42
43 458 29. Hikata T, Watanabe K, Fujita N, et al. Impact of sagittal spinopelvic alignment
44
45 459 on clinical outcomes after decompression surgery for lumbar spinal canal stenosis
46
47 460 without coronal imbalance. Journal of neurosurgery Spine 2015;23:451-8.
48
49
50 461 30. Beyer F, Geier F, Bredow J, Oppermann J, Eysel P, Sobottke R. Influence of
51
52 462 spinopelvic parameters on non-operative treatment of lumbar spinal stenosis.
53
54 463 Technology and health care : official journal of the European Society for Engineering

1
2
3
4 464 and Medicine 2015;23:871-9.
5

6 465 31. Sinaki M, Itoi E, Rogers JW, Bergstralh EJ, Wahner HW. Correlation of back
7
8 466 extensor strength with thoracic kyphosis and lumbar lordosis in estrogen-deficient
9
10 467 women. American journal of physical medicine & rehabilitation 1996;75:370-4.
11
12

13 468 32. Zhu Z, Xu L, Zhu F, et al. Sagittal alignment of spine and pelvis in
14
15 469 asymptomatic adults: norms in Chinese populations. Spine 2014;39:E1-6.
16
17

18 470 33. Gelb DE, Lenke LG, Bridwell KH, Blanke K, McEneaney KW. An analysis of
19
20 471 sagittal spinal alignment in 100 asymptomatic middle and older aged volunteers.
21
22 472 Spine 1995;20:1351-8.
23
24

25 473 34. Takeda N, Kobayashi T, Atsuta Y, Matsuno T, Shirado O, Minami A.
26
27 474 Changes in the sagittal spinal alignment of the elderly without vertebral fractures: a
28
29 475 minimum 10-year longitudinal study. Journal of orthopaedic science : official journal
30
31 476 of the Japanese Orthopaedic Association 2009;14:748-53.
32
33

34 477 35. Frobin W, Brinckmann P, Kramer M, Hartwig E. Height of lumbar discs
35
36 478 measured from radiographs compared with degeneration and height classified from
37
38 479 MR images. European radiology 2001;11:263-9.
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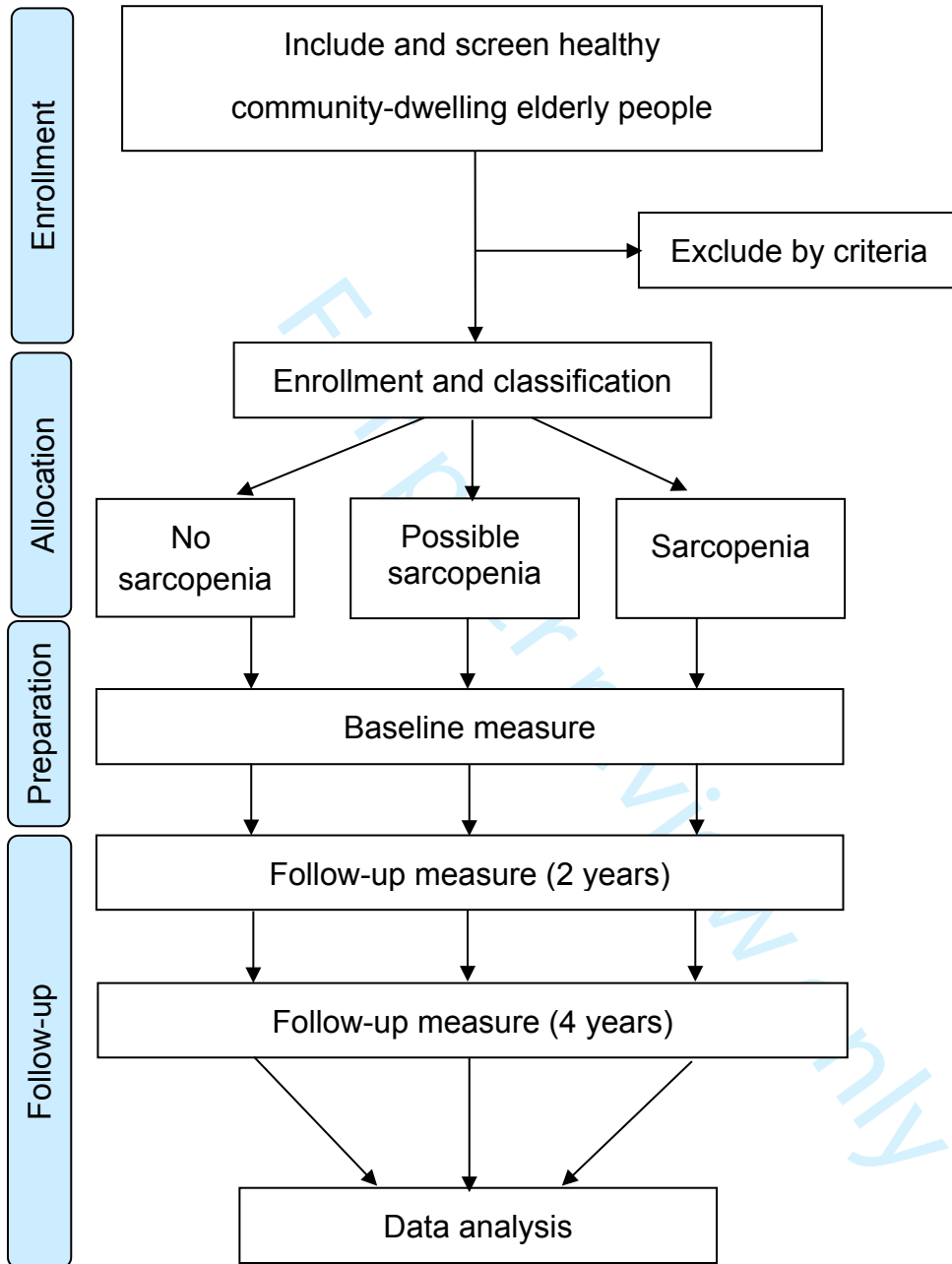
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481 **FIGURE LEGEND**

482 **Figure 1.** Flow diagram of the cohort study

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1 **Figure 1.**



BMJ Open

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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Keywords:	Sarcopenia, Spine < ORTHOPAEDIC & TRAUMA SURGERY, Paraspinal Muscles, Lumbosacral Region

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Manuscripts

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4 **1 Natural Aging Course of Paraspinal Muscle and Back Extensor**
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7 **2 Strength in Community-dwelling Older Adults (Sarcopenia of Spine,**
8
9 **3 SarcoSpine): A Prospective Cohort Study Protocol**

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24 **ABSTRACT**

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

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

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

43 **Trial registration number:** NCT03962530

44 STRENGTHS AND LIMITATIONS OF THIS STUDY

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

57 INTRODUCTION

58

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

66

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

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4 79 or nutritional support.
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10 81 Classical sarcopenia indices proposed by several sarcopenia working groups^{6,7} to
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12 82 date cannot be used to diagnose spinal sarcopenia. While feasible, inexpensive, and
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14 83 less radiation-exposed tools such as dual energy X-ray absorptiometry have been
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16 84 used to measure appendicular skeletal muscle mass, paraspinal muscle assessment
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18 85 still requires the use of spinal computed tomography (CT) or magnetic resonance
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20 86 imaging (MRI). In addition, spinal extensor strength measurement is necessary to
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22 87 confirm the function of the lumbar paraspinal muscle, but isokinetic strength
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24 88 measuring equipment for accurate measurement is not as feasible as a hand-grip
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26 89 strength dynamometer to evaluate sarcopenia. Furthermore, many older adults may
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28 90 experience pain during the measurement of spinal extension strength.
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37 92 Therefore, it is necessary to develop a simple, accessible, and clinically meaningful
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39 93 measurement index to confirm the function of spinal extensor muscles. In this
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41 94 prospective cohort study, we will investigate the basic data of sarcopenia and
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43 95 physical function as well as spine imaging (MRI and X-ray), back performance,
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45 96 spinal sagittal balance, and back extensor strength in 120 healthy older adults.
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47 97 Based on this, we will analyse the correlation between baseline sarcopenia, spinal
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49 98 functional index, spinal sagittal balance index, and physical function. Furthermore,
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51 99 we will observe the natural aging process of these indicators through long-term
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53 100 follow-up over 4 years.
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7 102 **Objectives**8
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10 103 1. To develop the concept of spinal sarcopenia in community-dwelling older
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12 104 adults.13
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15 105 2. In addition, we aim to observe the natural aging process of paraspinal muscle
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17 106 and back extensor strength and investigate the association between
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19 107 conventional sarcopenic indices and spinal sarcopenia.
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30 110 **METHOD AND ANALYSIS**31
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36 112 **Study design**37
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39 113 This is a prospective observational cohort study with 120 healthy community-
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41 114 dwelling older adults in a single center (SMG-SNU Boramae Medical Center).42
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44 115 Individual follow-up will last 4 years.
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51 117 **Participants and eligibility criteria**52
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54 118 Older adults (≥ 65 years old) who are community-dwellers and able to walk with or
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56 119 without assistive devices will be included. Participants who have experienced the
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4 120 following will be excluded: 1) low back pain with moderate severity (numeric rating
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6 121 scale⁸ 5 and over); 2) history of any types of lumbar spine surgery; 3) history of hip
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8 122 fracture surgery and arthroplasty of hip or knee; 4) contraindications for MRI (such
9
10 123 as cardiac pacemaker, implanted metallic objects, and claustrophobia); 5) disorders
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12 124 in central nervous system (such as stroke, parkinsonism, spinal cord injury); 6)
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14 125 cognitive dysfunction (Mini Mental State Examination score < 24); 7) communication
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16 126 disorder (such as severe hearing loss); 8) musculoskeletal condition affecting
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18 127 physical function (such as amputation of limb); 9) long-term use of corticosteroids
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20 128 due to inflammatory disease; 10) malignancy requiring treatment within 5 years; and
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22 129 11) other medical conditions which need active treatment; patients who refuse to
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24 130 participate in a study will also be excluded.
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30 131 Sarcopenia can be divided by two stages: 1) possible sarcopenia (PS) defined by
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32 132 low handgrip strength and/or low gait speed and 2) sarcopenia (SA) confirmed by
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34 133 low handgrip strength and/or low gait speed and low muscle mass defined by the
35
36 134 consensus report of the Asian working group for sarcopenia.⁶ A no sarcopenia (NS)
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38 135 group is added to this classification, and the study participants are classified into
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40 136 three groups (NS, PS, and SA) after the screening tests (Figure 1).
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48 138 **Outcomes measures**

49 50 51 139 Primary outcome measures

52 53 140 *1. Isokinetic back muscle strength*

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56 141 The investigators will use the isokinetic dynamometer (Biodex multi-joint
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4 142 system, Biodex Corporation, Shirley, NY, USA) to measure the torque of the
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6 143 back extensors. Briefly, the examination will be performed by seating the
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9 144 patient comfortably in the device, fixing both the thighs and the back to the
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11 145 chair using a strap, and asking the patient to hold the handle placed near the
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13 146 front, at the chest, to measure upper limb and hip joint motions. The
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16 147 dynamometer axis will be located on the anterior superior iliac spine of the
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18 148 patient's pelvis. All patients will be instructed to flex and extend the back five
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20 149 times at an angular velocity of 60°/sec as a warm-up before the examination.
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23 150 During the examination, patients will be instructed to execute flexion and
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25 151 extension of the back, with a maximum effort, 10 times at an angular velocity
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27 152 of 60°/sec. The back range of movement was 22 limited at 50°, with 30°
28
29 153 (-30°) of trunk flexion and 20° (+20°) of trunk extension, relative to the
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32 154 anatomical reference position (0°).⁹ The device will measure the peak torque
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34 155 (PT) (Nm) and the peak torque per body weight (PT/Bwt) (Nm/kg).¹⁰
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36 156 2. *Lumbar paraspinal muscle quantity and quality*

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38
39 157 Lumbar spine MRI will be performed using a 1.5-T scanner (Achieva 1.5 T;
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41 158 Philips Healthcare, Netherlands). Subjects will be placed in the supine
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43 159 position with the lumbar spine in a neutral position and a pillow under their
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46 160 head and knees. The imaging protocol will include sagittal T2-weighted fast
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48 161 spin echo imaging (repetition time, 3,200 ms/echo; echo time, 100 ms; echo-
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50 162 train length, 20; section thickness, 4 mm; and field of view, 300 × 300 mm)
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53 163 and axial T2-weighted fast spin echo imaging (repetition time, 3,500 ms/echo;
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55 164 echo time, 100 ms; echo-train length, 20; section thickness, 4 mm; and field
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4 165 of view, 200 × 200 mm). Axial images will be obtained for each lumbar
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6 166 intervertebral level (T12/L1-L5/S1) parallel to the vertebral endplates with five
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9 167 slices at each intervertebral level.

10
11 168 The measurement of the cross sectional area (CSA) and fatty infiltration ratio
12
13 169 (FI %) of the paraspinal muscles (erector spinae [ES], multifidus [MF], and
14
15 170 psoas major [PM]) will be performed with axial T2-weighted images using a
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17 171 radiological workstation (MEDIP; Medical IP, Seoul, South Korea) specially
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19
20 172 designed for such purposes. The measurement of ES and MF will be
21
22 173 performed from the level of L1/L2 to L5/S1 and that of PM will be performed
23
24 174 at the level of L4/5. The CSA will be measured by manually constructing free-
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26 175 draw points around the outer margins of the individual muscles using touch
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28 176 screen LCD monitor (XPS 15 9570, Dell, Round Rock, TX, USA) and digital
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30 177 touch screen pen (PN556W Dell Active Pen, Dell, Round Rock, TX, USA).
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32 178 The FI % is defined as the percentage of fatty infiltration area, which is
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34 179 obtained by dividing the fatty infiltration area by the total area. The CSA and
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36 180 FI % of paraspinal muscles will be separately measured on the bilateral sides,
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38 181 and mean values will be calculated.¹¹
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183 Secondary outcome measures

184 1. *Conventional sarcopenic indices*

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50 185 A. Appendicular skeletal muscle mass (ASM): Both dual-energy X-ray
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52 186 absorptiometry (Lunar iDXA for Bone Health; GE Healthcare,
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54 187 Schenectady, NY, USA) and bio-impedance analysis (InBody 720;
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4 188 Biospace, Seoul, South Korea) will be used to analyse body composition
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6 189 including lean body and fat masses. ASM will be calculated by obtaining
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9 190 the sum of the lean mass in bilateral upper and lower extremities¹² and
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11 191 standardized by being divided by the squared height value (ASM/Ht²,
12
13 192 kg/m²).

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16 193 B. Handgrip strength: It will be measured using a hand-grip dynamometer
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18 194 (T.K.K.5401; Takei Scientific Instruments, Tokyo, Japan)¹³, as described
19
20 195 previously¹⁴. Briefly, while sitting in a straight-backed chair with their feet
21
22 196 flat on the floor, patients will be asked to adduct and neutrally rotate the
23
24
25 197 shoulder, flex the elbow to 90°, and place the forearm in a neutral
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27 198 position, with the wrist between 0° and 30° extension and between 0° and
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29 199 15° ulnar deviation. Subjects will be instructed to squeeze the handle as
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31
32 200 hard as possible for 3 seconds, and the maximum contraction force (Kg)
33
34 201 will be recorded.

36 202 C. Short physical performance battery (SPPB): Functional examination
37
38 203 using SPPB derived from three objective physical function tests (i.e., the
39
40 204 time taken to cover 4 m at a comfortable walking speed, time taken to
41
42 205 stand from sitting in a chair 5 times without stopping, and ability to
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44
45 206 maintain balance for 10 s in three different foot positions at progressively
46
47
48 207 more challenging levels).¹⁵ A score from 0 to 4 will be assigned to
49
50 208 performance on each task, with higher scores indicating better lower
51
52 209 body function.

55 210 2. *Spine specific outcomes*

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4 211 A. Isometric back muscle strength: In addition to the isokinetic back muscle
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6 212 strength test, we will perform the isometric back muscle strength test
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8
9 213 using a handheld dynamometer (PowerTrack II; JTECH Medical, Salt
10
11 214 Lake City, UT, USA). This will involve the participant standing in full
12
13 215 extension with their back to a wall, midway between two vertically
14
15
16 216 oriented anchor rails, and feet flat on the floor with heels touching the
17
18 217 wall. An inelastic belt will be looped through the anchor rails, and secured
19
20 218 firmly around the participant, 1 cm below the anterior superior iliac
21
22
23 219 spines, in order to restrain movement and maintain participant contact
24
25 220 with the wall during the test. To standardise posture, arms will be crossed
26
27 221 over the chest, with fingertips level with the contralateral shoulders. The
28
29
30 222 participant will be instructed to flex forward approximately 15° at the hips
31
32 223 so the handheld dynamometer can be positioned posterior to the spinous
33
34 224 process of the seventh thoracic vertebrae. In this way, counter pressure
35
36 225 will be provided by the fixed wall behind the participants' back so that
37
38 226 variations in resistance by an examiner will be avoided.¹⁶
- 41 227 B. Spinal sagittal balance (SSB): For each participant, one lateral
42
43 228 radiograph of the whole spine will be made and digitized. All
44
45
46 229 measurements will be performed by means of imaging software
47
48 230 (INFINITT PACS M6; INFINITT Healthcare, Seoul, South Korea), as
49
50 231 previously described.^{17,18} Briefly, the following spinopelvic radiographic
51
52 232 parameters will be analysed: sacral slope (SS), pelvic incidence (PI),
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54
55 233 pelvic tilt (PT), lumbar lordosis (LL), thoracic kyphosis (TK), the ratio of LL

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4 234 to PI (LL/PI), PI-LL mismatch (PI-LL; the difference between the pelvic
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6 235 incidence and lumbar lordosis), and sagittal vertical axis (SVA). PI-LL will
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9 236 be used as the primary outcomes of SSB.¹⁹

10
11 237 C. Back performance scale (BPS): BPS consists of five tests: Sock Test, the
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13 238 Pick-up Test, the Roll-up Test, the Fingertip-to-Floor Test, and the Lift
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15 239 Test. The 5 tests comprising the BPS demonstrate associations with
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17 240 each other, and each test contributes to high internal consistency,
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19 241 implying that the tests share a common characteristic in measuring
20
21 242 physical performance.²⁰ The BPS sum score (0-15) is calculated by
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23 243 adding the individual scores of the 5 tests.

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27 244 D. Sorensen test: It is the most widely used test in published studies
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29 245 evaluating the isometric endurance of the trunk extensor muscles. The
30
31 246 test consists of measuring the amount of time a person can hold the
32
33 247 unsupported upper body in a horizontal prone position with the lower
34
35 248 body fixed to the examining table.²¹

39 249 3. *Other functional outcomes*

40
41 250 A. Berg balance scale (BBS): Balance and fall risk will be assessed using
42
43 251 BBS (range: 0–56; a lower score indicates a worse outcome).²²

44
45 252 B. Quality of life (QOL): It will be evaluated using the Euro Quality of Life
46
47 253 Questionnaire five-dimensional classification (EQ-5D; range: 0–1; a lower
48
49 254 score indicates a worse outcome).²³

50
51 255 C. Activities of daily living (ADLs): ADLs will be determined using the Korean
52
53 256 version of the modified Barthel index²⁴ (K-MBI; range: 0–100; a lower

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4 257 score indicates a worse outcome) and the Korean version of the
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6 258 Instrumental ADL (K-IADL; range: 0–3; a higher score indicates a worse
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9 259 outcome).²⁵

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11 260 D. Frailty: It will be assessed based on fatigue, resistance, ambulation,
12
13 261 illnesses, and loss of weight (FRAIL) using the Korean version of the
14
15 262 FRAIL scale (K-FRAIL; range: 0–5; a lower score indicates a worse
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17 263 outcome).²⁶

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20 264 4. *Serum examination*

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23 265 A. Serum chemistry, complete blood counts (CBC), blood urea nitrogen and
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25 266 creatinine will be obtained.

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27 267 B. Interleukin-6 (IL-6) level will be quantified by Green-Cross laboratory (GC
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29 268 lab, Seoul, Korea) using standard procedures.

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34 270 All outcome variables will be collected at baseline, 2 and 4 years. However, L-S
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36 271 spine MRI for lumbar paraspinal muscle quantity and quality will be performed only
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38 272 at baseline (Table 1).

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274 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

275 DEXA, Dual-energy X-ray absorptiometry; BIA, Bio-impedance analysis; MRI,

276 Magnetic resonance imaging; SPPB, Short Physical Performance Battery, QoL,

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277 Quality of life.

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279 **Data analysis**

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

291 **Sample size**

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

300

301 **Patient and public involvement**

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

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307 **ETHICS AND DISSEMINATION**

308 This protocol is approved by the institutional review board of Seoul Metropolitan
309 Government Seoul National University (SMG-SNU) Boramae Medical Center (IRB
310 No. 20-2019-19). The study will be performed in accordance with the relevant
311 guidelines of the Declaration of Helsinki, 1964, as amended in Tokyo, 1975; Venice,
312 1983; Hong Kong, 1989; and Somerset West, 1996.²⁷ Written informed consent for
313 all interventions and examinations will be obtained at patient admission. The Ethics
314 Board will be informed of all serious adverse events and any unanticipated adverse
315 effects that occur during the study. The study protocol has been registered at
316 Clinicaltrials.gov and will be updated. Direct access to the source data will be
317 provided for monitoring, audits, Research Ethics Committee (REC)/Institutional
318 Review Board (IRB) review, and regulatory authority inspections during and after the
319 study. All patient information will be coded anonymously, with only the study team
320 having access to the original data. The study results will be disseminated in peer-
321 reviewed publications and conference presentations.

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7 324 **DISCUSSION**8
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14 326 Skeletal muscle mass measurement to define sarcopenia has mainly been based on
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16 327 the sum of muscle mass in the limbs (appendicular limb muscle mass). However the
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18 328 question remains whether this sum of limb muscle mass is associated with muscle
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20 329 function throughout the whole body. Lee et al. reported that degenerative arthritis of
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22 330 the knee joint was associated with only lower limb muscle mass, but not with upper
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24 331 limb muscle mass.²⁸ Recently, Jeon et al. also suggested that the sum of limb
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26 332 muscle mass was not correlated with the radiological degenerative changes of the
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28 333 lumbar spine and hip joint.²⁹ Therefore, site-specific muscle mass investigation is
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30 334 necessary to evaluate the effect of skeletal muscle on specific regions.

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35 335 Currently, SSB is an important indicator of outcomes of lumbar spine surgery,³⁰ and
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37 336 even non-operative treatment of spinal stenosis.³¹ While SSB can be affected by
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39 337 sex³² and ethnicity,³³ aging is the most important cause of spinal sagittal
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41 338 imbalance.³⁴ Decreased lumbar lordosis is an important cause of spinal sagittal
42
43 339 imbalance, and it is known to originate from the wedging or decreased height of the
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45 340 intervertebral discs in the absence of vertebral compression fractures.^{35,36} However,
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47 341 spinal sagittal imbalance is difficult to explain only by the height of the intervertebral
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49 342 discs or vertebral bodies. Therefore, we can hypothesize that spinal sarcopenia is
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51 343 one of the causes of spinal sagittal imbalance which the current cohort study will
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53 344 prove.

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4 345 Several specific assessments such as cross-sectional area of paraspinal muscles,
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6 346 back muscle strength, and back performance test are required to evaluate spinal
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8 347 sarcopenia. However, unlike limb skeletal muscles, the functional evaluation of the
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10 348 spine corresponding to the center of the body is not practical. Thus, this cohort study
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12 349 will investigate the value of SSB as a substitute for back muscle strength and
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14 350 performance measurement. In other words, if back muscle strength and functional
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16 351 impairment are directly related to the spinal sagittal imbalance, a simple measurable
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18 352 SSB may be a useful index to represent spinal muscle function.
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27 354 **Authors' contributions**

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29
30 355 SYL conceived the study and is the principal investigator. JCK, SUL, SHJ, JYL, and
31
32 356 DHK contributed to the development of the study. All authors approved the version to
33
34 357 be published and are responsible for its accuracy.
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44
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46
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53 363 **Competing interests**

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57 364 None declared
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REFERENCES

1. Doherty TJ. Invited review: Aging and sarcopenia. *J Appl Physiol* (1985) 2003;95:1717-27.
2. Morley JE. Sarcopenia: diagnosis and treatment. *J Nutr Health Aging* 2008;12:452-6.
3. Delmonico MJ, Harris TB, Lee JS, et al. Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women. *J Am Geriatr Soc* 2007;55:769-74.
4. Pedone C, Costanzo L, Cesari M, Bandinelli S, Ferrucci L, Antonelli Incalzi R. Are Performance Measures Necessary to Predict Loss of Independence in Elderly People? *J Gerontol A Biol Sci Med Sci* 2016;71:84-9.
5. Masaki M, Ikezoe T, Fukumoto Y, et al. Association of sagittal spinal alignment with thickness and echo intensity of lumbar back muscles in middle-aged and elderly women. *Archives of gerontology and geriatrics* 2015;61:197-201.
6. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc* 2014;15:95-101.
7. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010;39:412-23.
8. Childs JD, Piva SR, Fritz JM. Responsiveness of the numeric pain rating scale in patients with low back pain. *Spine* 2005;30:1331-4.
9. Juan-Recio C, Lopez-Plaza D, Barbado Murillo D, Garcia-Vaquero MP, Vera-Garcia FJ. Reliability assessment and correlation analysis of 3 protocols to measure

- 1
2
3
4 389 trunk muscle strength and endurance. *J Sports Sci* 2018;36:357-64.
5
6 390 10. Lee HJ, Lim WH, Park JW, et al. The Relationship between Cross Sectional
7
8 391 Area and Strength of Back Muscles in Patients with Chronic Low Back Pain. *Annals*
9
10 392 of rehabilitation medicine 2012;36:173-81.
11
12
13 393 11. Sasaki T, Yoshimura N, Hashizume H, et al. MRI-defined paraspinal muscle
14
15 394 morphology in Japanese population: The Wakayama Spine Study. *PLoS One*
16
17 395 2017;12:e0187765.
18
19
20 396 12. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of
21
22 397 sarcopenia among the elderly in New Mexico. *American journal of epidemiology*
23
24 398 1998;147:755-63.
25
26
27 399 13. Pedrero-Chamizo R, Albers U, Tobaruela JL, Melendez A, Castillo MJ,
28
29 400 Gonzalez-Gross M. Physical strength is associated with Mini-Mental State
30
31 401 Examination scores in Spanish institutionalized elderly. *Geriatrics & gerontology*
32
33 402 international 2013;13:1026-34.
34
35
36 403 14. Ro HJ, Kim DK, Lee SY, Seo KM, Kang SH, Suh HC. Relationship Between
37
38 404 Respiratory Muscle Strength and Conventional Sarcopenic Indices in Young Adults:
39
40 405 A Preliminary Study. *Annals of rehabilitation medicine* 2015;39:880-7.
41
42
43 406 15. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-
44
45 407 extremity function in persons over the age of 70 years as a predictor of subsequent
46
47 408 disability. *N Engl J Med* 1995;332:556-61.
48
49
50 409 16. Harding AT, Weeks BK, Horan SA, Little A, Watson SL, Beck BR. Validity
51
52 410 and test-retest reliability of a novel simple back extensor muscle strength test. *SAGE*
53
54 411 *Open Med* 2017;5:2050312116688842.
55
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2
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4 412 17. Vialle R, Levassor N, Rillardon L, Templier A, Skalli W, Guigui P.
5
6 413 Radiographic analysis of the sagittal alignment and balance of the spine in
7
8 414 asymptomatic subjects. The Journal of bone and joint surgery American volume
9
10 415 2005;87:260-7.
11
12
13 416 18. Buckland AJ, Ramchandran S, Day L, et al. Radiological lumbar stenosis
14
15 417 severity predicts worsening sagittal malalignment on full-body standing
16
17 418 stereoradiographs. The spine journal : official journal of the North American Spine
18
19 419 Society 2017.
20
21
22 420 19. Koller H, Pfanz C, Meier O, et al. Factors influencing radiographic and clinical
23
24 421 outcomes in adult scoliosis surgery: a study of 448 European patients. European
25
26 422 spine journal : official publication of the European Spine Society, the European
27
28 423 Spinal Deformity Society, and the European Section of the Cervical Spine Research
29
30 424 Society 2016;25:532-48.
31
32
33 425 20. Strand LI, Moe-Nilssen R, Ljunggren AE. Back Performance Scale for the
34
35 426 assessment of mobility-related activities in people with back pain. Phys Ther
36
37 427 2002;82:1213-23.
38
39
40 428 21. Demoulin C, Vanderthommen M, Duysens C, Crielaard JM. Spinal muscle
41
42 429 evaluation using the Sorensen test: a critical appraisal of the literature. Joint Bone
43
44 430 Spine 2006;73:43-50.
45
46
47 431 22. Berg K, Wood-Dauphinee S, Williams JI. The Balance Scale: reliability
48
49 432 assessment with elderly residents and patients with an acute stroke. Scand J
50
51 433 Rehabil Med 1995;27:27-36.
52
53
54 434 23. Group TE. EuroQol-a new facility for the measurement of health-related
55
56
57
58
59
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- 1
2
3
4 435 quality of life. *Health policy* 1990;16:199-208.
- 5
6 436 24. Jung HY, Park BK, Shin HS, et al. Development of the Korean version of
7
8 437 Modified Barthel Index (K-MBI): multi-center study for subjects with stroke. *Journal of*
9
10 438 *Korean Academy of Rehabilitation Medicine* 2007;31:283-97.
- 11
12
13 439 25. Won CW, Yang KY, Rho YG, et al. The development of Korean activities of
14
15 440 daily living (K-ADL) and Korean instrumental activities of daily living (K-IADL) scale.
16
17 441 *Journal of the Korean Geriatrics Society* 2002;6:107-20.
- 18
19
20 442 26. Jung HW, Yoo HJ, Park SY, et al. The Korean version of the FRAIL scale:
21
22 443 clinical feasibility and validity of assessing the frailty status of Korean elderly. *Korean*
23
24 444 *J Intern Med* 2016;31:594-600.
- 25
26
27 445 27. Dale O, Salo M. The Helsinki Declaration, research guidelines and
28
29 446 regulations: present and future editorial aspects. *Acta anaesthesiologica*
30
31 447 *Scandinavica* 1996;40:771-2.
- 32
33
34 448 28. Lee SY, Ro HJ, Chung SG, Kang SH, Seo KM, Kim DK. Low Skeletal Muscle
35
36 449 Mass in the Lower Limbs Is Independently Associated to Knee Osteoarthritis. *PLoS*
37
38 450 *One* 2016;11:e0166385.
- 39
40
41 451 29. Jeon H, Lee SU, Lim JY, Chung SG, Lee SJ, Lee SY. Low skeletal muscle
42
43 452 mass and radiographic osteoarthritis in knee, hip, and lumbar spine: a cross-
44
45 453 sectional study. *Aging Clin Exp Res* 2019.
- 46
47
48 454 30. Hikata T, Watanabe K, Fujita N, et al. Impact of sagittal spinopelvic alignment
49
50 455 on clinical outcomes after decompression surgery for lumbar spinal canal stenosis
51
52 456 without coronal imbalance. *Journal of neurosurgery Spine* 2015;23:451-8.
- 53
54
55 457 31. Beyer F, Geier F, Bredow J, Oppermann J, Eysel P, Sobottke R. Influence of
56
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2
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4 458 spinopelvic parameters on non-operative treatment of lumbar spinal stenosis.
5
6
7 459 Technology and health care : official journal of the European Society for Engineering
8
9 460 and Medicine 2015;23:871-9.
10
11 461 32. Sinaki M, Itoi E, Rogers JW, Bergstralh EJ, Wahner HW. Correlation of back
12
13 462 extensor strength with thoracic kyphosis and lumbar lordosis in estrogen-deficient
14
15 463 women. American journal of physical medicine & rehabilitation 1996;75:370-4.
16
17
18 464 33. Zhu Z, Xu L, Zhu F, et al. Sagittal alignment of spine and pelvis in
19
20 465 asymptomatic adults: norms in Chinese populations. Spine 2014;39:E1-6.
21
22
23 466 34. Gelb DE, Lenke LG, Bridwell KH, Blanke K, McEneaney KW. An analysis of
24
25 467 sagittal spinal alignment in 100 asymptomatic middle and older aged volunteers.
26
27 468 Spine 1995;20:1351-8.
28
29
30 469 35. Takeda N, Kobayashi T, Atsuta Y, Matsuno T, Shirado O, Minami A.
31
32 470 Changes in the sagittal spinal alignment of the elderly without vertebral fractures: a
33
34 471 minimum 10-year longitudinal study. Journal of orthopaedic science : official journal
35
36 472 of the Japanese Orthopaedic Association 2009;14:748-53.
37
38
39 473 36. Frobin W, Brinckmann P, Kramer M, Hartwig E. Height of lumbar discs
40
41 474 measured from radiographs compared with degeneration and height classified from
42
43 475 MR images. European radiology 2001;11:263-9.
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4 477 **FIGURE LEGEND**

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6 478 **Figure 1.** Flow diagram of the cohort study
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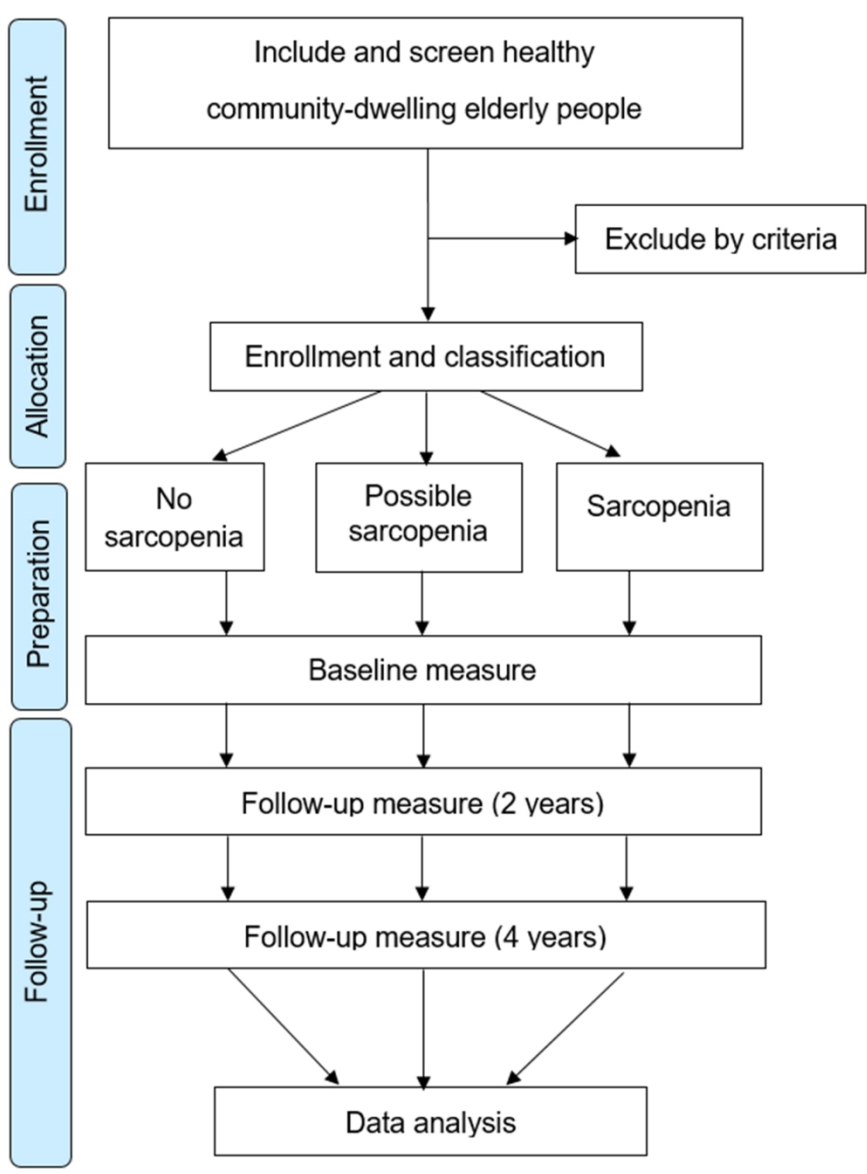


Figure 1. Flow diagram of the cohort study

190x254mm (300 x 300 DPI)