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Anatomically Matched Lower Limb Muscle-Specific Strength Using CT-Derived Quadriceps and Hamstring Volumes in Older Adults with Sarcopenia

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Abstract

Background

We aimed to estimate lower limb muscle-specific strength (MSS) by normalizing knee strength to computed tomography (CT)–derived volumes of the corresponding muscle groups and to examine its relationships with muscle quantity, absolute strength, and clinical outcomes in older adults with sarcopenia.

Methods

In this cross-sectional study, 50 older adults with sarcopenia (10 men, 40 women; mean age 71 ± 6.2 years) were assessed. Skeletal muscle index (SMI) was measured using bioelectrical impedance analysis (BIA), together with handgrip strength (HGS) and knee extensor and flexor strength. Quadriceps and hamstring volumes were quantified using automated three-dimensional CT volumetry. Extensor and flexor MSS were calculated by normalizing each maximal strength to the corresponding ipsilateral muscle volume. Clinical outcomes including physical performance, activities of daily living, falls efficacy, quality of life, fatigability, depressive symptoms, and cognitive function were also assessed.

Results

CT-derived volumes correlated highly with BIA-derived segmental lean mass (r = 0.852–0.905). SMI correlated with HGS and lower limb strength, and HGS correlated with knee strength but was not associated with extensor or flexor MSS. Extensor and flexor MSS were moderately correlated (r = 0.602). In exploratory analyses, Korean Falls Efficacy Scale scores correlated negatively with knee strength and both MSS measures (− 0.523 to − 0.412) but not with SMI or HGS.

Conclusions

CT-based muscle group-specific volumetry enabled anatomically matched estimation of lower limb MSS. MSS was distinct from conventional muscle quantity and absolute strength, and may provide complementary information on lower limb muscle function.

1. Introduction

Sarcopenia is an age-related condition characterized by loss of muscle quantity accompanied by declines in muscle strength and physical function, and is associated with an increased risk of disability, falls, and mortality [1, 2]. However, sarcopenia does not have a universally accepted definition that can be applied consistently in routine clinical practice [3]. The absence of a single, standardized definition of

sarcopenia has led to substantial heterogeneity in prevalence estimates, uncertainty in the selection of diagnostic cut-off points, and challenges in establishing coherent clinical care pathways [4, 5].

To date, multiple working groups, such as the Asian Working Group for Sarcopenia (AWGS) [6, 7], European Working Group on Sarcopenia in Older Persons [8], and the Foundation for the National Institutes of Health sarcopenia project [9], have proposed varying definitions of sarcopenia. In this context, the Global Leadership Initiative in Sarcopenia (GLIS) was convened to harmonize competing definitions into a unified classification system, with the aim of establishing a gold standard for sarcopenia assessment [5]. The GLIS has identified muscle strength, muscle quantity, and muscle-specific strength (MSS) as core components of sarcopenia, while reclassifying physical performance measures as outcomes rather than diagnostic criteria [5].

The AWGS 2025 consensus achieved a high level of alignment with the GLIS framework, yet it preserved guidance tailored to Asian populations. Notably, the revised consensus introduced a simplified diagnostic construct that defines sarcopenia solely by the concurrent presence of low muscle quantity and reduced muscle strength [7]. Furthermore, physical performance is no longer incorporated as a diagnostic component but is instead classified as an outcome indicator, explicitly recognizing that impairments in performance represent downstream consequences of muscle deterioration rather than defining the features of sarcopenia [7, 10, 11].

By expressing muscle strength relative to muscle quantity, MSS provides a composite index that relates force output to available muscle quantity, thereby complementing measures of muscle quantity or strength alone. This integrative measure allows the identification of individuals who maintain muscle quantity but have reduced muscle strength [10]. In addition, as noted above, the recent GLIS consensus formally recognizes MSS as a diagnostic component of sarcopenia [5]. This perspective reinforces functional capacity relative to muscle quantity as an additional dimension of sarcopenia assessment, complementing conventional measures of muscle quantity and absolute strength [5, 10].

Recent studies have operationalized MSS using handgrip strength (HGS) normalized to bioelectrical impedance analysis (BIA)–derived dominant upper limb muscle mass or total muscle mass, or to anthropometric measures such as calf circumference [10, 12]. Although BIA is practical, inexpensive, and suitable for community-based assessments, its accuracy in assessing muscle quantity is limited compared to that of standard imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI) [13]. More importantly, BIA-derived upper limb muscle quantity is a segment-level estimate rather than a measure based on the specific muscles responsible for grip force. Therefore, BIA-based MSS may not ensure exact anatomical correspondence between the measured strength and the muscle quantity used as the denominator [12].

These considerations highlight the importance of anatomical correspondence between measured strength and the muscle quantity used for normalization when operationalizing the MSS. Therefore, a muscle group-specific imaging approach may provide a more direct means of addressing the mismatch inherent in broader regional or segmental measures. CT-based three-dimensional volumetry enables

direct segmentation and quantification of individual muscle groups, allowing a more anatomically matched estimation of the MSS. Accordingly, the primary aim of this study was to estimate lower limb MSS by normalizing knee extensor and flexor strength to CT-derived three-dimensional volumes of the corresponding quadriceps and hamstring muscle groups, respectively. We additionally examined the relationships between the CT-based MSS and conventional muscle-quantity indices, absolute strength, and a range of clinically relevant measures, including physical performance and mobility, activities of daily living, falls, quality of life, fatigability, depressive symptoms, and cognitive function.

2. Methods

2.1. Study design and participants

Fifty patients aged 60 years or older with a prior diagnosis of sarcopenia who visited a tertiary hospital between September 2023 and December 2025 were included in this study. Eligible participants were recalled for a single study visit during which all study assessments and CT scans were performed on the same day. The exclusion criteria were as follows: 1) neurological disorders affecting gait; 2) orthopedic surgery within the previous 6 months; 3) central skeletal fractures within the past year; 4) clinically significant hepatic or renal dysfunction; 5) uncontrolled diabetes or hypertension; 6) advanced heart failure or chronic obstructive pulmonary disease; 7) liver cirrhosis (Child–Pugh B or C); 8) active malignancy requiring treatment; and 9) inability to perform muscle strength testing or cognitive impairment that interferes with study participation. Additional exclusions were made at the discretion of the principal investigator when study participation was considered inappropriate. This study was registered as an observational study with the Clinical Research Information Service (CRIS; KCT0011015).

2.2. Definition of sarcopenia

Sarcopenia was diagnosed based on the AWGS 2019 criteria [6]. The AWGS consensus identifies muscle quantity assessment as an essential element in the diagnosis of sarcopenia and recognizes MRI, CT, dual-energy X-ray absorptiometry, and BIA as acceptable measurement modalities [7]. In the present study, muscle quantity was assessed using BIA (InBody Co., Ltd., Seoul, Republic of Korea). Appendicular skeletal muscle mass was calculated as the sum of the segmental lean mass of both arms and legs, and SMI was calculated as appendicular skeletal muscle mass divided by height squared. Low muscle quantity was defined as an SMI of < 7.0 kg/m² in men and < 5.7 kg/m² in women. Muscle strength was assessed using HGS, with values < 28 kg in men and < 18 kg in women considered low. Physical performance was evaluated using usual gait speed and the five-time chair stand test and was considered low when either gait speed was < 1.0 m/s or the five-time chair stand time was ≥ 12 seconds. Sarcopenia was diagnosed in patients with low muscle quantity, accompanied by either low muscle strength or low physical performance.

2.3. CT acquisition and three-dimensional muscle volumetry

For MSS calculation, the muscle volume denominator was selected to correspond to the muscle group primarily responsible for each measured action. Accordingly, CT-based three-dimensional volumetry was used to quantify the quadriceps and hamstring muscle groups for knee extension and flexion, respectively.

A commercially available automated segmentation program (DeepCatch v1.3.0; MEDICAL IP Co., Ltd., Seoul, Republic of Korea), developed using a three-dimensional nnU-Net-based algorithm, was applied to the CT Digital Imaging and Communications in Medicine files. The program automatically segmented the quadriceps and hamstring muscle groups, generated three-dimensional masks, and calculated the volume of each muscle group [14, 15]. A representative example of the automated muscle segmentation and three-dimensional reconstruction is shown in Fig. 1.

CT-based automated segmentation with color-coded overlays and three-dimensional reconstruction of the quadriceps and hamstring muscle groups. (a) Three-dimensional reconstructed muscle masks. (b) Axial view. (c) Coronal view. (d) Sagittal view. CT, computed tomography

2.4. Muscle-strength assessment

HGS was assessed using a handgrip dynamometer (Takei Scientific Instruments Co. Ltd., Tokyo, Japan). Two trials were performed on each side, resulting in four measurements, and the highest value was used for analysis. Considering the limited availability of studies that have assessed lower limb muscle strength in Asian populations, the AWGS 2025 consensus continues to recommend HGS as the primary indicator of muscle strength [7, 16].

Lower limb muscle strength was assessed using the IB-LS device (InBody Co., Ltd., Seoul, Republic of Korea), according to the protocol described in previous studies [17, 18]. Knee extensor and flexor strengths were measured twice on each side. The highest knee extensor and flexor strengths were obtained across all trials, and both sides were used for analysis. The side on which each maximum value was obtained was recorded for ipsilateral muscle volume matching in the MSS calculation.

2.5. Calculation of MSS

MSS was operationalized as muscle strength normalized to the CT-derived three-dimensional volume of the anatomically corresponding muscle group, consistent with the conceptual definition of MSS as strength standardized to muscle quantity [5, 19]. Knee extensor MSS was calculated by dividing the highest knee extensor strength by the quadriceps muscle volume on the same side. Similarly, knee flexor MSS was calculated by dividing the highest knee flexor strength by the ipsilateral hamstring muscle volume. Thus, the sides used for extensor and flexor MSS calculation were determined independently according to the side with the highest strength for each movement.

Upper limb MSS was not calculated because HGS reflects the coordinated force generated by multiple forearm and intrinsic hand muscles and cannot be anatomically matched to a clearly defined muscle

compartment using the available CT protocol. Therefore, forearm CT muscle volume was included only to examine its correspondence with conventional upper limb lean mass.

2.6. Clinical outcome and screening measures

Clinical outcomes were selected based on the adverse health outcomes of sarcopenia recognized by the GLIS, including impaired physical performance, mobility limitations, disability in activities of daily living, falls, and poor quality of life [20]. Physical performance and mobility were assessed using the five-time sit-to-stand test (FTST) and gait parameters, including step length, gait speed, and step width. Disability in activities of daily living was evaluated using the Korean Activities of Daily Living (K-ADL) and Korean Instrumental Activities of Daily Living (K-IADL) scales. Fall-related outcomes included the Korean Falls Efficacy Scale (KFES) score and the number of falls reported during the preceding year. Quality of life was assessed using the Sarcopenia Quality of Life questionnaire (SarQoL) and the EuroQol five-dimension five-level questionnaire (EQ-5D-5L).

Fatigability was evaluated using the Pittsburgh Fatigability Scale, including its physical (PFS-physical) and mental (PFS-mental) subscales. Depressive symptoms and cognitive function were assessed using the Patient Health Questionnaire-9 (PHQ-9) and the Korean version of the Montreal Cognitive Assessment (MoCA-K), respectively. The Strength, Assistance with walking, Rise from a chair, Climb stairs, and Falls questionnaire (SARC-F) was administered as a symptom-based sarcopenia screening measure, rather than as a clinical outcome domain.

2.7. Statistical analysis

Normality was assessed using the Shapiro–Wilk test, Kolmogorov–Smirnov test, and skewness and kurtosis. Between-sex comparisons were performed using the independent-samples t-test for normally distributed variables and the Mann–Whitney U test for variables that did not satisfy the assumption of normality. Pearson's correlation analysis was used to examine the relationships between CT-derived muscle volumes and BIA-derived lean mass and the correlations between SMI, HGS, knee extensor and flexor strength, and their corresponding MSS measures, as all variables included in these analyses were normally distributed. Correlations between muscle parameters and clinical outcomes were examined using Pearson's correlation analysis for normally distributed variables and Spearman's rank correlation analysis for variables that did not satisfy the assumption of normality. The strength of correlation coefficients was interpreted as negligible (0.00–0.30), low (0.30–0.50), moderate (0.50–0.70), high (0.70–0.90), or very high (0.90–1.00) [21]. All statistical analyses were performed using SPSS software, version 21.0 (IBM Corp., Armonk, NY, USA), and statistical significance was set at $p < 0.05$.

3. Results

The baseline characteristics of the 50 participants (10 men and 40 women) are summarized in Table 1. The mean age of the study population was 71.0 ± 6.2 years. Men were significantly older and had greater height, body weight, SMI, HGS, and knee extensor and flexor strength than women (all $P < 0.05$). In contrast, no significant between-sex differences were observed in body mass index or MSS. Physical

performance, gait parameters, K-ADL and K-IADL scores, fall-related measures, quality of life, fatigability, depressive symptoms, cognitive function, and SARC-F scores are shown in Additional file Supplementary Table S1.

Table 1
Baseline demographics of participants

Age (years)	**All (n = 50)**	**Male (n = 10)**	**Female (n = 40)**
	71±6.2	**74.8±5.9***	**70.1±5.9***
Height (cm)	155.2±6.4	163.1±3.9**	153.2±5.3**
Weight (kg)	52.5±7.5	59.4±7**	50.7±6.7**
BMI (kg/m^2)	21.8±2.7	22.4±3	21.6±2.7
SMI (kg/m^2)	5.7±0.6	6.7±0.3**	5.4±0.4**
HGS (kg)	21.9±4.9	28.7±5**	20.3±3.2**
Knee extensor strength (kg)	22.9±7.5	28.7±10.1**	21.5±6.1**
Knee flexor strength (kg)	19±5.1	23.6±7.7*	17.8±3.6*
Knee extensor MSS (kg/cm^3)	0.028±0.001	0.025±0.001	0.029±0.008
Knee flexor MSS (kg/cm^3)	0.059±0.013	0.055±0.016	0.06±0.012

All data are presented as number (%) or mean±SDs. * $p < 0.05$ **$p < 0.01$

BMI: Body Mass Index, SMI: Skeletal Muscle Index, HGS: Hand Grip Strength, MSS: Muscle-Specific Strength

3.1. CT-derived muscle volume and BIA-derived lean mass

CT-derived muscle volumes showed strong positive correlations with the corresponding BIA-derived segmental lean mass measurements (Table 2). The mean volumes of the right and left arm muscles were 372.1 ± 77.3 cm^3 and 351.8 ± 82.6 cm^3, respectively. Both showed high to very high positive correlations with the corresponding BIA-derived arm lean masses (right, $r = 0.866$; left, $r = 0.905$; both $p < 0.01$). The mean volumes of the quadriceps and hamstring muscles were 845.2 ± 216.3 cm^3 and 324.2

± 66.0 cm³ on the right side and 805.6 ± 211.7 cm³ and 325.0 ± 66.7 cm³ on the left side, respectively. These total leg muscle volumes were highly correlated with the corresponding BIA-derived leg lean mass (right: r = 0.880; left: r = 0.852; both p < 0.01).

Table 2
Correlations between CT-derived muscle volume and BIA-derived lean mass

Body region	CT-derived muscle volume (cm^3)	BIA-derived lean mass (kg)	R
Rt. arm	372.1±77.3	1.59±0.34	0.866**
Lt. arm	351.8±82.6	1.57±0.34	0.905**
Rt. leg	1169.5±274	5.33±0.94	0.88**
Rt. quadriceps	845.2±216.3		
Rt. hamstring	324.2±66		
Lt. leg	1130.6±269.2	5.30±0.94	0.852**
Lt. quadriceps	805.6±211.7		
Lt. hamstring	325±66.7		

All data are presented as mean±SDs. R: Pearson correlation coefficient between the CT-based muscle volume and lean mass

**p < 0.01

BIA; Bioelectrical Impedance Analysis

Leg volume was defined as the sum of the quadriceps and hamstring volumes on the corresponding side.

3.2. Correlations between muscle quantity, muscle strength, and MSS

The correlations between SMI, HGS, knee extensor strength, knee flexor strength, extensor MSS, and flexor MSS are presented in Table 3. SMI showed a moderate positive correlation with HGS (r = 0.580, p < 0.01) and a weak positive correlation with knee extensor strength (r = 0.390, p < 0.01) and knee flexor strength (r = 0.486, p < 0.01). However, it was not significantly correlated with lower limb MSS. HGS was moderately correlated with both knee extensor strength (r = 0.560, p < 0.01) and knee flexor strength (r =

0.587, p < 0.01), but was not significantly associated with either MSS measure. Knee extensor strength was highly correlated with knee flexor strength (r = 0.809, p < 0.01). Knee extensor strength showed a weak correlation with flexor MSS (r = 0.484, p < 0.01), whereas knee flexor strength showed a weak correlation with extensor MSS (r = 0.408, p < 0.01). Extensor MSS and flexor MSS were also moderately correlated (r = 0.602, p < 0.01).

Table 3
Correlation among the muscle quantity, muscle strength, and MSS

SMI	**SMI**	**HGS**	**Knee extensor strength**	**Knee flexor strength**	**Knee extensor MSS**	**Knee flexor MSS**
		0.58**	**0.39****	**0.486****	**-0.271**	**-0.231**
HGS			0.56**	0.587**	0.132	0.103
Knee extensor strength				0.809**	0.681†	0.484**
Knee flexor strength					0.408**	0.627†
Extensor MSS						0.602**
Flexor MSS						

**p < 0.01

SMI: Skeletal Muscle Index, HGS: Hand Grip Strength, MSS: Muscle-Specific Strength

† Extensor/Flexor strength and their respective MSS share a common numerator; these correlations are mathematically dependent and not interpreted.

3.3. Correlations between muscle parameters and clinical outcomes

Considering the exploratory nature of the analysis and the number of correlations examined, the results are summarized with an emphasis on consistent patterns rather than on isolated significant associations. Among the clinical outcomes, KFES showed the most consistent pattern of association. KFES scores were negatively correlated with knee extensor strength (correlation coefficient = − 0.523, p < 0.01), knee flexor strength (− 0.421, p < 0.01), knee extensor MSS (− 0.412, p < 0.01), and knee flexor MSS (− 0.422, p < 0.01), whereas no significant correlations were observed with SMI (0.101) or HGS (− 0.238) (Table 4).

Isolated significant correlations were observed for SMI with PFS-mental (0.316, p < 0.05) and PHQ-9 (0.280, p < 0.05), knee extensor strength with SarQoL (0.363, p < 0.01), knee flexor strength with MoCA-K (0.285, p < 0.05), flexor MSS with MoCA-K (0.440, p < 0.01), and flexor MSS with PHQ-9 (− 0.325, p < 0.05). These associations did not form a consistent pattern across related clinical outcomes; therefore,

they are reported descriptively without individual interpretation. No significant correlations were observed between FTST, gait parameters, K-ADL, K-IADL, number of falls during the preceding 1 year, EQ-5D-5L, PFS-physical, or SARC-F.

Table 4
Correlation between the muscle parameters and clinical outcomes

SMI	**FTST**	**step length**	**step speed**	**step width**	**K-ADL**	**K-IADL**	**KFES**	**number of f/d**
	-0.023	**-0.053**	**-0.041**	**0.211**	**0.169**	**0.082**	**0.101**	**-0.177**
HGS	0.076	0.072	-0.26	-0.102	-0.084	0.012	-0.238	-0.131
Knee extensor strength	-0.016	0.127	0.027	0.019	-0.144	-0.037	-0.523**	-0.13
Knee flexor strength	0.008	0.121	0.034	0.002	-0.089	-0.06	-0.421**	-0.18
Extensor MSS	-0.008	0.114	0.085	-0.075	-0.153	-0.001	-0.412**	0.171
Flexor MSS	-0.088	0.082	0.001	-0.07	-0.163	-0.007	-0.422**	-0.104
*p < 0.05 **p < 0.01 SMI: Skeletal Muscle Index, HGS: Hand Grip Strength, MSS: Muscle-Specific Strength FTST: Five Times Sit-to-Stand Test, K-ADL: Korean Activities of Daily Living, K-IADL: Korean Instrumental Activities of Daily Living, KFES: Korean Falls Efficacy Scale, f/d: fall down								
	SarQoL	EQ-5D-5L	PFS-physical	PFS-mental	PHQ-9	MoCA-K	SARC-F	
SMI	-0.071	-0.17	0.152	0.316*	0.28*	-0.038	0.14	
HGS	0.155	0.071	-0.069	-0.015	0.091	0.134	-0.223	
Knee extensor strength	0.363**	0.035	-0.123	0.056	0.016	0.272	-0.159	
Knee flexor strength	0.22	0.029	-0.004	0.143	-0.069	0.285*	-0.262	
Extensor MSS	0.242	0.056	-0.13	-0.1	-0.047	0.245	-0.015	
Flexor MSS	0.274	0.162	-0.157	-0.163	-0.325*	0.44**	-0.276	
*p < 0.05 **p < 0.01								

SarQoL: Sarcopenia Quality of Life Questionnaire, EQ-5D-5L: EuroQOL 5 Dimension 5 Level Questionnaire, PFS: Pittsburgh Fatigability Scale, PHQ-9: Patient Health Questionnaire 9, MoCA-K: Korean version of the Montreal Cognitive Assessment, SARC-F: Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falls questionnaire.

4. Discussion

This study estimated lower limb MSS by normalizing knee extensor and flexor strength to the ipsilateral CT-derived three-dimensional volumes of the quadriceps and hamstring muscle groups, respectively. The CT-derived muscle volumes showed high to very high positive correlations with the corresponding BIA-derived segmental lean mass measurements. SMI was associated with HGS and absolute lower limb strength, but not with either lower limb MSS measure, whereas HGS was moderately associated with knee extensor and flexor strength, but not with their corresponding MSS measures. Among the exploratory clinical outcomes, KFES showed the most consistent pattern of association, with significant negative correlations with knee extensor and flexor strength and both lower limb MSS measures.

MSS represents muscle strength standardized to muscle quantity and has been recognized by the GLIS as a conceptual component of sarcopenia, alongside muscle quantity and strength [5, 19]. Muscle quantity provides the structural basis for force production; however, greater muscle quantity does not necessarily translate into greater muscle strength. In older adults and individuals with sarcopenia, reduced muscle strength may coexist with relatively preserved muscle quantity, reflecting age-related or pathological deterioration in muscle quality [12, 22]. Moreover, muscle strength may decline earlier and more rapidly than muscle quantity with aging, resulting in a progressive mismatch between muscle quantity and strength [23, 24]. Therefore, MSS may provide information regarding force-generating capacity relative to available muscle quantity.

The anatomical correspondence of the denominator remains an important issue in the operationalization of the MSS. Previous handgrip-based approaches have normalized HGS to the dominant upper limb muscle quantity, total muscle quantity, or calf circumference [10, 12]. Morimoto et al. noted that the corresponding muscle quantity would ideally be derived from the specific wrist and finger flexors and lumbrical muscles involved in grip generation. However, established methods for quantifying these small muscle groups are lacking [10, 12]. Similar concerns have been raised regarding lower limb indices. Previous studies normalized combined knee extensor and flexor torque to total leg lean tissue mass, thereby including the triceps surae, or normalized knee extensor torque alone to total leg lean tissue mass, which also includes the knee flexors and triceps surae [22, 25–27]. To improve anatomical correspondence, Francis et al. used combined knee extensor and flexor torque normalized to upper leg lean tissue mass [28]. Our study further refined this approach by separately matching knee extensor and flexor strengths to the ipsilateral quadriceps and hamstring volumes, respectively, thereby reducing the anatomical mismatch between measured strength and the muscle quantity used for normalization. The quadriceps and hamstring muscle groups were separately segmented, and the maximum knee extensor and flexor strength values were paired with the corresponding muscle volumes

on the same side. Thus, extensor and flexor MSS were independently calculated using action-specific and side-specific denominators. This approach extends previous regional methods by reducing the contribution of muscle groups that are not primarily responsible for the tested movement. Although the quadriceps and hamstrings do not account for all contributors to knee extension and flexion, respectively, their muscle volumes provide a closer anatomical correspondence to measured strength than whole leg or appendicular lean mass estimates.

CT-derived muscle volumes showed high to very high positive correlations with the corresponding BIA-derived segmental lean mass measurements, indicating broad consistency between the two measures of muscle quantity. However, unlike BIA, which estimates lean mass at the limb segment level and may be influenced by factors such as tissue hydration and fluid distribution, CT enables direct visualization and three-dimensional quantification of individual muscle groups [29, 30]. This anatomical specificity was particularly relevant to the present study because separate quantification of the quadriceps and hamstring muscle groups allowed knee extensor and flexor strengths to be normalized to their respective muscle volumes.

SMI showed a moderate positive correlation with HGS, which is consistent with previous studies that reported positive associations between SMI and HGS in older adults [31, 32]. In contrast, SMI showed only weak correlations with lower limb strength and was not significantly correlated with lower limb MSS. The absence of statistically significant correlations between SMI and MSS in this sample is consistent with MSS capturing information not fully redundant with overall muscle quantity; however, this finding should be interpreted with caution given the restricted range of SMI in a sarcopenia-only sample, the limited statistical power to detect correlations of the observed magnitude ($r = -0.271$ and -0.231), and the mathematical properties of ratio variables. This finding reinforces the conceptual separation between muscle quantity and size-normalized muscle function, and is broadly consistent with the GLIS framework, which recognizes muscle quantity, muscle strength, and MSS as distinct conceptual components of sarcopenia [5].

HGS showed moderate positive correlations with both knee extensor and flexor strength but was not significantly correlated with either knee extensor or flexor MSS. HGS is commonly used to assess muscle strength in patients with sarcopenia. However, the negligible association between HGS and lower-extremity MSS indicates that an upper-limb strength measure may not closely reflect volume-normalized lower-limb strength. This suggests that upper-limb strength may not serve as a proxy for volume-normalized lower-limb strength. Accordingly, HGS and lower limb MSS may provide complementary rather than interchangeable information regarding muscle function.

Extensor and flexor MSS values were moderately and positively correlated with each other. This association may reflect common individual characteristics that influence the size-normalized force-generating capacity of both lower limb muscle groups. This coherence may support the possibility that volume-normalized strength reflects shared individual-level characteristics of lower-limb muscle

function. However, given the cross-sectional design of the present study, the underlying mechanisms responsible for this relationship could not be determined.

In the present exploratory analysis, KFES showed the most consistent pattern of association among the clinical outcomes examined. Both knee extensor and flexor strength and their corresponding MSS measures were negatively correlated with KFES scores, indicating that lower absolute and volume-normalized lower-limb strength were associated with poorer falls efficacy. HGS was not significantly correlated with KFES in the present study, whereas both lower-limb strength and MSS showed significant negative correlations with KFES. This pattern is consistent with the possibility that lower-limb muscle parameters may be more closely related to falls efficacy than upper-limb strength, although the difference between these correlations was not formally tested. Both MSS and absolute lower-limb strength showed statistically significant correlations with falls efficacy. This is consistent with our earlier observation that MSS captures a region-specific, mass-independent property of muscle function and extends it by suggesting that this volume-normalized strength may be related to falls efficacy. Because falls efficacy is an important determinant of activity avoidance and future fall risk in older adults, the consistent relationship observed here supports the observed correlations between lower-limb MSS and KFES, which may warrant further investigation.

The major strength of this study lies in the use of CT-derived three-dimensional muscle volume to estimate anatomically matched lower limb MSS. The quadriceps and hamstring muscle groups were segmented separately, knee extensor and flexor strengths were assessed independently, and each maximum strength measurement was paired with the corresponding ipsilateral muscle volume. This approach reduces the denominator mismatch inherent in indices based on whole body, appendicular, or entire limb lean masses. Additional strengths include separate estimation of extensor and flexor MSS and comparison of CT-derived muscle volumes with conventional BIA-derived segmental lean mass measurements. Collectively, these methodological features provide a more anatomically specific framework for estimating lower limb MSS.

This study had some limitations. First, the relatively small sample size, female-dominant composition, single-center setting, and cross-sectional design limit the generalizability of the findings. All participants had sarcopenia, and controls without sarcopenia were not included. Therefore, the restricted ranges of muscle mass and strength may have influenced the observed correlations. Second, upper limb MSS was not calculated because HGS reflects the coordinated contributions of multiple forearm and intrinsic hand muscles, making it difficult to anatomically match HGS to a clearly defined muscle compartment using the available CT protocol [12]. This limits direct comparison with previous studies that employed handgrip-based MSS. Third, although the IB-LS has been validated [17, 18], it is not among the most widely used lower limb strength assessment devices in international research settings, and the generalizability of measurements obtained with this device requires further investigation. Fourth, the associations between muscle parameters and clinical outcomes were examined across multiple correlation analyses without adjustment for multiple testing; therefore, these exploratory findings should be interpreted cautiously. In addition, differences in the patterns of association across muscle

parameters were not evaluated by formal statistical comparisons of correlation coefficients and should not be interpreted as evidence that one measure was more strongly associated with an outcome than another. Finally, because MSS was calculated as a ratio of strength to muscle volume, the mathematical properties of ratio normalization may have influenced its relationships with measures of muscle quantity. Accordingly, the lack of significant correlations between MSS and SMI should not, by itself, be interpreted as evidence that MSS is independent of muscle quantity.

5. Conclusion

This study estimated lower limb MSS by anatomically matching knee extensor and flexor strengths with the ipsilateral CT-derived three-dimensional volumes of the quadriceps and hamstring muscle groups, respectively. CT-derived muscle volumes showed strong correlations with conventional segmental lean mass measurements, whereas SMI, absolute strength, and anatomically matched MSS showed different relationships with one another. In exploratory analyses, lower limb strength and MSS showed consistent associations with fall-related self-efficacy, suggesting the potential clinical relevance of anatomically matched lower limb MSS. Larger studies including individuals with a broader range of muscle health are needed to establish the reproducibility, reference values, and clinical utility of CT-derived anatomically matched MSS.

Abbreviations

ADL (within K-ADL) Activities of Daily Living

AWGS Asian Working Group for Sarcopenia

BIA Bioelectrical impedance analysis

BMI Body Mass Index

CT Computed tomography

DICOM Digital Imaging and Communications in Medicine

EQ-5D-5L EuroQol five-dimension five-level questionnaire

FES / KFES (Korean) Falls Efficacy Scale

FNIH Foundation for the National Institutes of Health

FTST Five-time sit-to-stand test

GLIS Global Leadership Initiative in Sarcopenia

HGS Handgrip strength

IADL Instrumental Activities of Daily Living

IRB Institutional Review Board

K-ADL Korean Activities of Daily Living

K-IADL Korean Instrumental Activities of Daily Living

KFES Korean Falls Efficacy Scale

MoCA-K Korean version of the Montreal Cognitive Assessment

MRI Magnetic resonance imaging

MSS Muscle-specific strength

PFS Pittsburgh Fatigability Scale

PFS-mental / PFS-physical Pittsburgh Fatigability Scale mental/physical subscales

PHQ-9 Patient Health Questionnaire-9

SARC-F Strength, Assistance with walking, Rise from a chair, Climb stairs, and Falls questionnaire

SarQoL Sarcopenia Quality of Life questionnaire

SMI Skeletal muscle index

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Keimyung University Dongsan Hospital, Daegu, Republic of Korea (Approval No.: DSMC 2023-02-061). All procedures were performed in accordance with the ethical standards of the Declaration of Helsinki. All participants provided written informed consent prior to inclusion in the study. The local Institutional Review Board approved the study protocol (Approval No.: DSMC 2023-02-061).

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to institutional data protection policies but are available from the corresponding author on reasonable

request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

GSJ designed the study. CP and AYY cleaned and analyzed the data. GSJ wrote the manuscript. CP provided guidance on statistical analysis. KTK revised the manuscript and provided guidance on the submission. KTK supervised the entire process. All authors reviewed the manuscript.

Clinical Trial Number

Not applicable

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Figures

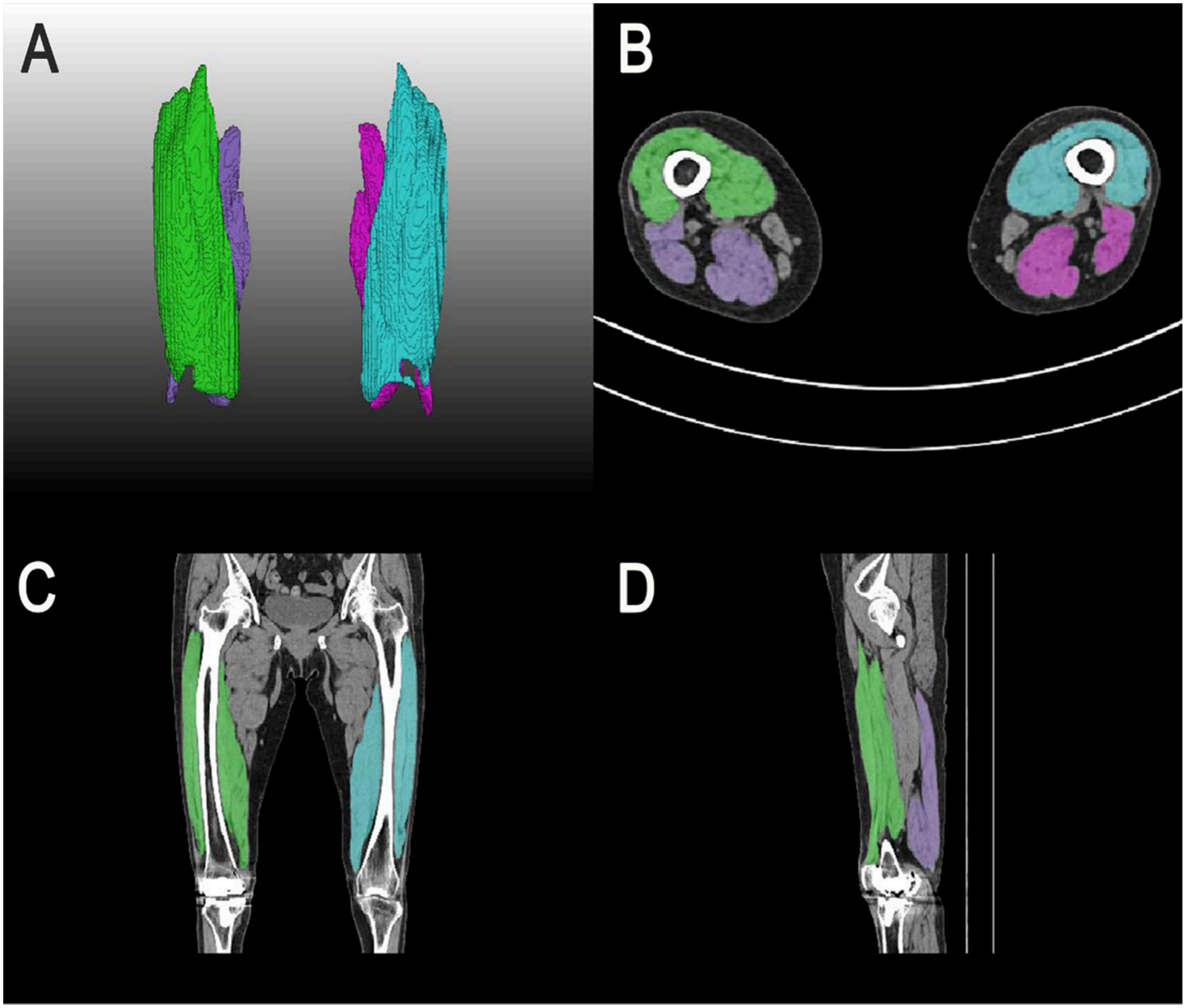


Figure 1

CT-based automated segmentation with color-coded overlays and three-dimensional reconstruction of the quadriceps and hamstring muscle groups. (a) Three-dimensional reconstructed muscle masks. (b) Axial view. (c) Coronal view. (d) Sagittal view. CT, computed tomography

Supplementary Files

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