Impact of sarcopenia on rehabilitation outcomes after total knee replacement in older adults with knee osteoarthritis

Chun-De Liao, Hung-Chou Chen, Shih-Wei Huang 💷 and Tsan-Hon Liou

Abstract

Introduction: Knee osteoarthritis (KOA) is associated with an increased risk of sarcopenia, and aging-related muscle deterioration continues after total knee replacement (TKR). Low skeletal muscle mass index may influence postoperative rehabilitation outcomes. Through this study, we aimed to investigate the impact of preoperative sarcopenia on clinical outcomes after postoperative rehabilitation in older Asian adults.

Methods: A total of 190 older adults (39 men, 151 women) were enrolled from two previous trials and were classified as having no sarcopenia, class I sarcopenia, or class II sarcopenia according to definitions provided by the Asian Working Group for Sarcopenia (AWGS) and the European Working Group on Sarcopenia in Older People (EWGSOP). All patients were retrospectively analyzed before (T_0) and after (T_1) TKR rehabilitation and 10 months after surgery (T_2) . The outcome measures included the timed up-and-go test (TUGT), gait speed (GS), timed chair rise (TCR), and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and physical difficulty (WOMAC-PF). With patient characteristics and T_0 scores as covariates, an analysis of variance was performed to identify intergroup differences in changes of all outcome measures at T_1 and T_2 .

Results: According to the definitions of both the AWGS and EWGSOP, patients with class I and class II sarcopenia exhibited minor changes in TUGT, GS, TCR, and WOMAC-PF at T₁ and T₂ (all p < 0.05), compared with those without sarcopenia. For patients classified as having sarcopenia based on AWGS and EWGSOP definitions, no significant intergroup differences in WOMAC pain score was observed at T₁ or T₂ (all p > 0.05).

Conclusions: Sarcopenia independently had negative impacts on the treatment effects of rehabilitation on physical mobility but not on pain outcome after TKR in older adults with KOA.

Keywords: osteoarthritis, physical function, rehabilitation, sarcopenia, total knee replacement

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Introduction

Knee osteoarthritis (KOA) and aging-related sarcopenia are high risk factors for physical disability in older populations. Individuals with KOA experience mobility impairment and limited function in their daily activities because of knee pain.^{1,2} Total knee replacement (TKR) surgery is recommended as an option for patients with severe pain in end-stage disease and have poor response to conservative management.³ The major treatment goals of TKR are pain relief and functional improvement. However, deficits in muscle function and physical mobility which are indicators of sarcopenia^{4,5} have been observed after TKR even when pain is decreased considerably. In general, individuals exhibit 28.1–40.9% lower leg strength,^{6,7} require 14.5–62.9% longer time for a timed up-and-go task (TUGT),^{6–8} and walk 13.9–58% shorter distance in the 6-min walk test⁷ than do their healthy peers over 2–12 months after TKR. In addition, no clinically meaningful difference in pain status was identified between Ther Adv Musculoskel Dis

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patients with high function and low function after TKR.⁹ Therefore, rather than pain status, skeletal muscle function may play a prominent role in mediating the effect of TKR on physical function.^{10,11}

Patients with KOA have lower lean mass than those without OA, and disease progression is attributable to aging-related decline in muscle mass.^{12–14} Lee *et al.*¹⁵ observed that a low skeletal muscle mass index in the legs is an independent risk factor for KOA. Similarly, Kim *et al.*¹⁶ reported that skeletal muscle mass index is negatively associated with the Kellgren–Lawrence grade (K-L grade) of radiographic KOA. Given that low muscle mass is associated with greater functional impairment¹⁷ and preoperative functional status predicts the functional recovery pattern,^{18,19} potential sarcopenia in older people with KOA may affect post-surgery outcomes.

Before and after TKR surgery, muscle attenuations have been observed in terms of decreased muscle mass²⁰ and volume²¹⁻²³ in the operated leg, accompanied by loss of strength.²² Therefore, sarcopenia in combination with muscle function deficits may occur preoperatively and could persist even after TKR. Early rehabilitation after TKR can improve muscle strength and function regardless of the training protocols used.24 However, it remains unclear whether patients who have sarcopenia preoperatively exhibit poor rehabilitation outcomes after TKR compared with their peers without sarcopenia. Identifying the effects of preoperative sarcopenia on rehabilitation outcomes after TKR might facilitate the optimization of treatment and identification of patients with a risk of poor rehabilitation outcomes.

Through this study, we aimed to identify the impact of preoperative sarcopenia on rehabilitation outcomes after TKR by comparing the differences in the treatment effects of postoperative rehabilitation between patients with KOA who were preoperatively classified as having sarcopenia and not having sarcopenia, and those with class I and class II sarcopenia. The study hypothesis was that compared with patients without sarcopenia, those who were preoperatively classified as having class I or class II sarcopenia would have minor changes in pain, physical mobility, and patient-reported functional outcomes in response to postoperative rehabilitation.

Methods

Ethics approval and study design

We adopted a retrospective design, used to evaluate the effects of body mass index (BMI) on postsurgery rehabilitation previously.25 All data used in the present study were collected from a rehabilitation center database. Our analysis of the patient data contained in the database was approved by the Institutional Review Board of Taipei Medical University (Trial number: 201209029 and N201605007). All procedures involving human participants followed the ethical standards of the institutional committee and the principles of the Declaration of Helsinki. All patients provided written informed consent before admitting baseline assessment. Patient characteristics including age, BMI, obesity, side of surgical leg, K-L grade of the surgical leg, and Cumulative Illness Rating Scale score, which assesses the comorbidity status of older individuals, were analyzed.²⁶ We used BMI≥27.0 to define obesity for the current Asian population.²⁷

Participants

All patients enrolled in this study were derived from two previous randomized control trials on the effects of post-surgery rehabilitation on clinical outcomes.^{28,29} The records of female patients aged 50–85 years who had undergone primary unilateral TKR between July 2008 and March 2019 were reviewed. Patients who had uncontrolled hypertension, diabetes, or neurologically impaired motor function of the lower extremities or underwent a revision TKR were excluded. A flowchart depicting the patient selection process and study group assignment is illustrated in Figure 1.

Sarcopenia identification

Before surgery, patient skeletal muscle mass was measured using bioelectrical impedance analysis by an InBody 220 apparatus (Biospace Co., Seoul, Korea). The device has been identified to be a valid skeletal muscle mass estimator.³⁰ Sarcopenia was identified based on skeletal muscle mass measurements (in kg), normalized for height to provide skeletal muscle index (SMI, in kg/m²). According to the consensus report of the Asian Working Group for Sarcopenia (AWGS),³¹ class I and class II sarcopenia were defined as skeletal muscle index 1 and 2 standard deviations (SDs)



Figure 1. Flow of patient enrollment and allocation throughout the present study.

AWGS, Asian Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia in Older People; LOCF, last observation carried forward; SMI, skeletal muscle mass index; TKR, total knee replacement.

below the reference sex-specific mean for younger individuals, respectively. We used the mean (SD) reference values of 10.87 (1.00) kg/m² and 7.88 (0.73) kg/m² for young Asian men and women, respectively.³² Accordingly, the cutoff values of the SMI for class I and class II sarcopenia are 9.87 kg/m² and 8.87 kg/m² for men, respectively, and 7.15 kg/m² and 6.42 kg/m² for women, respectively.³² Another definition of sarcopenia reported

by the European Working Group on Sarcopenia in Older People (EWGSOP) was used to identify any difference in the study results between the two (i.e. AWGS *versus* EWGSOP) different definitions of sarcopenia. The cutoff values of the SMI for moderate (i.e. class I) and severe (i.e. class II) sarcopenia in men are 10.76 kg/m² and 8.50 kg/m², respectively, and those for women are 6.76 kg/m² and 5.75 kg/m², respectively.³³

Sample size estimation

G-Power 3 was used to estimate the sample size required for an analysis of covariance (ANCOVA) in the study.³⁴ In a previous study,³⁵ the effect size estimated for postoperative rehabilitation was approximately 0.4 for the TUGT. With a statistical power of 0.8, an effect size of 0.4, an alpha of 0.05, a study group size of three, a numerator degree of freedom of two, and seven covariates (described below), we determined that a minimum sample size of 64 (21 for each group) was required to identify differences between the study groups. Considering the probability of patients being lost to follow-up, we enrolled 190 older patients in our study to ensure adequate statistical power.

Total knee replacement

Surgery procedures were performed by two experienced orthopedic surgeons. Each patient received a tricompartmental cemented TKR with a posterior stabilized prosthesis (Zimmer NexGen LPS-Flex Mobile) by using a minimally invasive surgical technique. Each patient received standardized perioperative care and postoperative physiotherapy until discharge.

Postoperative rehabilitation

Outpatient rehabilitation was initiated immediately after inpatient discharge. The rehabilitation program consisted of 24 exercise sessions within 2-3 months. Each patient received one of the following three type of exercises: elastic resistance exercise, balance training, and functional training that had been conducted as part of the postoperative rehabilitation program.^{28,29} The functional training consisted of warm-up, strengthening exercises, functional task-oriented exercises, endurance exercises, and cool-down. The elastic resistance exercise, which targeted muscle groups in the arms and legs, was designed according to previously established elastic exercise regimes for older women. The balance training, which targeted proprioception in the legs and postural control, has been described elsewhere. The attendance rate was recorded for each patient, and compliance to the prescribed postoperative rehabilitation protocols is presented as mean attendance rate.

Outcome measures

All outcome measurements were recorded at the baseline admission before rehabilitation, 4-month

follow-up postoperatively (the completion of outpatient rehabilitation), and 10-month follow-up postoperatively. The primary outcomes of interest included TUGT, gait speed, and timed chair rise (TCR) results, which have been used as functional sarcopenia parameters^{4,5} and effectively applied in our earlier study to assess outcomes after TKR.28 The TUGT was used to measure time required for a patient to rise from a standardized chair, walk 3m, turn around, and return to a seated position in the chair at a self-determined speed; if necessary, patients were allowed to use a walking aid during the task. Gait speed (in m/s) was measured using a 10-m walk task for each patient on the basis of the test data. TCR was employed to quantify performance in repeatedly transitioning from sitting to standing in a standard-height chair (with hands holding the waist) during a 30-s period.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has been well developed for patients with KOA to assess functional outcome after TKR. The Chinese version of the WOMAC questionnaire was used in this study.³⁶ The WOMAC questionnaire consists of three domains containing 24 items, with 5, 2, and 17 items assessing pain, stiffness, and physical difficulty (WOMAC-PF), respectively. The dimension scores for the WOMAC index range from 0 to 100, with 100 indicating the worst possible state.

Statistical analysis

Univariable comparisons of the muscle mass groups were performed for all variables at baseline. One-way analysis of variance was used to analyze continuous variables and chi-squared analysis was employed for categorical variables. The Kraus-Weber test was used for ordinal variables that lacked a normal distribution. ANCOVA was performed for each outcome measure to determine intergroup differences at 4- and 10-month follow-up assessments. The following factors were used as covariates to adjust the potential confounding effects on treatment outcomes: patient characteristics (i.e. age, sex, BMI, comorbidity score, K-L grade of the operated leg), exercise type, and baseline score of each outcome measure. The Bonferroni correction was performed for confidence interval adjustments. The last observation carried forward method was used for imputing the missing outcome data of discontinued patients. All differences with a *p*-value of <0.05 were regarded as statistically significant and presented as means and their SDs. SPSS Statistics (version 22.0; IBM, Armonk, NY, USA) was used for all analyses.

Results

After the exclusion of 40 patients who did not meet the inclusion criteria, 190 patients who underwent a primary unilateral TKR were included in the medical chart review (Figure 1). On the basis of the AWGS definition and the cutoff values of SMI for sarcopenia in Asian individuals, 69, 65, and 56 individuals were categorized as having no sarcopenia, class I sarcopenia, and class II sarcopenia, respectively. According to the EWGSOP definition of sarcopenia, 86, 79, and 25 individuals were categorized as having no sarcopenia, class I sarcopenia, and class II sarcopenia, respectively.

The demographic characteristics of the individuals are listed in Table 1. Age, age categories, rates of obesity, K-L grade of the involved leg, and BMI differed significantly among the three groups of patients classified based on the AWGS definition (all p < 0.01); similar results were observed in those classified based on the EWGSOP definition (all p < 0.05). For groups of patients defined as having sarcopenia according to both the AWGS and EWGSOP, no significant intergroup difference was observed in sex distribution, side of the operated leg, comorbidity score, type of rehabilitation, compliance, and adherence to postoperative rehabilitation (all p > 0.05). Significant intergroup differences in TUGT, gait speed, TCR, and WOMAC-PF results were observed at baseline in these patient groups (all p < 0.05). All outcome measures for the groups were confirmed to fit the Gaussian distribution.

The results of ANCOVA based on the AWGS and EWGSOP definitions for the clinical outcomes are presented in Table 2 and supplementary Table S1. Compared with patients classified as having class II sarcopenia according to the AWGS definition, those classified as not having sarcopenia had greater changes in the TUGT [adjusted mean difference (aMD) = -3.2s], gait speed (aMD = 0.57 m/s), TCR $(aMD = 2.9 \text{ repe$ $titions})$, and WOMAC-PF (aMD = -11.2) at 4 months after surgery, after control for patient characteristics (i.e. age, sex, BMI, comorbidity score, K-L grade of the operated leg), exercise type, and baseline score; such intergroup differences in mobility and functional measures remained significant 10 months after surgery (Table 2). At 4- and 10-month follow-up, compared with patients classified as having class I sarcopenia according to the AWGS definition, those without sarcopenia exhibited larger changes in all physical mobility and perceived functional outcomes (all p < 0.05). In addition, no significant difference in WOMAC pain scores was observed among the groups at any follow-up timepoint.

Based on the EWGSOP definition, compared with patients classified as having class II sarcopenia, those without sarcopenia exhibited greater changes in the TUGT, gait speed, TCR, and WOMAC-PF at 4- and 10-month follow-up (all p < 0.05). Significant differences in mobility and functional measures were also observed between patients without sarcopenia and those with class I sarcopenia at 4- and 10-month follow-up (all p < 0.05). In addition, no significant difference in WOMAC pain scores was observed between the EWGSOP-classified groups at any follow-up timepoint.

Discussion

In this study, the impact of sarcopenia on clinical outcomes after postoperative rehabilitation was investigated for individuals with KOA. Our results indicated that patients who were classified as having class I or class II sarcopenia based on the AWGS definition as well as the EWGSOP definition exhibited significantly minor improvements in mobility and WOMAC-PF outcome measures at 4 and 10 months after surgery, compared with those classified as having no sarcopenia. In addition, the results of the analyses based on the definitions of sarcopenia by the AWGS and EWGSOP demonstrated that patients with sarcopenia exhibited poorer performance in WOMAC-PF in response to postoperative rehabilitation than their peers without sarcopenia did, whereas none of the intergroup differences in the WOMAC pain scores were significant.

The minimal clinically important differences that are used to identify the relevant differences in the changes of outcome measures between study groups have been established for patients receiving TKR as follows: 0.1 m/s (3.94 inch/s) for gait speed;³⁷ 1.2 s for the TUGT;³⁸ 2.6 repetitions for TCR;³⁸ 4.8 and 13.5 points for the WOMACpain and WOMAC-PF, respectively.³⁹ In this study, the differences in such outcomes observed between patients with and without sarcopenia

Table 1. Demographic characteristics of patients.

| Items | AWGS definition | | | EWGSOP definition | | | | |
|------------------------------------------------------|-----------------------------------|-------------------------------------------|----------------------------------|---------------------|----------------------------------|----------------------------------------------|-----------------------------------------------|---------------------|
| | Nonsarcopenia (<i>n</i> = 69) | Class I sarcopenia (<i>n</i> = 65) | Class II sarcopenia (n=56) | <i>p</i> -value | Nonsarcopenia (<i>n</i> =86) | Class I sarcopenia (n=79) Mean ± SD | Class II sarcopenia (n=25) Mean ± SD | <i>p</i> -value |
| | $\textbf{Mean} \pm \textbf{SD}$ | Mean \pm SD | Mean ± SD | | Mean \pm SD | | | |
| Age (years) | 69.2±6.6 | $73.0\pm6.2^{\rm a}$ | $76.4\pm6.1^{\rm a}$ | <0.001 ^b | 70.9 ± 6.5 | 72.7 ± 6.6 | $78.1\pm6.6^{\rm a}$ | <0.001b |
| Age category, n (%) | | | | <0.001 ^b | | | | <0.001 ^b |
| <70 years | 45 (65.2) | 19 (29.2) | 8 (14.3) | | 43 (50.0) | 26 (32.9) | 3 (12.0) | |
| 70-79.9 years | 20 (29.0) | 36 (55.4) | 32 (57.1) | | 36 (41.9) | 40 (50.6) | 12 (48.0) | |
| ≥80years | 4 (5.8) | 10 (15.4) | 16 (28.6) | | 7 (8.1) | 13 (16.5) | 10 (40.0) | |
| Female, <i>n</i> (%) | 53 (76.8) | 51 (78.5) | 47 (83.9) | 0.60° | 74 (86.0) | 57 (72.2) | 20 (80.0) | 0.09° |
| BMI (kg/m²) | 24.7±3.9 | $26.7\pm3.0^{\text{a}}$ | $30.1\pm3.7^{\text{a}}$ | <0.001 ^b | 25.6 ± 3.6 | $27.3\pm3.9^{\text{a}}$ | $28.2\pm4.2^{\text{a}}$ | 0.002 ^b |
| SMI (kg/m²) | 8.37±1.16 | $7.36 \pm 1.08^{\text{a}}$ | $6.35\pm0.98^{\rm a}$ | <0.001 ^b | 7.67 ± 1.35 | $7.34 \pm 1.53^{\text{a}}$ | $6.87 \pm 1.57^{\text{a}}$ | 0.021 ^b |
| Obese, n (%)ª | 18 (26.1) | 27 (41.5) | 37 (66.1) | <0.001° | 31 (36.0) | 35 (44.3) | 16 (64.0) | 0.04° |
| TKR leg, right, <i>n</i> (%) | 43 (62.3) | 45 (69.2) | 41 (73.2) | 0.41° | 53 (61.6) | 60 (75.9) | 16 (64.0) | 0.22° |
| K-L grade, TKR leg, n (| %) | | | 0.002 ^c | | | | 0.005° |
| 3 | 45 (65.2) | 26 (40.0) | 21 (37.5) | | 49 (57.0) | 38 (48.1) | 5 (20.0) | |
| 4 | 24 (34.8) | 39 (60.0) | 35 (62.5) | | 37 (43.0) | 41 (51.9) | 20 (80.0) | |
| CIRS score | 8.67 ± 5.6 | 9.6 ± 5.4 | 9.6±5.2 | 0.51 ^b | 9.0 ± 5.6 | 9.2 ± 5.4 | 10.3 ± 5.4 | 0.59 ^b |
| Number of comorbiditie | es, n (%) | | | 0.41° | | | | 0.15 |
| ≤2 | 36 (52.2) | 41 (63.1) | 30 (53.6) | | 52 (60.5) | 43 (54.5) | 12 (48.0) | |
| 3 | 24 (34.8) | 16 (24.6) | 15 (26.8) | | 24 (27.9) | 25 (31.6) | 6 (24.0) | |
| ≥4 | 9 (13.0) | 8 (12.3) | 11 (19.6) | | 10 (11.6) | 11 (13.9) | 7 (28.0) | |
| Rehabilitation, n (%) | | | | 0.84c | | | | 0.20 ^c |
| Function training | 31 (44.9) | 34 (52.3) | 30 (53.6) | | 41 (47.7) | 36 (45.6) | 18 (72.0) | |
| Balance training | 29 (42.0) | 20 (30.8) | 16 (28.6) | | 31 (36.0) | 28 (35.4) | 6 (24.0) | |
| Resistance training | 9 (13.1) | 11 (16.9) | 10 (17.9) | | 14 (16.3) | 15 (19.0) | 1 (4.0) | |
| Adherence to treatment, <i>n</i> (%) ^e | 59 (85.5) | 55 (84.6) | 49 (87.5) | 0.90° | 74 (86.0) | 67 (84.8) | 22 (88.0) | 0.92° |
| Compliance (%) ^f | 84.2 ± 9.9 | 83.0 ± 10.7 | 83.1 ± 10.0 | 0.74 ^b | 83.5 ± 10.1 | 83.5 ± 10.7 | 83.3 ± 9.8 | 0.74 ^b |
| WOMAC-Pain (0–20) ^g | 12.8 ± 2.2 | 11.7 ± 3.2 | 11.6 ± 3.4 | 0.07 ^b | 12.1 ± 2.9 | 12.0 ± 3.0 | 12.1 ± 3.1 | 0.99 ^b |
| WOMAC-PF (0-68) ^g | 41.7±12.5 | $50.6 \pm 18.6^{\text{a}}$ | $54.4 \pm 19.2^{\text{a}}$ | <0.001 ^b | 42.5 ± 15.7 | $51.1\pm16.8^{\rm a}$ | $61.2\pm18.3^{\text{a}}$ | <0.001 ^b |
| Mobility measures ^g | | | | | | | | |
| TUG (s) | 12.3±2.6 | $13.9\pm3.7^{\text{a}}$ | $14.1\pm2.4^{\text{a}}$ | 0.001 ^b | 12.9±2.8 | 13.2 ± 2.3 | 14.1±1.9 | 0.04 ^b |
| GS (m/s) | 0.92±0.18 | $0.77\pm0.16^{\circ}$ | $0.69\pm0.20^{\rm a}$ | <0.001 ^b | 0.84 ± 0.20 | 0.78 ± 0.20 | $0.73\pm0.18^{\mathrm{a}}$ | 0.04 ^b |
| TCR (repetition) | 7.1±2.9 | 7.1 ± 3.4 | $5.1\pm2.8^{\circ}$ | <0.001 ^b | 7.2 ± 3.0 | 6.2±3.1 | $4.8\pm3.4^{\text{a}}$ | 0.03 ^b |

^aSignificant difference compared with the nonsarcopenia group; p < 0.05.

^bOne-way analysis of variance. ^cKruskal–Wallis Test.

^cKruskal-Wallis Test. ^dUsing the cutoff BMI≥27.0 for obesity in the Asian population. ^eData presented as the number of patients who completed the study. ^fData presented as mean attendance rate for all rehabilitation protocols. ^gData assessed after surgery and before postoperative rehabilitation. AWGS, Asian Working Group for Sarcopenia; BMI, basal metabolic index; CI, confidence interval; CIRS, Cumulative Illness Rating Scale; EWGSOP, European Working Group on Sarcopenia in Older People; GS, gait speed; K-L grade, Kellgren-Lawrence grading scale for severity of knee osteoarthritis; SD, standard deviation; SMI, skeletal muscle mass index; TKR, total knee replacement; TCR, timed chair rise; TUG, timed up-and-go; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; WOMAC-PF, WOMAC physical difficulty subscore.

were relatively small for both AWGS and EWGSOP definitions, especially WOMAC-pain and WOMAC-PF, despite being statistically significant. The results of this study indicate that sarcopenia has a significant but not clinically relevant impact on the ability of patients to perform daily living activities.

In this study, patients with AWGS-defined class II (mean age = 76.4 years) or class I (mean age = 73.0 years) sarcopenia were older than those without sarcopenia (mean age = 69.2 years), and similar results were observed in the groups of patients classified as having sarcopenia according to the EWGSOP definition. Our results are supported by previous studies that reported dramatic muscle mass loss occurring at ≥70 years of age.^{40,41} In addition, previous studies that have employed a muscle mass index to identify sarcopenia have reported 6.3-16.5% and 4.8-33.6% prevalence rates of class I and class II sarcopenia, respectively, among community-dwelling Asian women aged ≥ 70 years.^{32,40,42,43} In this study, among the 118 patients who were aged \geq 70 years, 46 (38.9%) and 48 (40.7%) were classified as having class I and class II sarcopenia, respectively, according to the AWGS definition; based on the EWGSOP definition, 53 (44.9%) and 22 (18.6%) patients were classified as having class I and class II sarcopenia, respectively. Compared with previous results, our findings may indicate that older individuals with KOA, particularly those with moderate-to-severe KOA, experience a higher prevalence of sarcopenia than their peers without KOA do.

In this study, patients with AWGS-defined class II sarcopenia had a higher mean BMI (30.1 kg/m^2) , and a higher proportion of such patients were obese (66.1%) compared with those without sarcopenia (24.7 kg/m² and 26.1%, respectively); similar results were observed among patients classified as having sarcopenia according to EWGSOP. Such findings corroborated the result that patients with class II sarcopenia exhibited poorer performance in mobility than those without sarcopenia did at the baseline assessment immediately after TKR. In previous studies, a high BMI has been revealed to negatively affect the mobility of older individuals.44,45 White et al.44 observed that obesity was significantly associated with walking capability independent of knee pain in older individuals with KOA. Vilaca et al.45 reported that older women with a higher BMI (30.9 kg/m²) walked a

shorter distance in the 6-minute walk test and required a longer duration in the TUGT than those with a lower mean BMI did (25.9 kg/m²). In addition, aging-associated low muscle mass contributes to physical limitations,^{41,46} whereas sarcopenia can coexist with a higher BMI (i.e. sarcopenic obesity), which tends to increase the risks of physical difficulty in older women.⁴⁶ Therefore, at baseline, patients with class II sarcopenia with older age, lower muscle mass index, and higher BMI may have poorer physical mobility than their peers without sarcopenia.

Obesity or a high BMI may negatively influence postoperative pain and physical functional outcomes in patients undergoing primary TKR.⁴⁷ The higher BMI observed among our patients who were classified as having class II sarcopenia by AWGS or EWGSOP definitions may have negatively affected their postoperative outcomes. However, after adjustments for BMI, the differences in mobility score changes remained significant among the study groups. Our results indicate that independent of the confounding effects of BMI (or obesity), sarcopenia appears to mediate the treatment efficacy of postoperative rehabilitation, with poorer improvements in physical mobility observed regardless of the definition of sarcopenia.

In the present study, significant differences in disease severity were observed among the groups of patients classified as having sarcopenia based on the AWGS or EWGSOP definition. Our results were supported by those of a previous study that indicated that low muscle mass is associated with KOA severity;¹⁶ accordingly, patients classified as having severe sarcopenia may experience a higher K-L grade than those without sarcopenia would. Therefore, a higher rate of K-L grade 4 (62.5% and 80.0% for AWGS and EWGSOP definition, respectively) could be observed for patients with class II sarcopenia than in those without sarcopenia (34.8% and 43.0% for AWGS and EWGSOP definitions, respectively). In addition, preoperative disease severity (i.e. pre-surgical K-L grade) has been reported to affect the outcomes of rehabilitation.48 After control for disease severity, patients with class II sarcopenia in this study exhibited minor changes in mobility and functional outcomes compared with their peers without sarcopenia; therefore, our results indicating that preoperative sarcopenia negatively affected the rehabilitation outcome, independent of the pre-surgical K-L grade.

| Measures | AWGS d | efinition ^a | | EWGSOP definition ^a | | | | |
|-------------------------|--------------------------------------------------|------------------------|---------------------------------------------------|--------------------------------|--------------------------------------------------|-----------------|---------------------------------------------------|------------------|
| | Nonsarcopenia <i>minus</i> class I sarcopenia | | Nonsarcopenia <i>minus</i> class II sarcopenia | | Nonsarcopenia <i>minus</i> class I sarcopenia | | Nonsarcopenia <i>minus</i> class II sarcopenia | |
| | Mean | (95% CI) | Mean | (SD) | Mean | (95% CI) | Mean | (95% CI) |
| TUG (s)♭ | | | | | | | | |
| 4 months | -1.6 | (-2.7, -0.4)*** | -3.2 | (-4.6, -1.8)*** | -1.7 | (-2.6, -0.7)*** | -1.8 | (-3.3, -0.3)* |
| 10 months | -2.2 | (-3.2, -1.2)*** | -4.6 | (-5.8, -3.4)*** | -2.2 | (–3.1, –1.3)*** | -3.8 | (-5.2, -2.4)*** |
| GS (m/s) | | | | | | | | |
| 4 months | 0.52 | (0.36, 0.68)*** | 0.57 | (0.39, 0.76)*** | 0.26 | (0.13, 0.39)*** | 0.32 | (0.10, 0.54)** |
| 10 months | 0.82 | (0.61, 1.04)*** | 0.92 | (0.67, 1.18)*** | 0.44 | (0.25, 0.63)*** | 0.54 | (0.23, 0.84)*** |
| TCR (repetition) | | | | | | | | |
| 4 months | 4.2 | (2.5, 6.0)*** | 3.1 | (0.9, 5.3)** | 3.2 | (1.1, 5.4)** | 3.8 | (0.3, 7.4)* |
| 10 months | 3.2 | (1.2, 5.2)** | 3.4 | (0.9, 5.8)** | 4.0 | (1.3, 6.8)** | 4.6 | (0.2, 9.1)* |
| WOMAC-Pain ^b | | | | | | | | |
| 4 months | 0.1 | (-0.6, 0.8) | -0.3 | (-1.1, 0.5) | 0.1 | (-0.4, 0.6) | -0.5 | (-1.4, 0.3) |
| 10 months | -0.5 | (-1.1, 0.1) | -0.4 | (-1.0, 0.2) | -0.1 | (-0.5, 0.3) | -0.4 | (-1.2, 0.3) |
| WOMAC-PF ^b | | | | | | | | |
| 4 months | -7.9 | (-12.4, -3.4)*** | -11.2 | (–16.7, –5.7)*** | -3.6 | (-7.0, -0.2)* | -8.6 | (-14.4, -2.7)** |
| 10 months | -8.4 | (–11.6, –5.2)*** | -10.3 | (-14.2, -6.4)*** | -3.7 | (-6.4, -0.9)** | -7.6 | (–12.0, –3.2)*** |

| Table 2. | Clinical | outcomes | at 4 and | 10 months | after surgery. |
|----------|----------|----------|----------|-----------|----------------|
|----------|----------|----------|----------|-----------|----------------|

*A significant difference between the compared groups; p < 0.05; **p < 0.01; ***p < 0.01.

^aAll data were adjusted by the baseline score and patient characteristics including age, sex, body mass index, comorbidity score, disease severity of the involved leg, and type of rehabilitation. Sex was coded as women=0 and men=1. Type of rehabilitation was coded as function training=1, balance training=2, and resistance training=3.

^bNegative values indicate that the nonsarcopenia group exhibited a performance superior to that of the compared group.

AWGS, Asian Working Group for Sarcopenia; CI, confidence interval; EWGSOP, European Working Group on Sarcopenia in Older People; GS, gait speed; TCR, timed chair rise; TUG, timed up-and-go; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; WOMAC-PF, WOMAC physical difficulty subscore.

> Aging-related muscle mass deterioration was identified to be associated with the severity of knee pain,⁴⁹ particularly in older women with radiographically mild KOA.⁵⁰ For mild KOA (K-L grade=2), appendicular muscle mass relative to body weight was reported to be significantly lower in patients with knee pain than in those without knee pain, whereas no such difference was noted for moderate-to-severe KOA (K-L grade \geq 3).⁵⁰ On the basis of previous results, low muscle mass may not be a major determinant of pain status at end-stage KOA, which may explain our finding that no significant difference in pain reduction responded to rehabilitation among muscle-mass

groups since all patients in this study were diagnosed as having moderate-to-severe KOA (K-L grade \geq 3) preoperatively. In addition, patients classified as having class I or class II sarcopenia according to AWGS or EWGSOP definitions experienced minor changes in mobility tasks and WOMAC-PF scores compared with those without sarcopenia; these results indicate that sarcopenia is most likely to negatively affect physical mobility but not pain outcomes after TKR.

Because of their lower physical status at baseline, the class II sarcopenia individuals were expected to have poor compliance to postoperative exercise training compared with patients without sarcopenia, who exhibited a higher level of physical function before outpatient rehabilitation. However, our results demonstrated that patients with class I or class II sarcopenia completed the rehabilitation protocols with an approximate mean attendance rate of 83.0–83.5%, which was comparable to the corresponding rates of patients without sarcopenia (mean attendance rate, 83.5–84.2%), regardless of the definition of sarcopenia or the type of exercise. In addition, no significant difference was observed in the proportion of patients from the different study groups who completed the study. Therefore, TKR followed by early rehabilitation is not contraindicated in Asian elder people with sarcopenia.

Study limitation

Our findings are subject to certain limitations. First, all patients in each study group undertook a different type of exercise, which may have influenced the postoperative outcomes despite the equal distribution of three rehabilitation types among the groups. However, all analyses for rehabilitation outcomes were controlled for exercise type; therefore, the results of this study were assumed to be independent of the type of exercise. In addition, owing to the limited sample size, we could not conduct a subgroup analysis to identify any difference between the three rehabilitation types for each study group. Future studies with larger sample sizes are warranted to compare the responses to rehabilitation types between patients with and without sarcopenia. Second, medication prescribed for pain control and the use of walking aids during the mobility tests also represent potential confounding factors. We did not consider drug use for pain or walking aid use in our analysis of the results of the mobility measures. Future studies on whether pain medications or walking aid use has a significant intragroup contribution to changes in post-surgery outcomes after rehabilitation are warranted. Third, only individuals with KOA were included in our study. Therefore, our results might not be generalizable to all TKR types. Further investigation on whether the effects of sarcopenia on postoperative rehabilitation outcomes in patients with other preoperative diagnoses (e.g. rheumatoid arthritis) are similar to those for KOA is necessary. Fourth, patient satisfaction regarding surgical outcomes was not measured in this study, because patients' perspective is becoming increasingly important in clinical management and the satisfaction outcome likely extends beyond improved mobility and pain relief after TKR.51

Whether the significant differences in functional capacity affected how patients perceived their postoperative rehabilitation outcomes remained unclear. Fifth, muscle mass outcome was not assessed after TKR in the present study. As postoperative muscle mass was assessed for only some of the included patients (n=60), we were unable to analyze muscle mass outcomes. Therefore, the effects of rehabilitation interventions on changes in sarcopenia status for each study group were unclear. Future studies are warranted to identify whether preoperative sarcopenia affects sarcopenia status after postoperative rehabilitation. Finally, potential confounders, such as disease duration⁵² and preoperative functional status,¹⁹ may have made contributions when measuring treatment efficacy and post-surgery outcomes. However, disease duration and preoperative functional status were not assessed or included as covariates for analysis in this study; therefore, differences in treatment effects among the study groups may been overestimated.

Conclusions

The minor changes in mobility outcomes (i.e. TUGT, gait speed, and TCR results) observed in the sarcopenia groups relative to the nonsarcopenia group suggest that a low muscle mass index preoperatively may limit the effectiveness of postoperative outpatient rehabilitation on physical outcome in older adults with KOA. However, no negative impacts for the postoperative pain outcome were identified. In addition, using two different definitions (i.e. AWGS and EWGSOP definitions) for classifying patients with sarcopenia did not affect the study results. The results of this study suggest that preoperative sarcopenia should be considered for assessing rehabilitation outcomes after TKR, particularly physical mobility and function.

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Supplemental material

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