Retrospective study of relationship between vastus medialis volume on SPECT-CT and outcome of unilateral total knee arthroplasty

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Abstract
Although the importance of quadriceps femoris function was reported previously, little is known about volume-related factors and their effects on clinical outcomes after total knee arthroplasty (TKA). We sought to determine whether there was a bilateral difference in vastus medialis muscle volume measured on single-photon emission computed tomography–computed tomography (SPECT-CT) in patients who underwent unilateral TKA. We also aimed to determine whether vastus medialis volume was related to osteoarthritis (OA) severity or scintigraphic uptake degree around the knee joint on SPECT-CT. And finally, we attempted to investigate the factors, such as vastus medialis volume and scintigraphic uptake degree, associated with the functional outcomes of TKA.

This retrospective study included 50 patients (41 female, 9 male) undergone unilateral TKA due to primary OA. The maximal cross-sectional area of the vastus medialis was measured on axial SPECT-CT images. Scintigraphic uptake degrees and Kellgren-Lawrence (K-L) grade at the tibiofemoral joints were assessed. We compared maximal cross-sectional area of the vastus medialis on SPECT-CT for difference of bilateral lower limbs. We also analyzed the relationship between volume of vastus medialis and scintigraphic uptake measured on SPECT-CT and the severity of OA on conventional radiographs. The clinical outcomes were evaluated using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index at baseline and at 1 and 2 years after surgery. The relationship between preoperative muscle volume and scintigraphic uptake on SPECT-CT was analyzed.

The amount of muscle volume measured on SPECT-CT was smaller in operated limb in patients who underwent unilateral TKA. Preoperative vastus medialis muscle volume was not related to preoperative OA severity measured on conventional radiographs and scintigraphic uptake on SPECT-CT. However, a decreased vastus medialis muscle volume was related to worse clinical outcomes after TKA (P=.045), whereas the degree of scintigraphic uptake on SPECT-CT was not associated with postoperative clinical outcomes.

Muscle volume of vastus medialis was decreased in the operated knee than in the nonoperated knee, and that was correlated with worse postoperative results. Even if the preoperative volume of vastus medialis were not related to OA severity on conventional radiographs and scintigraphic uptake on SPECT-CT, preservation and improvement of the muscle mass of the knee undergoing TKA is important.

Abbreviations: AP = anteroposterior, CSA = cross-sectional area, CT = computed tomography, ICCs = intraclass correlation coefficients, K = Kappa, K-L = Kellgren-Lawrence, MRI = magnetic resonance imaging, OA: osteoarthritis, PA = posteroanterior, PACS = picture archiving and communication system, PJI = periprosthetic joint infection, SPECT-CT = single-photon emission computed tomography–computed tomography, TKA = total knee arthroplasty, WOMAC = Western Ontario and McMaster Universities Osteoarthritis.

Keywords: quadriceps femoris, single-photon emission computed tomography–computed tomography, total knee arthroplasty, vastus medialis.
1. Introduction

The quadriceps femoris muscle contributes to maintaining normal knee function and stability by distributing potentially harmful loads during heel-strike and stabilizing varus and valgus moments.\(^1\) Patients with advanced knee osteoarthritis (OA) may have quadriceps femoris muscle weakness that is probably related to OA progression and symptom aggravation.\(^2\)\(^,\)\(^3\) Furthermore, considering the important role of the quadriceps femoris muscle in artificial joint function, its condition can substantially affect total knee arthroplasty (TKA) outcomes.\(^4\)\(^,\)\(^5\) Therefore, assessment of quadriceps femoris muscle condition is crucial to establishing management plans for patients with advanced knee OA and predicting TKA outcomes.\(^6\)\(^,\)\(^7\) Although the importance of quadriceps femoris muscle function was reported previously,\(^8\)\(^,\)\(^9\) little is known about factors related to quadriceps femoris muscle volume and its effects on TKA clinical outcomes.

There is no gold standard for measuring quadriceps femoris muscle volume of patients undergoing TKA. Some authors measured quadriceps femoris muscle volume using magnetic resonance imaging (MRI). However, this approach may be impractical, as it is expensive to use in otherwise healthy patients undergoing TKA.\(^8\) Previous studies found that the maximum cross-sectional area (CSA) of the vastus medialis muscle, which is easily assessed on CT, has a good correlation with total quadriceps femoris muscle volume.\(^9\)\(^,\)\(^10\) Of the 4 muscles comprising the quadriceps femoris muscle, the vastus medialis has received most attention because a decrease in its function is suspected to be the key contributor to symptoms and functional deterioration in patients with knee OA.\(^11\)\(^,\)\(^12\) Therefore, the vastus medialis muscle volume measured on CT could be used as a proxy to predict quadriceps femoris muscle volume in patients undergoing TKA.

For evaluating knee OA progression, single-photon emission computed tomography–computed tomography (SPECT-CT) is sensitive to changes in osteoblastic metabolism; metabolic changes indicate stress in the subchondral bone, which is well-correlated with symptoms.\(^13\)\(^,\)\(^14\) Using SPECT-CT, a multifactorial approach could be possible for assessing quadriceps femoris muscle volume with conventional CT images.

Here, we sought to determine whether there was an inter-limb difference in the vastus medialis muscle volumes measured on SPECT-CT in patients after unilateral TKA. We also aimed to determine whether vastus medialis muscle volume was related to OA severity or scintigraphic uptake degree around the knee joint on SPECT-CT. And finally, attempted to investigate the factors, including preoperative vastus medialis muscle volume and scintigraphic uptake degree, associated with the functional outcomes of TKA. We hypothesized that the vastus medialis muscle volume would be wider in the nonoperated limb in patients who underwent unilateral TKA. The muscle volume would be adversely related with OA severity and scintigraphic uptake degree on SPECT-CT. We also hypothesized that increase vastus medialis volume and the low scintigraphic uptake would be associated with better TKA outcomes.

2. Materials and methods

For this retrospective observation study, patients who failed conservative treatment with stage 3,4 unilateral primary varus gonarthrosis according to the Kellgren-Lawrence grade and underwent unilateral TKA from 2011 to 2016 was included this study. Patients who met the following criteria were enrolled: undergone unilateral TKA; underwent standing full-limb anteroposterior (AP) radiograph and standing AP and 45° posteroanterior (PA) radiographs and SPECT-CT of the knee joint before surgery; and clinical assessments included Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index from preoperative state to 2 years postoperatively. We reviewed a collected database of 88 patients who met the inclusion criteria using medical records. Of them, 38 were excluded for the following reasons: follow-up less than 2 years; preoperative valgus deformity; revision TKA; history of operation around the knee, hip, or spine or fracture or septic arthritis involving the knee, hip, or spine; rheumatoid arthritis; and condition that highly compromises patient activity, such as stroke. Fifty patients who underwent unilateral TKA were finally included in this study. All patients gave the consents to use their data for this study, and this study was approved by the Ethics Committee of University Hospital before commencement (No.10-2019-58).

We used standing full-limb AP radiograph. The standing AP and 45° PA radiographs were also used to determine radiographic OA severity with the Kellgren-Lawrence (K-L) grading system.\(^15\)\(^,\)\(^16\) The higher of the measured grades on the 2 radiographs was used. The standing full-limb AP radiograph was obtained using a 35.5 × 129.5 cm grid cassette at a source-to-image distance of 240 cm using a UT 2000 X-ray machine (Philips Research, Eindhoven, the Netherlands) running at 90 kV and 50 mA/s. While checking the standing full-limb AP radiograph, foot rotation was held constant by reference to a foot template on the platform of the radiographic system. In addition, the appropriateness of the knee position (with the patella facing forward) was confirmed on a preview monitor before final radiograph acquisition (Fig. 1).

SPECT-CT images were obtained before TKA using an In finia Hawkeye 4 device (GE Healthcare, Milwaukee, WI), which incorporates CT and a bone scan into a one-step procedure. Each patient was injected with 1110 MBq (30 mCi) Tc-99m hydroxy-methylene diphosphonate, and images were obtained. Four hours after the injection, multiplanar 2-dimensional SPECT images were reconstructed in 3 phases (SPECT: 128 × 128 matrix; 32 frames; 35 seconds per frame; step-and-shoot). Multisilic CT images (140 kV, 70–100 mA) of the entire lower extremity were obtained via multi-planar reconstruction (slice thickness: 2.95 mm; pitch: 1.9 mm; reconstruction interval: 2.95 mm). All radiological images were digitally stored on a picture archiving and communication system (PACS).

The CSA of the vastus medialis was measured on axial SPECT-CT images using PACS software (M-view; Marotech, Seoul, Korea) (Fig. 2). The level showing maximal CSA of the vastus medialis was 20.8% of the femoral length from the most distal end of the lateral femoral condyle on the coronal plane of CT scans of the femur (SD, 2.1%; range, 15.8–27.2%). The maximal CSA of the vastus medialis was divided by BMI and then multiplied by 10\(^\text{4}\) (VmCSA) m\(^4\)/kg to correct bias caused by differences in the heights and weights of individual patients. The degree of scintigraphic uptake at the levels of the tibiofemoral joint was assessed and graded using the scale previously reported: grade 0, no uptake; grade 1, higher uptake than normal cancellous bone; grade 2, same uptake as the articular surface; and grade 3, higher uptake than the articular surface.\(^13\) (Fig. 3). Between the grades measured in the medial and lateral compartments, the higher grade was used.

Clinical outcome evaluations were performed by a single clinical investigator, and the evaluations were conducted preoperatively and at 1 and 2 years after surgery. Outcomes were evaluated using the WOMAC index (Fig. 4).
All statistical analyses were performed using SPSS for Windows (version 19.0; SPSS, Chicago, IL); P values < .05 were considered significant. Differences in the CSA and VmCSA between the 2 lower limbs in unilateral TKA were evaluated using the paired t-test. The associations between VmCSA and scintigraphic uptake degree on SPECT-CT and preoperative factors such as K-L grade on conventional radiographs were determined using analysis of variance. Multivariable analysis was performed to confirm whether VmCSA and scintigraphic uptake degree were associated with TKA outcomes after the adjustment for potential confounders including age, BMI, K-L grade, mechanical axis deviation, preoperative clinical score, and postoperative time as independent variables using a generalized estimating equation to account for the correlation from the same subject. To determine the intra- and interobserver reliabilities of the radiographic and scintigraphic assessments, 2 orthopedic surgeons assessed 30 randomly selected knees twice at a 4-week interval. The intra- and interobserver reliabilities of measurements of the maximum CSA were assessed by calculating intraclass correlation coefficients (ICCs); the reliabilities of uptake grading on SPECT-CT were evaluated using Kappa (K) statistics. The ICCs for the intra- and interobserver reliabilities were 0.80 (range, 0.67–0.88) and the K coefficient was 0.92 (range, 0.67–0.88). Thus, the reliabilities were satisfactory. For sensitivity analysis, we performed a bootstrap resampling technique with 10,000 replicates to examine uncertainty of variables in the model. We could not find any significant bias from the sensitivity analysis.

3. Results

Mean patient age was 70 (range, 56–82) years. There were 41 female patients (82%). The mean body mass index (BMI) was 27 kg/m² (Table 1). The vastus medialis muscle volume was larger in the non-operated limb than in the operated limb in patients who underwent unilateral TKA. The mean VmCSA was greater in the nonoperated limb than in the operated limb (464.7 vs 419.1 cm²; P < .001) (Table 2).

The preoperative OA severity on conventional radiographs and the degree of scintigraphic uptake on SPECT-CT were not related to the preoperative vastus medialis muscle volume. The preoperative K-L grade and scintigraphic uptake were not related to the VmCSA of the operated and nonoperated limbs (P > .05) (Table 3).

Decreased vastus medialis muscle volume was related to a worse clinical outcome after TKA. A lower VmCSA was related to a higher WOMAC index (P < .047). Scintigraphic uptake on SPECT-CT was not associated with clinical outcome after

Figure 1. Preoperative radiographs of 71-year-old woman who underwent a left side total knee arthroplasty. (A) Standing full-limb anteroposterior, (B) 45° flexion posteroanterior (PA). This radiograph indicates K-L grade 4. (C) SPECT -CT indicates grade 3 on the left and grade 1 on the right.
surgery ($P = 0.064$). Confounding factors, including age, preoperative K-L grade, and postoperative time, were related to clinical outcome. Older age at the time of unilateral TKA and more severe preoperative OA on conventional radiographs were associated with worse clinical outcomes ($P < 0.001$ and $P = 0.038$, respectively). The clinical symptoms improved with time until 2 years after surgery ($P = 0.002$). BMI, mechanical axis deviation, and preoperative WOMAC score were not associated with clinical outcomes after surgery. There was no difference between the operated and nonoperated limbs to compare these factors ($P = 0.124$) (Tables 4 and 5).

4. Discussion
The principal finding of this study was that muscle volume of vastus medialis decreased in the operated knee than in the nonoperated knee, and that was correlated with worse postoperative results. However, the preoperative degree of scintigraphic uptake on SPECT-CT was not correlated with muscle volume or clinical outcome after TKA. In patients with end-stage knee OA requiring TKA, it may be reasonable to speculate that OA severity could be related to vastus medialis muscle volume because their knees have not been used properly.
for a long period of time. Therefore, if scintigraphic uptake degree on SPECT-CT is related to OA severity, scintigraphic uptake degree may be related to vastus medialis muscle volume. However, scintigraphic uptake degree was not related to vastus medialis muscle volume or clinical outcome following TKA.

We found that the nonoperated limb had a greater vastus medialis muscle volume than the limb subjected to unilateral TKA. Although there are conflicts in the association between quadriceps femoris muscle strength and knee OA severity,\(^1\) some studies reported that individuals with severe arthritis showed decreased quadriceps femoris muscle strength.\(^{18,19}\) Other study reported that there was no difference in muscle thickness between the operated and nonoperated knees in the TKA group.\(^2\) In this study, the lower vastus medialis muscle volume of the operated limb could be explained by pain, stiffness, reduced range of motion reported in previous studies.\(^{18,19}\)

The smaller CSA of the vastus medialis, which reflects the quadriceps femoris muscle, was recently found to be related to poorer outcomes after TKA. The quadriceps femoris muscle contributes to joint stability in terms of varus and valgus moments in combination with the hamstrings,\(^3\) weakness of these muscle could result in instability and malalignment, which worsen arthritis. Mizner et al\(^6\) found that the condition of the quadriceps femoris muscle will substantially affect the postoperative outcome after TKA.

Several studies have proposed factors to predict the outcome after TKA. Some studies have proposed that higher K-L grade was a strongly related risk factor for subsequent TKA in the nonoperated limb after unilateral TKA, whereas age, sex, BMI did

| Table 1 | Patient characteristics. |
|---------|--------------------------|
| Variables | Mean ± SD | Range |
| Sex (female/male) | 41/9 | NA |
| Age, yr | 70 ± 6.6 | 56–82 |
| BMI, kg/m² | 27 ± 4.2 | 17.8–38.1 |

*BMI=body mass index; NA=not applicable; SD=standard deviation.

1 Data are presented as number of patients.

| Table 2 | An inter-limb difference in the vastus medialis muscle volumes measured on SPECT-CT in patients who underwent unilateral TKA. |
|---------|-------------------------------------------------------------|
| Variables | Operated limb (n=50) | Nonoperated limb (n=50) | P |
| CSA, cm² | 11.2 (3.5) | 12.4 (3.6) | <.001 |
| VmCSA, m⁴/kg | 419.1 (123.2) | 464.7 (133.1) | <.001 |

Data are presented with mean with standard deviation in the parenthesis.

CSA=cross sectional area, VmCSA=the maximal cross-sectional area (CSA) of the vastus medialis was divided by BMI and then multiplied by 10⁴. |
not affect the progression of OA in the nonoperated limb to TKA. In the current study, the K-L grade was associated with the clinical outcome and the BMI did not influence the outcome; this is similar to results from previous studies. In contrast, age was found to be the single most predictive value of subsequent TKA. Hence, patients with older age should anticipate worse clinical outcome following TKA. Ritter et al. reported that age was found to be the single most predictive value of subsequent TKA. Hence, patients with older age should anticipate worse clinical outcome following TKA; however, it was proven that scintigraphic uptake grade was related to VmCSA and the clinical outcome after TKA. On the contrary, the scintigraphic uptake location is known to be associated with the painful regions at the time SPECT-CT is performed. Our findings suggest that scintigraphic uptake on SPECT-CT was beneficial only when it was used to assess the present symptom, not when it was used to predict prognosis after surgery.

The strength of this study was that although no clear association was found, efforts were made to find the relationship between degree of scintigraphic uptake (bone metabolism) and the patient’s knee condition before and after TKA using SPECT-CT. Some limitations should be noted when interpreting our findings. First, the sample size was relatively small. Furthermore, the subject group was predominantly female. There may be differences in the results of studies between men and women of the relationship between muscle strength and postoperative

### Table 3
Preoperative vastus medialis muscle volume (VmCSA) according to preoperative Kellgren-Lawrence grade and scintigraphic uptake degree on SPECT-CT in patients who underwent unilateral TKA.

| Variables | Kellgren-Lawrence grade | P | Scintigraphic uptake on SPECT-CT | P |
|-----------|-------------------------|---|-------------------------------|---|
| Operated limb (n = 50) | Operated limb (n = 50) | Operated limb (n = 50) | Operated limb (n = 50) | Operated limb (n = 50) |
| NA | NA | NA | NA | NA |
| 1 (n = 5) | 2 (n = 2) | 3 (n = 25) | 4 (n = 23) | 0 (n = 0) | 1 (n = 2) | 2 (n = 2) | 3 (n = 46) |
| 368.3 | 408.8 | 434.1 | 0.660 | NA | 489 | 419.4 | 416.5 | .730 |
| 0.124 | 0.304 | 0.429 | 0.208 | 0.001 | 0.001 | 0.001 | 0.001 |

NA = not applicable; VmCSA = the maximal cross-sectional area (CSA) of the vastus medialis was divided by BMI and then multiplied by 10^4.

### Table 4
Factors associated with WOMAC index in patients who underwent unilateral TKA (univariable analysis).

| Variable | Estimate | SE | Z | P | 95% CI | Lower | Upper |
|----------|----------|----|---|---|--------|-------|-------|
| Age      | 0.507    | 0.152 | 3.330 | .001 | 0.208 | 0.805 |
| BMI      | 0.344    | 0.094 | 0.873 | .383 | -0.429 | 1.117 |
| CSA      | -0.005   | 0.004 | -1.499 | .134 | -0.012 | 0.002 |
| VmCSA    | -0.201   | 0.100 | -2.002 | .045 | -0.397 | -0.004 |
| Scintigraphic uptake | 2.528 | 1.956 | 1.852 | .064 | -0.147 | 5.202 |
| K-L grade | 2.590 | 1.044 | 2.252 | .024 | 0.504 | 4.596 |
| Mechanical axis deviation | 0.137 | 0.226 | 0.606 | .545 | -0.306 | 0.579 |
| Preoperative WOMAC index | 0.177 | 0.121 | 1.470 | .142 | -0.059 | 0.414 |
| Operated vs nonoperated limb | 3.842 | 2.500 | 1.537 | .124 | -1.057 | 8.742 |
| Postoperative time | -4.294 | 1.428 | -3.007 | .003 | -7.093 | -1.495 |

BMI = body mass index, CI = confidence interval, CSA = vastus medialis cross sectional area, K-L grade = Kellgren-Lawrence grade, Scintigraphic uptake = scintigraphic uptake grade on SPECT-CT, SE = standard error, VmCSA = the maximal cross-sectional area (CSA) of the vastus medialis was divided by BMI and then multiplied by 10^4.

P values marked in bold indicate numbers that are statistically significant.

### Table 5
Factors associated with WOMAC index in patients who underwent unilateral TKA (multivariable analysis).

| Variable | Estimate | SE | Z | P | 95% CI | Lower | Upper |
|----------|----------|----|---|---|--------|-------|-------|
| Age      | 0.622    | 0.159 | 3.908 | <.001 | 0.310 | 0.934 |
| VmCSA    | -0.184   | 0.093 | -1.989 | .047 | -0.366 | -0.003 |
| K-L grade | 2.014 | 0.969 | 2.077 | .038 | 0.114 | 3.914 |
| Preoperative WOMAC index | 0.886 | 0.120 | 0.712 | .476 | -0.150 | 0.321 |
| Postoperative time | -4.551 | 1.461 | -3.115 | .002 | -7.414 | -1.688 |

CI = confidence interval, K-L grade = Kellgren Lawrence grade, SE = standard error, VmCSA = the maximal cross-sectional area (CSA) of the vastus medialis was divided by BMI and then multiplied by 10^4.

P values marked in bold indicate numbers that are statistically significant.
clinical outcome. Therefore, care must be taken to apply our results to patients with different sex distributions. However, OA is common in female populations; thus, our findings can provide valuable information. Second, we used SPECT-CT images to measure the maximum CSA of the vastus medialis muscle; this measurement may be less precise than that afforded by MRI. However, several studies have shown that CT affords satisfactory accuracy when used to measure thigh muscle parameters. In addition, our intra- and interobserver reliabilities were satisfactory. Third, this study was performed retrospectively. Thus, there can be some potential source of bias. Due to the sex ratio tendency to woman and small sample size of this study, generalizability is limited. Prospective study with larger sample size should be performed in the future.

5. Conclusion
Muscle volume of vastus medialis decreased in the operated knee than in the nonoperated knee, and that was correlated with worse postoperative results. Even if the preoperative volume of vastus medialis were not related to radiographic OA severity, preservation and improvement of the muscle mass of the knee undergoing TKA is important.

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