

Fig. 2. The gait kinematics and kinetics for each walking speed. The dashed lines represent mean values for the preferred walking speed. The solid lines represent the mean values for the faster walking speed. The thick lines are for the involved side. † Statistically significant for the intra-limb comparison in the involved side, and ‡ in the contralateral side. †‡ Statistically significant for the inter-limb comparison.

and kinetics during stance can be attributed to dysfunction of the involved-side knee extensors resulting from knee reconstruction. Five of eight patients kept their knee extended during early stance, and one did not extend the knee after mid-stance, whereas two patients exhibited a two-peak knee flexion, the so-called “double knee action.” All patients tended not to change the gait biomechanics of the operated knee when walking faster, although different walking patterns were exhibited. We also observed an increased involved-side knee flexion during swing at a faster walking speed; however, an asymmetric change in joint kinetics (i.e., maximal knee extension moment and ankle plantarflexion moment) cannot explain the increased involved-side knee flexion during swing. In view of the internal muscle activities, simulation studies suggest that the activity of the rectus femoris during early swing prevents excessive knee flexion [24,25]. Thus, the inactivity of the rectus femoris previously reported in this patient population [7] might increase the involved-side knee flexion during swing during faster walking speeds, which indicates that decelerating knee flexion during swing is difficult. The asymmetric change in the maximal dorsiflexion angle during late stance could be associated with those in maximal ankle plantarflexion moment and ankle concentric power, indicating that the patients could not increase the forces generated by the involved-side plantarflexors.

Walking faster, or increasing the walking distance per unit time, requires additional mechanical work. Therefore, we can evaluate the gait asymmetry from the viewpoint of mechanical work by observing the changes in joint power (work per unit time) during faster walking. Joint power analysis showed that the two hip power parameters on both sides increased at a faster speed, although the change in contralateral maximal hip concentric power during early stance was marginally statistically significant. Conversely, the knee and ankle power changed asymmetrically. The greater ankle eccentric power during stance on the involved side, which has not been observed in the contralateral side or in healthy subjects [15,16,20,21], could be attributed to the decreased knee angular movement during this phase. Decreased involved-side knee flexion during early stance, regardless of gait pattern, may alter ankle joint power, because a greater angular acceleration and deceleration are required if the knee flexion is small after initial contact.

Our study has several limitations. First, our study size was small ($n = 8$), preventing us from guaranteeing the statistical power in each comparison, which would allow discussion of only the detected differences. Thus, we carefully focused on gait parameters that were not significantly different between the two walking speeds considering the intra- and inter-limb difference and variation. Second, the heterogeneous patient characteristics made

the target population less specific, which often occurs in this patient population [3,12,13]. This heterogeneity might have increased the variability of gait parameters and also weakened the statistical power. However, we believe that the inclusion and exclusion criteria of this study enabled us to recruit patients with good functional outcomes, which validates our comparison. Third, there may have been selection bias; the patient population achieved good functional outcomes (they could walk without an assistive device). Patients with compromised physical function might choose a different strategy to cope with the loss of lower limb function and also with the reduced second peak in vertical ground reaction force. Lastly, we have some other methodological problems; we did not set a target walking speed for preferred and faster walking because walking ability varied among the patients. Although we attempted to distract patients from focusing on the force plates during measurement, the size of the forceplates used for this study might have restricted step length, especially during fast walking because we considered only those trials in which foot contact on the force plates was achieved by both feet. We also lack information on muscle activities and the muscle strength of the hip extensors and plantarflexors which would help elaborate the discussion.

In conclusion, we observed that patients tended to rely on the bilateral hip, ankle, and contralateral knee to generate the additional power needed for walking faster. Kinetic analysis revealed that patients did not increase the involved-side vertical body support during late stance to walk faster, which is associated with a small increase in ankle plantarflexion moment and concentric power. In patients who underwent endoprosthetic knee replacement who need to walk faster, our study findings indicate the lower limb muscles that should be trained (the bilateral hip extensors, contralateral knee extensors, and bilateral plantarflexors). Conversely, for those who experienced fatigue or pain in specific lower limb muscles or joints, our study findings could help manage and redistribute the mechanical load on the lower limbs. The ability to vary the walking speed could be important to improve the quality of life of patients who undergo endoprosthetic knee replacement.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Extension gap needs more than 1-mm laxity after implantation to avoid post-operative flexion contracture in total knee arthroplasty

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Abstract

Purpose In total knee arthroplasty (TKA), a high soft-tissue tension in extension at the time of operation would cause a post-operative flexion contracture. However, how tight the extension gap should be during surgery to avoid a post-operative flexion contracture remains unclear. The hypothesis is that some laxity in the intraoperative extension gap is necessary to avoid the post-operative flexion contracture.

Methods A posterior-stabilized TKA was performed for 75 osteoarthritic knees with a varus deformity. The intraoperative extension gap was measured using a tensor device that provides the gap length and the angle between the femoral component and the tibial cut surface. The medial component gap was defined as the gap calculated by subtracting the selected thickness of the tibial component, including the polyethylene liner, from the extension gap at the medial side. Then, the patients were divided into three groups according to the medial component gap, and post-operative extension angle measured 1 year after the surgery was compared between each groups.

Results One year post-operatively, a flexion contracture of more than 5° was found in 0/34 patients when the medial component gap was more than 1 mm, in 2/26 (8 %)

patients when the gap was between 0 and 1 mm, and in 3/15 (20 %) patients when the gap was <0 mm. Three factors were associated significantly with the post-operative extension angle: age, preoperative extension angle, and medial component gap.

Conclusion The intraoperative extension gap is related to the post-operative extension angle. Surgeons should leave more than 1-mm laxity after the implantation to avoid the post-operative flexion contracture. As a clinical relevance, this study clarified the optimal extension gap to avoid the post-operative flexion contracture.

Level of evidence Prospective comparative study, Level II.

Keywords Total knee arthroplasty · Flexion contracture · Extension gap · Soft-tissue tension

Introduction

It is important to avoid flexion contractures after total knee arthroplasty (TKA). When a flexion contracture is present post-operatively, the quadriceps muscle must generate an increased force to stabilize the flexed knee during weight-bearing. This force is distributed between the posterior half of the tibial plateau and the patellofemoral joint [1, 15]. Therefore, patients with persistent flexion contractures can experience anterior knee pain and altered gait mechanics, and thus be dissatisfied with their arthroplasty [13, 21, 25].

Risk factors for post-operative flexion contractures have been reported as having a preoperative flexion contracture, male gender, and/or advanced age [11, 21]. Additionally, it has been shown that a greater post-operative flexion contracture forms with higher soft-tissue tension in extension at the time of operation [2, 4, 23]. By contrast, loose soft tissue would cause instability in extension that may relate

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to a patient's symptom or implant survival [22, 24]. However, optimal soft-tissue tension is generally determined by the experience and feeling of the individual surgeons, and there is no report, which evaluated quantitatively the relationship between the intraoperative extension gap and post-operative flexion contracture. It remains unclear how tight the knee can be left in extension during surgery to avoid a post-operative flexion contracture. It would be very helpful if a single numerical value could be determined that serves as a target for the appropriate soft-tissue tension in TKA. With this numerical target, surgeon can intraoperatively determine the optimal soft-tissue tension to avoid the post-operative flexion contracture.

This study evaluated the effect of an intraoperative extension gap on post-operative flexion contractures. The extension gap was measured with a tensor device in the presence of the femoral component, and the post-operative flexion contracture was evaluated with radiographs. The hypothesis is that some laxity in the intraoperative extension is necessary to avoid the post-operative flexion contracture. The aim of this study is to clarify the optimal extension gap to avoid it. Further, the risk factors associated with post-operative flexion contracture were examined using multiple linear regression analysis with age, body mass index (BMI), preoperative flexion contracture, intraoperative soft-tissue tension, and/or sagittal alignment of components.

Materials and methods

Fifty-nine patients who had surgery for the treatment for advanced medial compartment osteoarthritis were recruited prospectively, and 75 knees were performed implantation with the Nexgen Legacy Posterior-Stabilized prosthesis (Zimmer, Warsaw, USA). The patient population comprised 53 women and 6 men with a median age of 77 (range 51–89). None of the subjects had a history of knee injuries or ipsilateral lower extremity surgery prior to TKA.

A single experienced surgeon (SM) performed all operations. Measured resection technique was used for bone cutting. The components were aligned perpendicular to the mechanical axis. For the femur, it was rotationally aligned to the surgical epicondylar axis. For the tibia, the rotational alignment was adjusted to the anteroposterior axis connecting the medial third of the patellar tendon attachment and the centre of the cut surface. Following the bone resections of femur and tibia, and the removal of osteophytes, soft-tissue balancing of the knee was adjusted to be within 5° of imbalance at extension. The knee was confirmed having achieved full extension when the trial components were inserted.

Assessment of “component gap” in extension

The extension gap was measured with the femoral trial component using an offset-type tension device (ORF-tensor®; Zimmer). The tension device consists of three parts: an upper seesaw plate, a lower platform plate, and an extra-articular main body and presents two measurements: the centre joint gap and the angle between the seesaw plate and the platform plate (Fig. 1a). The surgeon can evaluate soft-tissue balance under a constant joint distraction force between the seesaw plate and the platform plate from 133.4 N to 355.84 N, using a specially made torque drive. The joint distraction force was set at 176.4 N, following a report that the joint gap at full extension with 176.4 N of joint distraction force corresponded most closely to the insert thickness [14]. After finishing cutting bones and ligament balancing, the femoral trial component was inserted and the tension device was installed between the femoral trial component and the cutting surface of the tibia with the patella was reduced. The distraction force of 176.4 N was applied to the tension device using torque driver for exclusive use, and the gap length and the angle between the seesaw plate and the platform plate was measured.

The measurements with the tensor were obtained three times by one surgeon (SM), and the average was used for data. The average errors between repeated measurements for the joint gap and angle were 0.5 mm and 0.4°, and the intraclass correlation coefficients (ICC) for the measurements of the joint gap and angle were 0.98 and 0.90, respectively, in our previous study [19]. To evaluate the average errors and the intraobserver reproducibility, the measurement was taken three times by one examiner (SM) on the nine knees randomly selected from the study group. These data were obtained using the same tension device and performing same surgeon as this study. By making these measurements and measuring the transverse diameter of the tibial component, the extension gap at the centre of the medial compartment—called the “medial extension gap”—can be calculated with the following formula: “centre joint gap”— $0.25 \times$ “diameter of tibial component” $\times \tan$ “varus angle” (Fig. 1b) [19]. To evaluate intraoperative soft-tissue tension, a “medial component gap” was defined, which was the distance calculated by subtracting the selected thickness of the tibial component including the polyethylene liner from the medial extension gap (Fig. 1c) [19]. Although the extension gap at the lateral side can also be obtained by calculating in the same way, only the values from the medial side was assessed for this investigation because all cases were varus knees and the medial extension gap was smaller than the lateral extension gap.

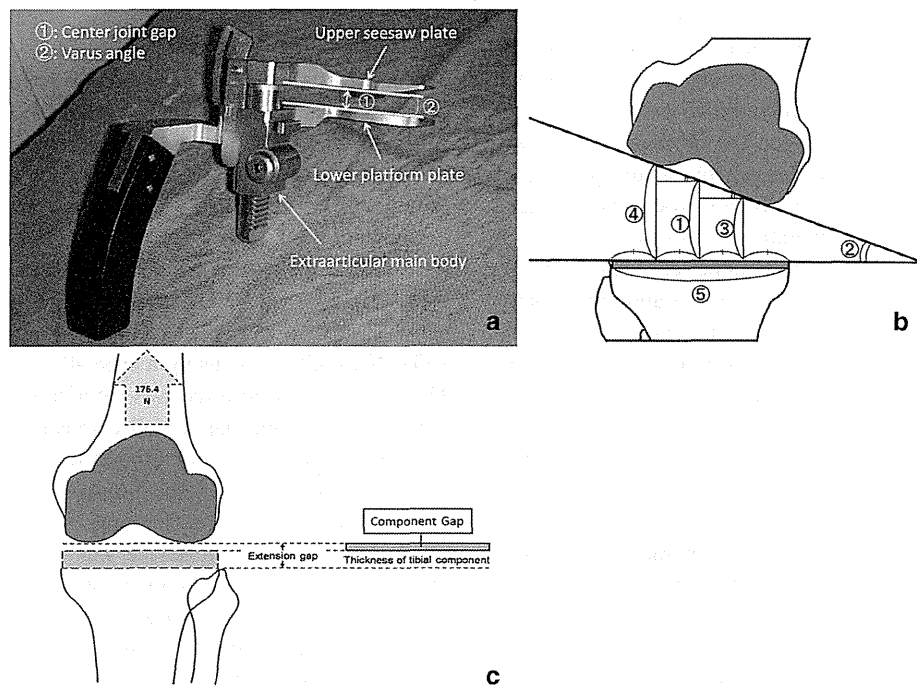


Fig. 1 **a** The tension device consists of three parts: an upper seesaw plate, a lower platform plate, and an extra-articular main body. This device can be used in the presence of the femoral component. Two measurements were taken: ① the centre joint gap and ② the angle between the seesaw plate and the platform plate. **b** The diagram illustrates the following parameters: ① centre joint gap, ② varus angle, ③ medial joint gap, ④ lateral joint gap, and ⑤ transverse

diameter of the tibial component. Using these measurements, we calculated the medial and lateral joint gaps as follows: ③ = ① - $0.25 \times ⑤ \times \tan ②$ and ④ = ① + $0.25 \times ⑤ \times \tan ②$. **c** The extension gap with the femoral component was measured by applying 176.4 N of distraction force. The component gap was defined as the distance that was calculated by subtracting the thickness of the tibial component including the polyethylene liner from the extension gap

Assessment of post-operative extension angle

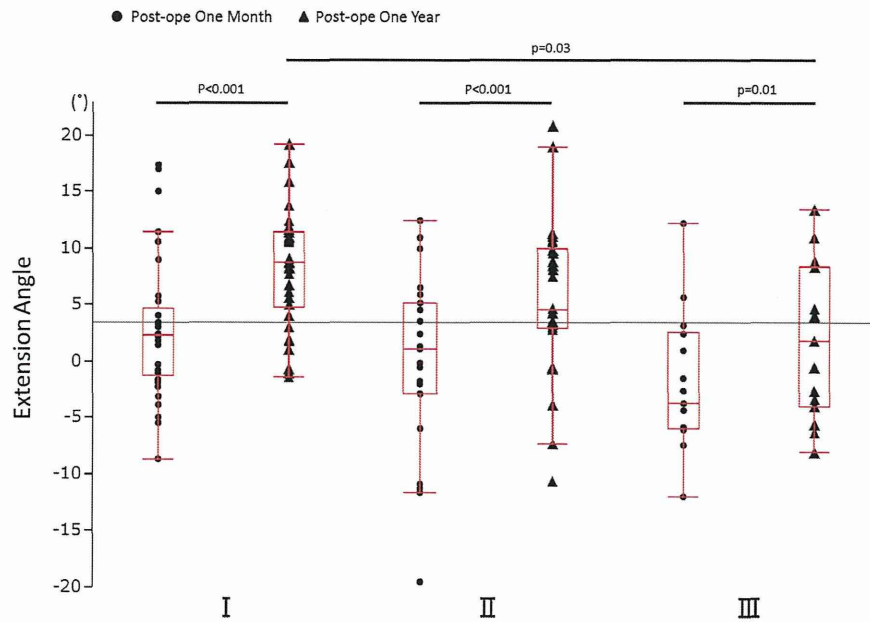
To assess the extension angle accurately, a lateral radiograph of the knee in passive full extension was used before surgery, at 1 month, and at 1 year post-operatively. The radiographs were taken with the heel supported 10 cm off the table and the patients were asked to relax the knee for extension. The extension angle was the angle measured between the axis of the distal femur and the axis of the proximal tibia from true lateral radiographs. The sagittal alignment of components was evaluated using the same radiograph. When the value was expressed as a positive value, the component was aligned in flexion relative to the axis of the distal femur and to the axis of the proximal tibia. Furthermore, full-length weight-bearing anteroposterior radiographs were taken with the patella positioned at the centre of the femoral condyles. The hip–knee–ankle angle defined the angle between the mechanical axes of the femur and the tibia, which was the line connecting the centre of the hip with that of the knee and the centre of the knee with that of the ankle joint. A positive value was expressed as varus. In addition to radiographic analysis, the Knee Society pain score was used for evaluation preoperatively

and at 1 year post-operatively. This study was approved by the institutional review board of Institutional Review Board in Kyushu University (ID number of the approval: 24–25). To participate in this study, informed consent was obtained from all the patients.

Statistical analysis

To investigate the relationship between the intraoperative laxity at the medial component gap and the incidence of post-operative flexion contracture, the patients were divided into three groups according to the medial component gap: Group I, patients whose medial component gap was more than 1 mm; Group II, whose gap was between 0 and 1 mm; and Group III, whose gap was <0 mm. We examined the changes of the extension angle from 1 month to 1 year after surgery in each group using a paired *t* test. The mean post-operative extension angle was compared among the groups using ANOVA with a Tukey–Kramer post hoc test. The rates of post-operative flexion contracture and hyperextension at 1 year after surgery were compared among the groups using Pearson Chi-square test. Flexion contracture was defined as the knee whose flexion angle

Fig. 2 Comparison of mean post-operative extension angle at 1 month and 1 year after surgery, categorized by the medial component gap. In all the groups, the extension angle significantly improved from 1 month to 1 year after surgery. The mean post-operative extension angle of Group III was significantly smaller than that of Group I, significant at $p < 0.05$



(the angle between the axis of the distal femur and the axis of the proximal tibia on radiograph in full extension) was more than 5°. Hyperextension was defined as a knee whose extension angle was more than 10° [21]. A power analysis was performed to estimate the required sample size. When standard deviation was assumed to be 6.5, the difference in post-operative knee extension angle among the groups was assumed to be 3°. To achieve 80 % power ($\alpha = 0.05$), the estimated sample size was 71 knees.

To investigate the risk factors associated with the post-operative extension angle at 1 year, multiple linear regression analysis was performed using six risk variables: age, BMI, preoperative extension angle, medial component gap, and sagittal alignments of the femoral and tibial components. JMP® statistical software (version 9; SAS Institute, Inc, Cary, NC, USA) was used to analyse the data. The level of significance was determined as $p < 0.05$.

Results

The mean component gaps were 1.0 ± 1.5 mm on the medial side and 3.7 ± 2.0 mm on the lateral side. The mean extension angle measured by a lateral radiograph of the knee in full extension was $-1.2^\circ \pm 8.2^\circ$ preoperatively, $0.8^\circ \pm 6.9^\circ$ at 1 month, and $6.0^\circ \pm 6.5^\circ$ 1 year after surgery. In groups categorized by the medial component gap, there were significant improvements in the extension angle from 1 month to 1 year after surgery in all groups. The mean post-operative extension angle of Group III was significantly smaller than Group I ($p < 0.05$) (Fig. 2). A total of five patients (7 %) had a residual flexion

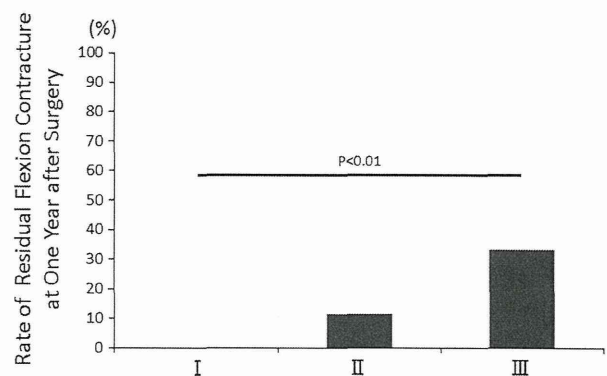


Fig. 3 Rate of residual flexion contracture in patients 1 year after surgery in groups categorized by the medial component gap. When the medial extension gap was smaller than the thickness of the tibial component including the polyethylene liner, it was associated with a higher risk of post-operative flexion contracture, significant at $p < 0.05$

contracture 1 year after surgery. The degrees of extension contractures were the range of 5.6–10.6. There were no patients with a residual flexion contracture 1 year after surgery in Group I, whereas there were some in Groups II and III. The rate of residual flexion contracture in Group III was significantly greater than that in Group I (Fig. 3). The mean Knee Society pain score was significantly improved from 35.9 ± 14.2 (mean \pm SD) preoperatively to 95.2 ± 5.1 1 year post-operatively ($p < 0.0001$). The mean hip–knee–ankle angle was significantly improved from $13.8^\circ \pm 4.8^\circ$ preoperatively to $0.5^\circ \pm 2.9^\circ$ 1 month post-operatively ($p < 0.0001$) on the full-length weight-bearing anteroposterior radiographs. The sagittal alignment

Table 1 Demographic characteristics of enrolled patients

Variable	I	II	III
Number of knees	34	26	15
Age (years) ^a	76 ± 7	74 ± 6	74 ± 8
Sex (% male) ^b	10	4	13
Diagnosis (% osteoarthritis)	100	100	100
Preoperative extension angle ^a	7 ± 7	-3 ± 11	-1 ± 8
Preoperative hip–knee–ankle angle (°) ^a	13 ± 5	15 ± 5	14 ± 4
Preoperative knee society score ^a	40 ± 14	32 ± 14	34 ± 16
Post-operative knee society score ^a	95 ± 6	96 ± 4	96 ± 3

^a Values are expressed as mean ± SD

^b Because there were few men, it was not possible to analyse differences between men and women

was $0.1^\circ \pm 2.9^\circ$ on the femoral component and $5.0^\circ \pm 2.7^\circ$ on the tibial component. No patient had evidence of clinical instability or anterior knee pain on physical examination. There were no differences among groups in age, preoperative extension angle, hip–knee–ankle angle, or Knee Society pain score (Table 1).

With the use of the regression equation featuring the six independent variables studied, three were significantly associated with post-operative extension angle: age, preoperative extension angle, and the medial component gap. There were significantly negative correlations between age and the post-operative extension angle. On the other hand, there were positive correlations between the post-operative extension angle and the preoperative extension angle, and between the post-operative extension angle and the medial component gap.

The variation in the post-operative extension angle accounted for 35 % ($R^2 = 0.35$). It had significant correlations with age ($p = 0.03$), preoperative extension angle ($p < 0.0001$), and medial component gap ($p = 0.02$), but not with BMI (n.s.), sagittal alignment of femoral component (n.s.), and sagittal alignment of tibial component (n.s.). The relationship showed that greater age and a larger preoperative flexion contracture and a smaller component gap were associated with a greater risk of flexion contracture formation.

Discussion

The most important finding in this study is that to avoid post-operative flexion contracture, a 1-mm medial component gap, which is quantitatively measured using a tensor device, should be left during TKA surgery for varus knees. The appropriate soft-tissue tension needed at the time of operation to avoid post-operative flexion contracture

formation has not yet been known. Surgeons try to find an optimal thickness of polyethylene liners by manual varus–valgus testing, but accuracy depends on the experience of the individual surgeon. Therefore, many surgeons try to become skilled in getting a feel for proper tensioning. However, objective data are needed to determine the proper tension in order to avoid a post-operative flexion contracture. In this study, we used the extension gap, which was measured with a tensor device, as an objective parameter evaluating intraoperative soft-tissue tension. Although the extension gap has been commonly used as a guide to perform the bone cut and the soft-tissue release at the time of operation [2, 9, 16, 26], it has not been used as a prognostic indicator of post-operative results. The “component gap” was defined as a value calculated by subtracting the thickness of the selected tibial component from the extension gap with the femoral component. This is the first study, to our knowledge, that examined whether the measured extension gap could be a useful indicator for post-operative flexion contracture.

This study focused on the “component gap”, which is one of the references for intraoperative soft-tissue tensioning. The “component gap” can be adjusted by surgical procedures, such as bone cutting, ligament releasing, and the selection of components. Our results showed that when the medial component gap was <0.0 mm, it was associated with a greater risk of flexion contracture (20 %). The risk was decreased to 8 % when the medial component gap ranged from 0.0 to 1.0 mm and it was 0 % when more than 1.0 mm. Therefore, this study suggests that the medial component gap should be more than 1.0 mm to avoid post-operative flexion contracture formation.

Evaluation of the extension gap and the extension angle is important to explore what extent of intraoperative soft-tissue tension is needed to fully extend the knee post-operatively. The recent review by Asano et al. [2] has shown that higher intraoperative soft-tissue tension was more likely to lead to flexion contracture formation. Koh et al. assessed the extension space, which is defined as the gap calculated by subtracting the femoral and tibial component thickness, including the PE insert, from the extension gap. Their results showed a counterintuitive finding that larger extension gap was more frequent than in the no-flexion contracture group [10]. These studies did not show what extent of tension was appropriate to avoid a contracture. The authors measured the extension angle in increments of 5° using a goniometer, and the extension gap was evaluated without the femoral component. The accumulation of errors from positioning the limb, positioning the goniometer, and rounding the angle to the nearest 5° might result in a substantial measurement error. Some authors report that radiographic measurements are more accurate than using a goniometer [6, 7, 12]. Therefore, the

extension angle was measured by radiography in this study. Additionally, it is possible that the extension gap was overestimated in the absence of the femoral component. The extension gap is usually measured by using a spacer block or a tension device; however, in most cases, it is evaluated without the femoral component [2, 5, 9, 10, 16, 26]. Recently, it was reported that the extension gap is overestimated when measured without the femoral component because the tension of posterior capsule decreases without the posterior femoral condyle [17, 18]. Therefore, the current study measured the extension gap in the presence of the femoral component. Aunan et al. [3] measured intraoperative component gap by custom-made spatulas that can be used with the femoral and tibial components. This can be another method to evaluate the component gap intraoperatively.

According to this study, to avoid a post-operative flexion contracture, the thickness of the tibial component should be 1.0–2.0 mm smaller than the measured extension gap with the femoral component at 176.4 N force applications. The component gap at the medial side was assessed by calculating from the centre gap and the inclination angle of the extension gap. It should be noted that the medial extension gap is smaller than the centre gap if varus imbalance is left in extension. For example, a 4° residual varus imbalance would decrease the medial extension gap by 1 mm compared with the centre extension gap if the width of tibia is 70 mm. Therefore, even if the surgeon selected the thickness of tibial insert as 1 mm thinner than the indicated centre gap, the component gap would be <1 mm at the medial side in this situation. As a result, the risk of post-operative flexion contracture increases.

The results of this study suggest that age, a preoperative flexion contracture, and intraoperative soft-tissue tension are related to post-operative flexion contracture formation. BMI and sagittal alignment of components are not significantly associated with post-operative flexion contracture formation. It is well known that preoperative flexion contracture is a potential risk factor [11, 21], and there are some reports that increasing age is a risk factor [8, 21]. The results of this study agree with those previous studies. The current study also showed that intraoperative soft-tissue tension is related to post-operative flexion contracture formation.

There are some limitations to this study. First, this study was limited to the medial compartment of osteoarthritic knees in which surgery had been performed with the posterior-stabilized prosthesis. Therefore, valgus knees or other diseases cannot be generalized by our results. Secondly, in the present study, the offset-type tension device (ORF-tensor®; Zimmer) with the joint distraction force was applied at 176.4 N. Therefore, different results would be obtained if different device or distraction forces were used. Third, measured resection technique was used and only the

extension gap was evaluated. Pang HN et al. [20] reported that using computer-assisted gap balancing technique, post-operative flexion contracture was few than measured resection technique. Therefore, using different surgical technique may bring different results, and the flexion gap and flexion–extension gap mismatch cannot be made mention from our study. Laxity about the same as in extension gap will remain in flexion gap, if the extension gap and flexion gap are equal. However, leaving flexion gap laxity of one to 2 mm will not occur flexion instability. Fourth, there is a possibility that the thickness of cement would influence to the actual extension gap, because the component gap was measured before cementing. However, its influence should be minimal. Lastly, this study did not define what extent of component gap size was acceptable, because there were few cases where the component gap was too large.

Conclusion

Intraoperative soft-tissue tension affected the formation of a post-operative flexion contracture. The “component gap” derived from the extension gap with the femoral component and the thickness of the tibial component can be one of the parameters used to evaluate intraoperative soft-tissue tension. When the medial component gap was more than 1.0 mm, it was associated with a low risk of flexion contracture formation. The component gap is a useful reference to select the proper thickness of the tibial component for the extension gap in TKA.

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Ultrasound Can Detect Macroscopically Undetectable Changes in Osteoarthritis Reflecting the Superficial Histological and Biochemical Degeneration: Ex Vivo Study of Rabbit and Human Cartilage

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Abstract

Recognizing subtle cartilage changes in the preclinical stage of osteoarthritis (OA) is essential for early diagnosis. To this end, the ability of the ultrasound signal intensity to detect macroscopically undetectable cartilage change was investigated. In this study, cartilage of rabbit OA model and human OA samples was examined by macroscopic evaluation, ultrasound signal intensity, histology with Mankin scores, and Fourier transform infrared imaging (FTIR) analysis. Rabbit OA was induced by anterior cruciate ligament transection and evaluated at 1, 2, 4 and 12 weeks. Twenty human samples were harvested during total knee arthroplasty from OA patients who had macroscopically normal human cartilage (ICRS grade 0) on the lateral femoral condyle. In the animal study, there was no macroscopic OA change at 2 weeks, but histology detected degenerative changes at this time point. Ultrasound signal intensity also detected degeneration at 2 weeks. In human samples, all samples were obtained from macroscopically intact site, however nearly normal ($0 \leq$ Mankin score < 2), early OA ($2 \leq$ Mankin score < 6), and moderate OA ($6 \leq$ Mankin score < 10) samples were actually intermixed. Ultrasound signal intensity was significantly different among these 3 stages and was well correlated with Mankin scores ($R = -0.80$) and FTIR parameters related to collagen and proteoglycan content in superficial zone. In conclusion, ultrasound can detect microscopic cartilage deterioration when such changes do not exist macroscopically, reflecting superficial histological and biochemical changes.

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Introduction

Osteoarthritis (OA) is a slow progressive degenerative joint disease and is a leading cause of impaired mobility in the elderly [1]. Although it is clear that the early diagnosis of OA is important, there is no established method to detect very early or subtle changes in the OA cartilage. Clinically, plain radiographs are still the gold standard for staging OA. However, in the early stage of OA, little or no changes are apparent in plain radiographs [1]. Magnetic resonance imaging is more powerful tool than plain radiographs for the early diagnosis of OA, however cost and availability still remain significant hurdles [2]. It is useful to develop methods to detect such early changes in the cartilage. Moreover, basic studies detecting subtle changes in the cartilage matrix that accompany the progression of OA are pivotal in improving diagnostic methods.

Quantitative ultrasound is a candidate method for detecting subtle changes in the cartilage [3]. Various unique ultrasound devices have been used to investigate cartilage and the potential of

ultrasound to evaluate subtle changes in the cartilage is promising [3,4]. We developed our ultrasound noncontact method to evaluate the cartilage in an animal model. More recently, an ultrasound noncontact arthroscopy probe was used to evaluate knee and elbow cartilage during surgery [5,6,7]. Our recent report shows that the ultrasound signal intensity (US signal intensity) is useful for differentiating normal (ICRS grade 0) from slightly degenerated cartilage (ICRS grade 1) [7]. We believe that this ultrasonic noncontact probe is useful in evaluating subtle changes in the cartilage.

Our hypothesis is that the US signal intensity is sufficiently sensitive to detect the microscopic degeneration of articular cartilage. Therefore, we determined whether ultrasound can detect macroscopically undetectable histological changes in OA by using a rabbit OA model. We also used human macroscopically intact cartilage samples (ICRS grade 0) to clarify the ability of ultrasound to differentiate cartilage that has such intact surface.