Correlation of Knee Instability With Alignment And Repetitive Physical Activity In Patients With Knee Osteoarthritis: A Cross-Sectional Study

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Abstract

Objectives. Malalignment, dynamic knee instability, and repetitive physical activity are considered biomechanical risk factors for knee osteoarthritis (KOA), though the correlations among these factors are poorly understood. The purpose of this study was to elucidate the relationship between knee instability and alignment, and to determine the effects of repetitive physical activity on knee instability in patients with KOA.

Methods. The study subjects were 68 patients with radiographic tibiofemoral KOA and 68 control subjects. Each participant underwent clinical evaluation, muscle strength test, radiography, and knee instability test. Instability was evaluated before and after repetitive stepping exercise using triaxial accelerometer.

Results. Mediolateral acceleration correlated (p<0.01) with two coronal alignments (mechanical axis; HKA and joint line convergent angle; JLCA). Pearson correlation coefficient was small (r=0.23-0.24) before but increased after stepping (r=0.28-0.33). Increased mediolateral acceleration after stepping correlated with JLCA (r=0.37, p<0.001). There were significant differences in coronal alignments, gait speed, mediolateral acceleration, and accelerations in all directions between the control and KOA groups. Anteroposterior acceleration did not correlate with sagittal knee alignment. Multiple logistic regression analysis identified HKA/JLCA, and increased mediolateral acceleration after stepping as significant diagnostic predictors of KOA.

Conclusion. We found a direct relationship between knee instability and knee alignment or repetitive physical activity. Repetitive stepping activity significantly increased mediolateral acceleration in KOA patients, compared to the control. Stepping increased the correlation between mediolateral acceleration and coronal alignment. In knees with large JLCA, repetitive stepping provided much larger mediolateral instability. Our results suggest that, in addition to JLCA, the increase in mediolateral acceleration after repetitive physical activity, possibly contributes to the development of KOA.

Trial registration

Tan-nan Regional Medical Center TRMC No. 2018-1

Introduction

Malalignment of the knee is a major risk factor for the development and progression of knee osteoarthritis (KOA) (1–3). Evidence suggests that changes in the geometry of the articular surface affect the biomechanical properties of the joint, which can ultimately result in damage of the articular cartilage (4–7). Another pathological factor in KOA is mechanical stress resulting from high physical activity of daily living or occupation (8–12). For example, prolonged or repeated squatting (8, 10, 11) and stressful stair climbing activity are considered risk factors for KOA (8, 9, 12), although a few groups have argued that high physical activity is not associated with the incidence or worsening of KOA (13, 14).
Knee joint laxity and instability are also major factors that contribute to the physical function of the knee joint and risk factors for KOA (15–20). In this regard, varus thrust during walking is considered a risk factor for radiographically-confirmed progression of medial (RKOA) (21, 22), and for the development and worsening of MRI-confirmed medial tibiofemoral lesion (23). Knee thrust is usually diagnosed by physical examination, though Change et al (24) used a motion analysis system to demonstrate a close association in OA patients between knee thrust and peak varus angle and angular velocity. However, only a few studies have examined the direct relationship between knee instability and alignment or physical activity. Kuroyanagi et al (25) used the varus-valgus angle, representing the amount of thrust, and demonstrated its correlation with radiographic alignment. Our group reported an increase in the antero-posterior and mediolateral laxity of the knee after stair climbing in patients with mild KOA (26). However, the knee joint laxity was only measured in that study under static conditions. To our knowledge, there is no information on dynamic knee joint instability during physical activity in RKOA.

Figure 1 illustrates the pathological relationship between the above-mentioned mechanical factors and RKOA. To our knowledge, little is known regarding the correlation of knee instability or alignment with repetitive physical activity. Since early 1990s, several studies applied accelerometry to evaluate the knee joint under dynamic instability conditions (27–31). For example, a significant decrease in the lateral thrust, as measured by accelerometry, was reported in patients with varus OA knees using lateral wedge insole (28). Advanced technological development in accelerometry was applied by Turcot et al (31) to determine tri-axial instability of the tibiofemoral joint.

We hypothesized that significant relationships exist between knee instability or alignment with repetitive physical activity. To test our hypothesis, we determined the relationship between dynamic knee joint instability and coronal/sagittal knee alignment, and the effect of repetitive physical activity on knee instability in patients with RKOA. We used tri-axial accelerometry to evaluate tibiofemoral instability. Repetitive squatting has been reported previously to study the effects of high physical activity on the knee joint (8, 10, 11), however, this form of activity could potentially cause considerable pain in patients with KOA. For this reason, we used stepping exercise in this study as representative high physical activity in daily living. The main purpose of this study was to elucidate the relationship between knee instability and alignment, and to determine the effects of repetitive physical activity on knee instability in patients with RKOA.

Methods

Subjects

City dwellers aged ≥ 50 years were invited through advertisements to volunteer in this study. Power analysis using G Power 3.1.9 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) estimated participation of at least 64 subjects in order to detect group differences, with two-tailed α of 0.05, power of 80%, and effect size of 0.5. We excluded subjects with patellofemoral malalignment, diagnosed previously with rheumatoid arthritis or severe spinal stenosis, and also subjects who had undergone knee
surgery previously, as well as paraplegic subjects and those who could not stand on one leg or climb up/down stairs. All subjects underwent radiological assessment of the knee for KOA using the Kellgren-Lawrence (K/L) scoring system (in this system, grade 0 signifies no OA and grade 4 represents severe OA). Based on the results of radiographic examination, the selected study subjects were 68 participants (34 men and 34 women) with radiographic K/L grade 0–1 (here called the control group), and 68 (34 men and 34 women) with K/L grade 2–4. Only the index knee was selected for analysis in each participant. There were no significant differences in age and side of the knees between the control and OA groups. However, the body mass index (BMI) of the OA group was significantly larger than that of the control (Table 1).

| Table 1 | Demographic data |
|---------|------------------|
|         | RKOA group (n = 68, rt/lt) | Control group (n = 68, rt/lt) | P value* | Effect size Cohen' |
| K-L grade | | | |
| 0 | 0 | 25 (16/9) | |
| 1 | 0 | 43 (21/22) | |
| 2 | 27 (14/13) | 0 | |
| 3 | 15 (8/7) | 0 | |
| 4 | 26 (16/10) | 0 | |
| Side | right | 38 | 37 | 0.86 |
|      | left | 30 | 31 | |
| Age, years | 69.0 (8.0) | 67.1 (8.1) | 0.18 | 0.23 |
| Gender | Males | 34 | 34 | |
|        | Females | 34 | 34 | |
| BMI, kg/m² | 25.0 (3.0) | 23.6 (3.6) | 0.02 | 0.40 |

Data are mean (SD) or number of subjects.

* by unpaired t-test (continuous variables) or chi-square test (categorical variables)

RKOA: radiographic knee osteoarthritis

K-L: Kellgren and Lawrence, BMI: body mass index
All participants provided written informed consent according to the Declaration of Helsinki. The study protocol was approved by the Ethics Review Committee of Tan-nan Regional Medical Center, Fukui (TRMC 2018-1).

**Clinical evaluation**

Subjects were asked to fill in the knee injury and osteoarthritis outcome score (KOOS) (32). KOOS assesses five outcomes; pain, symptoms, activity of daily living (ADL), sport and recreational function, and knee-related quality of life. The KOOS meets the basic criteria of outcome measures and is used to evaluate the course of knee injury and treatment outcome (32). Since the study subjects were patients with primary KOA, we evaluated the activities of daily living (KOOS-A), pain (KOOS-P), and OA-related symptoms (KOOS-S).

**Assessment of muscle strength**

The isokinetic strength of the quadriceps and hamstring muscles was evaluated by the Biodex System Dynamometer (Biodex Medical Systems, NY) at angular speed 60°/sec. Each subject was tested three times and the highest value was chosen for analysis.

**Radiography**

Standing radiographs of the knee in anteroposterior (AP), lateral, and skyline views were obtained in all participants. Furthermore, all subjects underwent fluoroscopic-assisted, standing AP and full length AP radiographs in a semi-flexed position. The AP radiograph of the knee was obtained with the radiographic beam pointing parallel to the medial tibial plateau. The full length one-leg standing AP radiograph of the leg was used to express the varus valgus alignment of the leg using the mechanical axis; the hip-knee ankle angle (HKA), which represents the angle between the line connecting the center of the femoral head and the center of the tibia plateau and the line connecting the center of the tibia plateau and center of the ankle, (Fig. 2a). The joint line convergent angle (JLCA) (33) was obtained using the one-leg standing AP radiograph. The JLCA represents the angle between the line connecting the most distal point of the medial and lateral femoral condyles and the line connecting the proximal medial and lateral edges of the tibia plateau (Fig. 2b). Using the AP radiographs, the medial slope angle of the tibia plateau (MS) was defined as the angle between the line connecting the proximal medial and lateral edges of the tibia plateau and the line connecting the two points of center of the tibial shaft (7 cm and 12 cm distal to the tibial plateau) (Fig. 2b). Finally, the posterior slope angle of the medial tibial condyle (PS) was measured. It represents the angle between the line connecting the anterior and posterior edges of the medial tibial condyle and the line of the anterior margin of the tibia, distal to the tibial tubercle (Fig. 2c).

**Accelerometry**

Three small triaxial accelerometric wireless sensors (WAA-006™, Tekscan, MA) were attached to the fibular head, lateral femoral condyle, and lateral side of the leg, with skin tape and 7 cm-wide Velcro band. A pressure sensor (FlexiForce™, Nitta, Japan) was also attached to the heel with skin tape. The subject was instructed to walk on a 10 m flat floor at own comfortable natural speed, then step up and down 20
times on a 20 cm-high stepper, and finally walk on the flat floor. The sampling rate was 1 kHz for accelerometry and 50 Hz for the heel pressure sensor. The data of the femur, tibia and heel pressure sensors were synchronized, and the difference in accelerometry between the femur and the tibia was analyzed (WAA Data Analyzer, ATR-Promotions, Kyoto, Japan). The data were filtered using a Butterworth low-pass filter with a cutoff frequency of 10Hz, and the triaxial acceleration of the femur relative to the tibia was obtained (Fig. 2). The range between the positive peak and the following negative peak was defined as the magnitude of the acceleration. The first 10 acceleration waves starting from the heel were selected and the average values were used for the following analysis.

**Statistical analysis**

Reproducibility of measurements of accelerometry of the knee joint was tested in 10 KOA patients on two separate days. The average intraclass correlation (ICC) for antero-posterior direction was 0.99 before stepping and 0.93 after stepping. The ICC for mediolateral direction was 0.97 before stepping and 0.86 after stepping and for proximal and distal direction, it was 0.90 before stepping and 0.95 after stepping.

The association between accelerometry and the alignments was analyzed using Pearson's correlation analysis.

Two-tailed unpaired t-test and multiple logistic regression analysis were used for analysis of the clinical outcome, knee muscle strength, radiographic, gait speed and accelerometric data comparison between the OA and control groups. Effect size as Cohen's $d$ (34) was calculated to scale and rank the difference in all measures between the two groups.

All statistical analyses were conducted using the EZR software ver. 1.27 (35), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics. The level of statistical significance was set at $p < 0.05$.

**Results**

All subjects completed the study protocol without additional knee pain.

Mediolateral acceleration correlated significantly ($p < 0.01$) with two coronal alignments (mechanical axis; HKA and joint line convergent angle; JLCA). The Pearson correlation coefficient was small ($r = 0.23–0.24$) before stepping, and increased after stepping ($r = 0.28–0.33$). The increase in mediolateral acceleration after stepping correlated significantly and largely ($r = 0.37, p < 0.001$) with JLCA.

MS did not correlate with mediolateral acceleration before stepping (bZ) ($p = 0.11$) and poorly ($r = -0.18, p < 0.05$) after stepping (aZ).

In the sagittal plane, PS did not correlate with acceleration in the antero-posterior direction; bY, aY, and a-bY ($p = 0.92, 0.57, and 0.18$ respectively) (Table 2).
### Table 2
Relationship between acceleration and alignment in the coronal and sagittal planes.

| Parameter 1 | Parameter 2 | Pearson's correlation coefficient | 95% CI          | P value |
|-------------|-------------|----------------------------------|-----------------|---------|
| bZ          | HKA         | 0.24                             | 0.08–0.40       | < 0.01 |
| bZ          | JLCA        | 0.23                             | 0.07–0.39       | < 0.01 |
| bZ          | MS          | -0.14                            | -0.30–0.03      | 0.11   |
| aZ          | HKA         | 0.28                             | 0.12–0.43       | < 0.01 |
| aZ          | JLCA        | 0.33                             | 0.17–0.48       | < 0.001|
| aZ          | MS          | -0.18                            | -0.33 – -0.008  | < 0.05 |
| a-b Z       | HKA         | 0.22                             | 0.05–0.38       | < 0.05 |
| a-b Z       | JLCA        | 0.37                             | 0.21–0.51       | < 0.001|
| a-b Z       | MS          | -0.16                            | -0.32– -0.005   | 0.057  |
| bY          | PS          | -0.009                           | -0.18–0.16      | 0.92   |
| aY          | PS          | 0.05                             | -0.12–0.22      | 0.57   |
| a-b Y       | PS          | 0.12                             | -0.05–0.28      | 0.18   |

95%CI: 95% confidence interval, HKA: hip-knee-ankle angle in the coronal plane, MS: medial slope angle of the tibial plateau in the coronal plane, JLCA: joint line convergence angle in the coronal plane, PS: posterior slope angle of the medial tibial plateau in the sagittal plane, bZ, aZ, bY, aY: average acceleration of anteroposterior (Y), and mediolateral (Z) directions before (a) and after (b) stepping.

a-b Z (Y): difference of mediolateral (anteroposterior) acceleration after stepping.

All KOOS parameters (KOOS-A, KOOS-P, KOOS-S) and isokinetic muscle strength (quadriceps and hamstring) were significantly lower in the RKOA (p < 0.0001, each), compared with the control subjects. Within the coronal alignments, HKA and JLCA were larger (p < 0.0001), and MS smaller (p < 0.01) significantly in the RKOA group, but not the sagittal knee alignment (PS) (p = 0.14), compared with the control group (Table 3).
Table 3
Patient-reported outcome measures (KOOS), isokinetic muscle strength, alignment, and accelerometry

| KOOS                          | RKOA group n = 68 | Control group n = 68 | P value | Effect size Cohen’ d |
|-------------------------------|-------------------|----------------------|---------|----------------------|
| Activities of daily living    | 75.9 (10.6)       | 88.5 (10.2)          | < 0.001 | 1.22                 |
| Pain                          | 69.2 (14.2)       | 93.1 (9.6)           | < 0.001 | 1.99                 |
| Symptoms                      | 66.4 (16.4)       | 90.1 (12.7)          | < 0.001 | 1.63                 |

Isokinetic knee muscle strength

| Muscle and Location           | RKOA group         | Control group        | P value | Effect size Cohen’ d |
|-------------------------------|-------------------|----------------------|---------|----------------------|
| Quadriceps, Nm/kg             | 0.78 (0.34)       | 1.10 (0.31)          | < 0.001 | 0.99                 |
| Hamstrings, Nm/kg             | 0.39 (0.22)       | 0.64 (0.32)          | < 0.001 | 0.92                 |

Alignment

| Angle and Location            | RKOA group         | Control group        | P value | Effect size Cohen’ d |
|-------------------------------|-------------------|----------------------|---------|----------------------|
| HKA, °                        | 7.5 (4.4)         | 3.9 (3.0)            | < 0.001 | 0.98                 |
| JLCA, °                       | 3.9 (2.1)         | 1.2 (0.8)            | < 0.001 | 1.69                 |
| MS, °                         | 85.1 (1.9)        | 86.2 (2.3)           | < 0.01  | 0.50                 |
| PS, °                         | 77.5 (1.8)        | 78.1 (2.9)           | 0.14    | 0.26                 |
| Walking speed, m/s            | 0.72 (0.15)       | 0.85 (0.15)          | < 0.001 | 0.84                 |

Accelerometry

| Acceleration and Direction    | RKOA group         | Control group        | P value | Effect size Cohen’ d |
|-------------------------------|-------------------|----------------------|---------|----------------------|
| bX, m/s²                      | 0.69 (0.31)       | 0.61 (0.18)          | 0.07    | 0.32                 |
| bY, m/s²                      | 0.61 (0.21)       | 0.56 (0.16)          | 0.13    | 0.27                 |
| bZ, m/s²                      | 0.54 (0.20)       | 0.46 (0.12)          | < 0.01  | 0.49                 |
| aX, m/s²                      | 0.87 (0.40)       | 0.71 (0.20)          | < 0.01  | 0.51                 |
| aY, m/s²                      | 0.75 (0.28)       | 0.63 (0.19)          | < 0.01  | 0.50                 |
| aZ, m/s²                      | 0.69 (0.26)       | 0.52 (0.13)          | < 0.001 | 0.83                 |

Data are mean and (standard deviation).

RKOA: radiographic knee osteoarthritis, HKA: hip-knee-ankle angle in the coronal plane, MS: medial slope angle of the tibial plateau in the coronal plane, JLCA: joint line convergence angle in the coronal plane, PS: posterior slope angle of the tibial plateau in the sagittal plane, bX, bY, bZ, aX, aY, aZ: average acceleration of proximal-distal (X), anteroposterior (Y), and mediolateral (Z) directions before (b) and after (a) stepping. a-b X, a-b Y, a-b Z: difference of acceleration after stepping in X, Y, Z directions.
|                       | RKOA group n = 68 | Control group n = 68 | P value  | Effect size Cohen' d |
|-----------------------|--------------------|----------------------|----------|----------------------|
| a-b X, m/s²           | 0.18 (0.17)        | 0.10 (0.08)          | < 0.01   | 0.60                 |
| a-b Y, m/s²           | 0.14 (0.13)        | 0.08 (0.09)          | < 0.01   | 0.54                 |
| a-b Z, m/s²           | 0.14 (0.10)        | 0.05 (0.05)          | < 0.001  | 1.22                 |

Data are mean and (standard deviation).

RKOA: radiographic knee osteoarthritis, HKA: hip-knee-ankle angle in the coronal plane, MS: medial slope angle of the tibial plateau in the coronal plane, JLCA: joint line convergence angle in the coronal plane, PS: posterior slope angle of the tibial plateau in the sagittal plane, bX, bY, bZ, aX, aY, aZ: average acceleration of proximal-distal (X), anteroposterior (Y), and mediolateral (Z) directions before (b) and after (a) stepping. a-b X, a-b Y, a-b Z: difference of acceleration after stepping in X, Y, Z directions.

The walking speed of the OA group was significantly slower (p < 0.001) than that of the control. Before stepping, acceleration of the OA group was significantly larger than the control group in only mediolateral direction (bZ). However, accelerations after stepping and the change in acceleration after stepping were significantly larger in both proximal-distal (aX and a-bX) and anteroposterior directions (aY and a-bY), as well as mediolateral direction (aZ and a-bZ) (p < 0.01). (Table 3).

Multiple logistic regression analysis was performed using RKOA (KL2-4) as the outcome with six independent variables (BMI, KOOS-P, quadriceps muscle strength, walking speed, a-b Z (or bZ), and JLCA (HKA or MS)). The following six models were used with these variables: a-b Z and JLCA (model 1), a-b Z and HKA (model 2), a-b Z and MS (model 3), bZ and JLCA (model 4), bZ and HKA (model 5), and bZ and MS (model 6). After accounting for all the variables, both JLCA and HKA significantly (p < 0.05) affected the diagnosis of RKOA (models 1, 2, 4, 5), while MS did not (models 3 and 6). In addition, a-b Z significantly (p < 0.001) discriminated RKOA from non-OA (models 1–3), while bZ did not (models 4–6) (Table 4).
### Table 4
Results of logistic regression analysis with the stepwise procedure for the diagnosis of radiographic knee osteoarthritis

| Variables     | Odds ratio | 95% CI      | P value |
|---------------|------------|-------------|---------|
| **Model 1**   |            |             |         |
| KOOS-pain     | 0.86       | 0.81–0.93   | < 0.001 |
| JLCA, °       | 4.77       | 2.04–11.2   | < 0.001 |
| a-b Z, 10m/s² | 8.11       | 2.36–2.79   | < 0.001 |
| **Model 2**   |            |             |         |
| KOOS-pain     | 0.86       | 0.81–0.97   | < 0.001 |
| HKA, °        | 1.38       | 1.07–1.78   | < 0.05  |
| a-b Z, 10m/s² | 8.09       | 2.65–24.7   | < 0.001 |
| **Model 3**   |            |             |         |
| KOOS-pain     | 0.86       | 0.81–0.91   | < 0.001 |
| a-b Z, 10m/s² | 8.78       | 3.01–25.6   | < 0.001 |
| **Model 4**   |            |             |         |
| KOOS-pain     | 0.86       | 0.83–0.93   | < 0.001 |
| JLCA, °       | 4.83       | 2.35–9.93   | < 0.001 |
| **Model 5**   |            |             |         |
| KOOS-pain     | 0.87       | 0.83–0.92   | < 0.001 |
| HKA, °        | 1.41       | 1.14–1.74   | < 0.01  |
| **Model 6**   |            |             |         |
| KOOS-pain     | 0.87       | 0.84–0.91   | < 0.001 |

95% CI: 95% confidence interval, KOOS: Knee Injury and Osteoarthritis Outcome Score, HKA: hip-knee-ankle angle in the coronal plane, JLCA: joint line convergence angle in the coronal plain, a-b Z: difference of acceleration after stepping in mediolateral direction

### Discussion
In this study, we measured dynamic knee instability using tri-axial accelerometer before and after repetitive stepping activity and demonstrated significant relationship between mediolateral knee instability and coronal alignment of the knee.
In the coronal plane, the load distribution across the femorotibial joint is estimated predominantly in knees with normal alignment. Knees with varus deformity receive the total load almost entirely on the medial compartment (36). The mechanical stress concentrated on the medial compartment produces high adduction moment of the knee and opening of the lateral side of the joint, which is described as varus thrust (37). The degree of lateral opening is indicated directly by JLCA and indirectly by HKA. Accordingly, mediolateral acceleration, which quantitatively represents varus thrust, likely correlates significantly with HKA and JLCA.

Maeyama and coworkers (38) measured three directions of acceleration. They reported that the overall magnitude of acceleration of the dysplastic hip was significantly larger than that of the contralateral normal hip. They found a significantly high correlation between radiographic center-edge angle and the overall magnitude of acceleration ($r=-0.73$, $p<0.0001$). The hip joint has ball and socket anatomy, which is supported by many muscles multi-directionally. Thus, instability related to the bony structure is often strongly responsible for dynamic joint instability. On the other hand, the anatomical morphology of the knee joint is more complex. In addition, the joint is supported by not only the surrounding muscles, but also by a series of ligaments, supporting structures and soft tissues. Therefore, any instability associated with the bony structures, described as knee alignment, may be less responsible for dynamic knee instability.

The JLCA has been used recently to describe the magnitude of medial and lateral coronal soft tissue laxity in tibial osteotomy for KOA (39). Although the JLCA reflects the effect of soft tissue laxity, and it varies greatly in subjects with KOA (40), its significance in the understanding of the pathogenesis of KOA is unclear. In the present study, JLCA correlated significantly with the $a-b$ Z, indicating JLCA may be a valuable marker to estimate mediolateral acceleration after stepping activity. In addition, multiple logistic regression analysis identified it as a marker for the radiographic diagnosis of KOA. Therefore, JLCA could be a potentially useful radiographic index for evaluation of KOA pathology.

The MS/PS is the anatomical angle of the tibia plateau that reflects joint configuration. Driban et al (6) showed that a greater coronal tibial slope significantly affected the load distribution, and it was associated with increased risk of incident accelerated KOA, particularly among knees with malalignment. On the other hand, using a musculoskeletal model for healthy adults, Van Rossom et al (7) demonstrated that small changes in coronal tibial slope had a less pronounced effect on the load distribution, though coronal plane malalignment significantly affected it. In the present study, although the MS was significantly smaller (proximal tibial surface inclines more medially) in patients with RKOA compared to that of the control, it was not helpful in the diagnosis of KOA even after adjustment for other variables. Furthermore, we did not find the significant difference of PS between the control and RKOA groups, and the PS did not correlate with acceleration in the antero-posterior direction. In this regard, Van Rossom et al (7) reported that transverse plane malalignment only minimally affected the load distribution. Further research is needed to determine how individual joint geometry influences knee joint instability and the risk of KOA.
Our results also showed significantly larger mediolateral acceleration in patients with RKOA, compared with the control. However, the difference became insignificant after adjustment for all other variables.

Turcot et al (31) demonstrated significant high acceleration in anteroposterior and mediolateral directions in patients with KOA compared to the control, and concluded that the accelerometric method used in their study could discriminate between asymptomatic subjects and patients with medial KOA. They also indicated that the difference between their results and those reported by Lafortune et al (27) were probably related to differences in gait velocity, location of the accelerometer, and sensor fixation method. Walking speed is a major factor affecting gait (41). However, we instructed our subjects to walk at their own natural pace so as to conduct the test under similar daily activity. In fact, our RKOA patients walked significantly slower than the control (p < 0.0001, Cohen's d = 0.84). With respect to the placement of the accelerometer, the femoral sensor was attached on the lateral epicondyle of the femur, while the tibial sensor was fixed to the fibular head. These sites were easy to locate on the skin. In addition, accelerometer should be placed on the lateral aspect of the leg for more accurate measurement (42). In our study, we measured body synchronous movements through the use of several sensors with good reproducibility of the obtained relative femorotibial acceleration. Care should also be taken to reduce artifacts produced by the sensor-skin mounting technique. In this regard, the use of exoskeleton may be advantageous relative to skin tape, although we used skin tape and firmly rapped wide Velcro band when placing the sensors on the skin.

After adjustment for all variables, the only significant difference in acceleration between RKOA patients and the control group was the average increase in mediolateral acceleration after repetitive stepping. Mediolateral instability occurred much more in patients with RKOA after 20 stepping activities on the 20cm-high stepper.

Lueponsak et al (43) reported that among several daily living activities, descending stairs was associated with the highest forces across the knees and hips. Sahlström et al (44) applied gait analysis and demonstrated that climbing stairs is associated with a significant increase in knee moment in healthy subjects. Another study showed that malalignment and overweight can increase mechanical stress on the knee joint (45). In addition to our previous study in patients with KOA (26), a few studies also reported that certain physical exercises can induce knee joint laxity in athletes (46–48).

With regard to the soft tissues around the knee joint, previous studies demonstrated a strong relationship between decreased stiffness and reduced strength of the medial collateral ligament under cyclic loading (46). Others reported greater co-contraction of the medial muscle in response to medial knee joint laxity in patients with medial KOA (49). In our study, isokinetic knee muscle strength was significantly lower in the OA group compared to the control subjects. In this regard, muscle weakness is a known risk factor for KOA (50–51). In the elderly, repetitive physical exercise, such as stepping exercise, even for a relatively short period of time, may cause muscle fatigue (52) and reduce stiffness of the collateral ligament (46), as the knee becomes more unstable.
In this study, JLCA significantly correlated with medio-lateral acceleration after repetitive stepping (aZ and a-b Z). This suggests that knees with large JLCA are potentially susceptible to the development or progression of KOA. Our study also demonstrated a significant increase in mediolateral acceleration in KOA patients after repetitive stepping, compared with non-OA subjects. In addition, a-b Z was a significant independent marker of KOA, suggesting that such activities during daily living are probably associated with the pathogenesis of KOA.

Our study has certain limitations. With regard to the stepping protocol, we set the height of the step and frequency of stepping up and down so that all subjects were able to complete the test without suffering further knee pain. The results would have been different if the exercise level had been harder or tailored to the daily activity of the individual patient. Nevertheless, the results showed significantly larger post-exercise increase in mediolateral acceleration in patients with RKOA relative to the non-OA control, suggesting repetitive physical exercise may play a role in mechanical pathology for KOA. Another limitation of the study was the cross-sectional design. Further longitudinal studies are needed to determine whether coronal alignment abnormality and increased acceleration after repetitive stepping are risk factors for the development or progression of KOA.

**Conclusions**

In summary, we found a direct relationship between knee instability and knee alignment or repetitive physical activity. Repetitive stepping activity resulted in a significant increase in mediolateral acceleration in RKOA patients, compared to the control. The correlation between mediolateral acceleration and coronal alignment increased after stepping compared with before stepping. In knees with large JLCA, repetitive stepping activity provided much larger mediolateral instability. Our results suggest that increases in mediolateral acceleration after repetitive physical activity as well as JLCA seem to contribute to the pathogenesis of KOA.

**Abbreviations**

- a-b X (Y or Z): difference in acceleration after stepping in proximal-distal (antero-posterior or medio-lateral) direction
- b(a)X (Y or Z): acceleration before (after) stepping in proximal-distal (antero-posterior or medio-lateral) direction
- HKA: hip-knee-ankle angle
- JLCA: joint line convergence angle
- KOA: knee osteoarthritis
- KOOS: the knee injury and osteoarthritis outcome score
MS: medial slope angle of the proximal tibia
PS: posterior slope angle of the proximal tibia
RKOA: radiographic knee osteoarthritis

Declarations

Ethics approval and consent to participate

All participants provided written informed consent. This study was approved by the Human Ethics Committee of Tan-nan Regional Medical Center (protocol #2018-1).

Consent for publication

Consent for publication was obtained from all participants.

Availability of data and materials

The datasets used and analyzed in this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors’ contributions

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Conflict of interest

All authors declare no conflict of interest.

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**Figures**

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**Figure 1**

![Diagram](image_url)

Knee joint instability

- ?
- Malalignment

- ?
- Repetitive physical activity

Knee osteoarthritis
Association between three risk factors for knee osteoarthritis. The relationship between dynamic knee instability and alignment or repetitive physical activity is unknown.

Figure 2

Radiographic parameters used in the present study. (a) The hip-knee-ankle angle (HKA) (α) from the full length weight bearing AP radiograph of the leg. (b): The joint line convergent angle; JLCA (β) and the medial tibial slope angle; MS (γ) from the weight bearing AP radiograph of the knee. (c) The posterior slope angle of the medial tibial condyle; PS (δ) from the lateral radiograph of the knee.
Figure 3

Typical mediolateral acceleration waves of the tibiofemoral joint from representative patient with knee OA and control subject.

Supplementary Files

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