Osteoarthritis and Cartilage 27 (2019) 248–256

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Trunk movement asymmetry associated with pain, disability, and quadriceps strength asymmetry in individuals with knee osteoarthritis: a cross-sectional study

H. Iijima † ‡ § *, R. Eguchi ||, T. Aoyama ‡, M. Takahashi †

† Department of System Design Engineering, Faculty of Science and Technology, Keio University, Yokohama, Japan
‡ Department of Physical Therapy, Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto, Japan
§ Japan Society for the Promotion of Science, Tokyo, Japan
|| School of Science for Open and Environmental Systems, Graduate School of Science and Technology, Keio University, Yokohama, Japan

ARTICLE INFO

Article history:
Received 16 July 2018
Accepted 29 October 2018

Keywords:
Knee osteoarthritis
Harmonic ratio
Improved harmonic ratio
Knee pain
Disability
Quadriceps strength asymmetry

SUMMARY

Objective: This study examined 1) the clinical relevance of trunk movement asymmetry, which was evaluated using a trunk-mounted inertial measurement unit (IMU), and 2) the relationship between trunk movement asymmetry and lower limb muscle strength asymmetry in individuals with knee osteoarthritis (OA).
Design: One-hundred-thirty-one participants (mean age, 74.2 years; 71.8% female; Kellgren and Lawrence [K&L] grade ≥1) underwent gait analysis at their preferred pace for IMU-based measurement of trunk movement asymmetry (harmonic ratio [HR] and improved HR). The isometric strength of quadriceps and hip abductors was evaluated using a hand-held dynamometer. Pain and disability level were evaluated using a validated self-reported questionnaire. Multiple regression analyses with covariate adjustment were performed to examine the relationship between trunk movement asymmetry (independent variable) and pain, disability level, or muscle strength asymmetry (dependent variables).
Results: Individuals with severe knee OA (K&L grade ≥3) had increased trunk movement asymmetry in the medio-lateral axis compared to those with a K&L grade of 1. Increased trunk movement asymmetry was associated with a greater knee pain and disability. The increased trunk movement asymmetry was significantly associated with an increase in the asymmetry of quadriceps strength, but not with asymmetry in the strength of hip abductor.
Conclusion: Our findings indicate that increased medio-lateral trunk movement asymmetry may be an indicator of impairment, rather than adaptation, in individuals with knee OA. This preliminary finding warrants validation by future study. Paying close attention to medio-lateral trunk movement asymmetry may be key to our understanding of OA-related pain and disability.

Introduction

Knee osteoarthritis (OA) is a leading cause of knee pain and functional disability[1]. Patients with knee OA show biomechanical deviations in multiple joints during level walking, possibly due to efforts made to avoid pain and minimize stress to the knee joint[2]. As these deviations are performed to compensate for the ipsilateral limb, they may increase the joint load on the contralateral limb[2], which may cause knee OA to progress in the contralateral limb[3]. Better understanding of knee OA-related biomechanical deviations during level gait is therefore crucial for clinicians and physical therapists.

OA-related biomechanical deviations accompany gait asymmetry[4–6]. This provides a valuable insight into the adapted gait strategy used by patients with knee OA. The harmonic ratio (HR) is a representative measure of gait asymmetry calculated via spectral analysis of acceleration time-series signals[7,8], generally acquired using an inertial measurement unit (IMU) attached to the lower trunk. Recently, Pasciuto *et al.* demonstrated that an

* Address correspondence and reprint requests to: H. Iijima, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan. Tel: 81-45-563-1141; Fax: 81-45-566-1660.

E-mail addresses: iijima.hirotaka.4m@yt.sd.keio.ac.jp (H. Iijima), eguchi.ryo@keio.jp (R. Eguchi), aoyama.tomoki.4e@kyoto-u.ac.jp (T. Aoyama), takahashi@sd.keio.ac.jp (M. Takahashi).

https://doi.org/10.1016/j.joca.2018.10.012
1063-4584/

improved HR (iHR) was both more reliable and easier to interpret than a traditional HR[9]. These HR techniques have been applied to characterize patients with pathologies[10,11]; for example, a lower medio-lateral HR was associated with greater disability in stroke patients[10]. Considering that lower HRs were found in individuals in the early stage of Parkinson's disease, whose stride length and stride time were similar to those of age-matched healthy older adults[11], HR techniques would be able to characterize subtle biomechanical deviations that are not recognized using typical spatiotemporal gait parameters. However, OA-related alterations in these measures have not been addressed, and their clinical relevance remains unclear. Furthermore, whether gait variability determined using HR indicates impairment or adaptation is not fully understood. Medio-lateral trunk movement asymmetry has been suggested to serve a different function in locomotor control in comparison to other orientations of asymmetry[12]. These results suggest that investigating IMU-based trunk movement asymmetry in individuals with knee OA, particularly in the medio-lateral axis, and clarifying its clinical relevance would improve our understanding of OA-related disability and biomechanical deviations.

Lower limb muscle weakness and strength asymmetry are factors potentially involved in OA-related gait asymmetries. Weak quadriceps and hip abductor muscles are features of knee OA[13,14], and contraction of these muscles plays a role in the three-dimensional regulation of the center of mass during normal walking[15]. Conversely, displacing the trunk laterally shifts the center of gravity and allows the body to balance over the stance leg with minimal muscular support at the hip and knee joints, which causes an imbalance in muscle strength between limbs. Laroche *et al.* revealed that older women with quadriceps strength asymmetry had greater asymmetry and variability in their spatiotemporal gait parameters[16]. However, we are unaware of any studies examining the relationship between trunk movement asymmetry and muscle strength asymmetry in the lower limbs of individuals with knee OA.

This cross sectional study of individuals with knee OA aimed to examine 1) the clinical relevance of trunk movement asymmetry, using HRs and iHRs, and 2) the relationship between trunk movement asymmetry and lower limb muscle strength asymmetry. We hypothesized that 1) individuals with more severe knee OA had a higher degree of trunk movement asymmetry, which is associated with a greater knee pain and disability and 2) increased trunk movement asymmetry is associated with a greater degree of quadriceps and hip abductor muscle strength asymmetries.

Methods

Participants

Elderly participants who had reported knee pain within the last month were identified using a mail-based survey and invited to Kyoto University in September 2017. The minimum number of participants was set based on the minimum sample size required to ensure adequate statistical power; however, no restrictions were imposed on the upper limit owing to the observational nature of the study. The ethical committee of Kyoto University approved the study (approval number: C1297), and written informed consent was obtained from all participants prior to enrollment. The eligibility criteria included (1) age $\geq$45 years; (2) a Kellgren and Lawrence [K&L] grade $\geq$1, using the original scale[17], in one or both knees, in the medial tibiofemoral compartment, evaluated using weight-bearing antero-posterior radiographs; (3) knee pain during daily living within the past 30 days; and (4) the ability to walk independently on a flat surface without ambulatory assistive devices. Participants with bilateral knee OA were not evaluated separately from those with unilateral OA; both bilateral and unilateral OA cases were included in this study. The exclusion criteria included (1) a history of knee surgery, (2) rheumatoid arthritis, (3) a periarticular fracture, or (4) the presence of neurological problems. We included patients with a K&L grade $\geq$1 because a pre-radiographic diagnosis of knee OA, particularly K&L grade 1, predicts radiographic OA progression to at least grade 2 within 3–5 years[18,19].

Measurements and procedures

The following measurements were performed on all participants: (1) IMU-detected HR and iHR during level walking, (2) muscle strength, and (3) OA-related self-reported measures of knee pain and disability.

IMU-detected HR and iHR during level walking

Instrumentation. Linear lower trunk acceleration was measured along three orthogonal axes (medio-lateral, vertical, and antero-posterior) using a single IMU (TSND151, ATR-Promotions Co., Ltd., Kyoto, Japan) with a sampling frequency of 200 Hz [Fig. 1(A)]. Acceleration values were expressed as a sensor coordinate system (reported in the x, y, and z fields of the sensor). Footwear influences balance[20,21], walking speed[21], and vertical acceleration produced by heel strike[22]; thus, to prevent potential bias from footwear, all participants wore standard shoes (LD AROUND M, Mizuno, Tokyo, Japan) mounted with a pressure sensor (force register sensors Model 402, Interlink Electronics Inc., CA, USA) on both feet. The sensor-mounted shoes can precisely detect the time point of heel contact that is required for stride segmentation and calculation of HR and iHR. Although the footwear was novel for each participant, all subjects reported that the shoes were comfortable. Data were sampled at 100 Hz.

Procedures for gait analysis. After fitting of the lower trunk-mounted IMU and footwear, participants underwent gait analysis on a 14 m walkway at their preferred pace. Participants stood still for 3 s and walked the full 14 m, although only a designated 10-m distance was analyzed to exclude the first and last two to three steps[23]. As HR is gait velocity-dependent[24], each patients' gait velocity (m/s) was calculated based on a time measured by an experienced physical therapist using a stopwatch, and was subjected to statistical analysis.

Data reduction and calculation of HR and iHR. Figure 1 in the Supplemental Appendix S1 describes the data reduction process for HR and iHR calculations. After stride segmentation and offset correction, a low-pass fourth-order Butterworth filter with a cutoff frequency of 20 Hz was applied[25].

The HR was calculated by decomposing filtered acceleration signals into harmonics using a discrete Fourier transform [Fig. 1(B)]; the summed amplitudes of the first 10 even harmonics were then divided by the summed amplitudes of the first 10 odd harmonics for vertical and antero-posterior accelerations, and vice-versa for medio-lateral accelerations[24]. The iHR was also calculated. iHR is thought to have less variability than traditional HR and measures range from 0 (total asymmetry) to 100 (total symmetry), allowing intuitive interpretation[9]. The iHR is calculated as the ratio between the power of the even harmonic over the total power of the signal, as shown in Supplemental Appendix S1, Method 1. All data analyses were performed using MATLAB version R2017a (MathWorks Inc., 3 Apple Hill Drive, Natick, MA, USA).

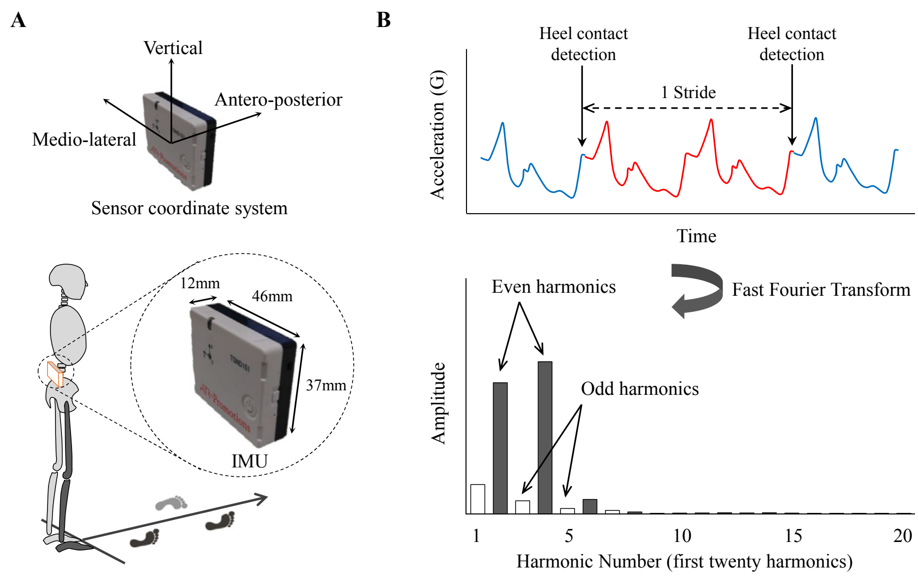

Fig. 1. Experimental setting (A) and illustration of the discrete fast Fourier transform processing applied to acceleration data (B). Harmonic content of the acceleration signals in each direction (expressed as a sensor coordinate system) was extracted using a fast Fourier transform. Using even and odd harmonics, harmonic ratio [HR] and improved HR (iHR) were calculated (see Supplemental Appendix S1, Method 1). White and black bars indicate odd and even harmonics, respectively.

Muscle strength

The maximum isometric quadriceps and hip abductor muscle strengths (Nm/kg) in both legs were measured using a hand-held dynamometer (HHD; μTas F-1, Anima Corp., Tokyo, Japan) according to a method previously validated for use in community-dwelling elderly fallers[26]. Measurement procedures for each muscle are provided in Supplemental Appendix S1, Method 2.

The minimum detectable change (MDC_{95}) was calculated using 100 randomly selected participants (i.e., 200 knees) to determine the smallest degree of change outside of the muscle strength testing error-range. The MDC_{95} was 0.227 Nm/kg and 0.132 Nm/kg in quadriceps and hip abduction strengths, respectively. The intra-rater reliability was excellent for quadriceps strength (intra-class correlation [$ICC_{1,1}$]: 0.939; 95% CI: 0.921, 0.954) and hip abductor strength ($ICC_{1,1}$: 0.936; 95% CI: 0.916, 0.951).

The absolute difference in quadriceps and hip abductor muscle strengths between the two lower limbs was calculated. For interpretation purposes, the quadriceps asymmetry index (Asy_{Quad}) was also calculated (see Supplemental Appendix S1, Method 2).

OA-related self-reported measure of knee pain and disability

The severity of knee pain and degree of disability were evaluated using the Japanese Knee Osteoarthritis Measure (JKOM) subcategory “pain and stiffness” (0–32 points) and “activities of daily living” (0–40 points)[27]. The JKOM “activities of daily living” scale relies on daily activities, such as use of stair, knee bending, standing up from a sitting position, walking, shopping, removing socks, and both light and heavy household chores. For each subscale, higher scores indicate a worse condition (range: 0–4 points; 0 indicates no pain or difficulty, and 4 represents extreme pain or difficulty). The concurrent and construct validities of the JKOM were established by comparing it with the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the Medical Outcomes Study 36-item Short-Form Health Survey[27].

Patients’ characteristics and covariates

Demographic characteristics, severity of radiographic OA, bilateral definite radiographic OA (K&L grade ≥2 in both knees), and bilateral knee pain were assessed as covariates (see Supplemental Appendix S1, Method 3). As part of the patients’ characteristics, participants underwent a visual analog score for knee pain, anatomical axis angle with sex-specific correction[28], Timed Up and Go test[29], and five-repetitive chair stand test[30] were also evaluated.

Statistical analyses

At least 84 participants were required for the present study, accounting for a potential 10% dropout rate due to exclusion criteria and missing data (see Supplemental Appendix S1, Method 4). To characterize trunk movement asymmetry associated with knee OA, the HR and iHR were compared between different degrees of radiographic disease severity, using an analysis of covariance with adjustments for age (continuous), female sex, BMI (continuous), and gait velocity (continuous). As few participants had severe radiographic disease (K&L grade = 4), participants with K&L grade = 3 and 4 were combined into one level and included in an ordinal scale (1: K&L grade = 1; 2: K&L grade = 2; 3: K&L grade = 3 or 4). A Jonckheere–Terpstra trend test[31] was performed to test the hypothesis that trunk movement asymmetry increases over time with increased K&L grade. The Jonckheere–Terpstra test[31] is a rank-based nonparametric test that can be used to determine if there is a statistically significant trend between an ordinal independent variable (i.e., K&L grade) and a continuous dependent variable (i.e., trunk movement asymmetry).

To examine the clinical relevance of the HR and iHR in individuals with knee OA, multiple regression analyses were performed with HR (continuous) and iHR (continuous) as independent variables and JKOM “pain and stiffness” (continuous) or “activities of daily living” (continuous) as the dependent variable. In these analyses, in addition to the covariates mentioned above, K&L grade (ordinal), bilateral knee pain (0: absence, 1: presence), and bilateral radiographic OA (0: absence, 1: presence) were also included as covariates. We checked the regression model features by comparing the residuals vs fitted values (i.e., the residuals had to be normally distributed around zero), and independence between observations. A post-hoc mediation analysis was performed to determine whether the significant relationship detected between lower medio-lateral iHR and greater disability was mediated by severe knee pain in accordance with previously described method[32]. In this analysis, severe knee pain (JKOM "pain and stiffness" score) was identified as a potential mediator. The full mediation analysis for the selected mediator involved fitting two linear models in order to deconstruct the total effect into both direct and indirect effects of lower medio-lateral iHR on greater disability (see Supplemental Appendix S1, Fig. 2).

Additional multiple regression analyses were performed to examine the association between the HR and iHR as independent variables with the lower limb muscle strength difference (continuous) as the dependent variable. As muscle strength was calculated with an adjustment for body mass, BMI was not included as a covariate, although the other variables mentioned above were included as covariates. These covariates were chosen a priori on the basis of clinical judgment and previous studies demonstrating that these factors may be associated with upper trunk acceleration[24,33,34], trunk kinematics[5] and each outcome variable[35]. These factors would not feature on the causal-response pathway between HR/iHR and each outcome variable. All statistical analyses were performed using JMP Pro 13.0 (SAS Institute, Cary, NC, USA) or SPSS Statistics for Windows, Version 23.0 (IBM Corp., NY, USA). A P-value <0.05 was considered to be statistically significant.

Results

Of the 196 participants initially recruited, 134 (68.4%) randomly selected participants underwent a lower trunk-mounted IMU-based gait analysis. Of these, 3 (2.2%) were excluded due to pre-radiographic OA (K&L grade = 0). Thus, 131 participants were included in the final analysis (mean age, 74.2 [65–88] years; mean BMI: 21.7 kg/m^2, 71.8% female) (Table I).

Individuals with moderate to severe knee OA had a higher medio-lateral trunk movement asymmetry

Table II shows the comparison of the HR and iHR between participants stratified by their knee K&L grade. Overall, the HR and iHR were similar in individuals with a K&L grade of 1 and 2. HR and iHR were slightly lower in patients with a K&L grade of 3 or 4, compared to those with a K&L grade of 1 and 2. No severity-dependent trend in K&L grade was identified by the trend test. Notably, individuals with a K&L grade of 3 or 4 had a significantly higher medio-lateral HR than those with a K&L grade of 1, after adjustment for covariates. The medio-lateral HR in non-index knees with a K&L grade of 3 or 4 was also higher than those from knees with a K&L grade of 1 (difference in mean: 0.160; 95% CI: 0.013 to 0.310).

Medio-lateral trunk movement asymmetry was associated with greater disability

Multiple linear regression (Table III) revealed that increased medio-lateral HR and iHR (i.e., lower trunk movement asymmetry) were associated with a lower score (i.e., lower knee pain and disability) in the JKOM "pain and stiffness" and "activities of daily living" subcategory after adjustment for covariates, although the significance of this relationship was only confirmed using the iHR. Vertical and antero-posterior HR and iHR were not significantly associated with the score from the JKOM "activities of daily living." A mediation analysis revealed that severe knee pain was a significant mediator between lower iHR and greater disability (direct effect: −0.031, 95% CI: −0.079, 0.018 points; indirect effect: −0.037, 95% CI: −0.081, −0.001 points). Furthermore, increased vertical HR and vertical and antero-posterior iHR were significantly associated with better Timed Up and Go function (see Supplemental Appendix S1, Table I).

Table I
Participants' characteristics (n = 131)

Age, years	74.2 ± 5.81
Female, no. (%)	94 (71.8)
Height, m	1.56 ± 0.09
Mass, kg	53.1 ± 8.22
BMI, kg/m^2	21.7 ± 2.52
Index knee corrected AAA, °	178.3 ± 3.85
Index knee K&L grade, no. (%)	
Grade 1	43 (32.8)
Grade 2	71 (54.2)
Grade 3	15 (11.5)
Grade 4	2 (1.5)
Lateral type knee OA, no. (%)	7 (5.3)
Bilateral knee OA, no. (%)	62 (47.3)
Bilateral knee pain, no. (%)	71 (54.2)
VAS score for knee pain, mm	14.0 ± 20.2
JKOM, points	
Pain and stiffness	3.85 ± 4.64
Activities of daily living	2.56 ± 3.60
Participation in social activities	2.10 ± 1.93
General health conditions	1.54 ± 1.34
Total score	10.0 ± 9.58
Physical Performance	
Gait velocity, m/s	1.57 ± 0.22
Timed Up and Go test, s	5.49 ± 1.28
Five-repetitive chair stand test, s	7.55 ± 1.92
HR	
Medio-lateral	1.65 ± 0.42
Vertical	2.58 ± 0.82
Antero-posterior	2.60 ± 0.83
iHR	
Medio-lateral	80.2 ± 9.65
Vertical	92.5 ± 6.48
Antero-posterior	91.6 ± 7.74
Muscle strength	
Quadriceps	
Index knee, Nm/kg	1.27 ± 0.44
Non-index knee, Nm/kg	1.30 ± 0.41
Difference between limbs, Nm/kg	0.16 ± 0.14
Asy_{Quad}, %	12.3 ± 9.70
Hip abductor	
Index knee, Nm/kg	0.91 ± 0.33
Non-index knee, Nm/kg	0.90 ± 0.35
Difference between limbs, Nm/kg	0.13 ± 0.13

AAA: Anatomical axis angle; BMI: Body mass index; HR: Harmonic ratio; iHR: Improved harmonic ratio; K&L: Kellgren and Lawrence; OA: Osteoarthritis; VAS: Visual analog scale; JKOM: Japanese Knee Osteoarthritis Measure; Asy_{Quad}: Quadriceps asymmetry index.
Except where otherwise indicated, values are mean ± SD.

Medio-lateral trunk movement asymmetry was associated with quadriceps strength asymmetry

Increased medio-lateral HR and iHR (i.e., lower trunk movement asymmetry) were associated with decreased quadriceps strength asymmetry after adjustment for covariates (Table IV). The vertical and antero-posterior HR and iHR were not significantly associated with quadriceps strength asymmetry. Neither the HR nor the iHR were associated with hip abductor strength asymmetry as well as quadriceps and hip abductor strength values themselves (see Supplemental Appendix S1, Table II).

Figure 2 displays a graphic illustration of the relationship between difference in quadriceps strength or Asy_{Quad} and medio-lateral trunk asymmetry. The difference in quadriceps strength and Asy_{Quad} had a similar linear relationship with trunk movement asymmetry, regardless of the measure used (HR and iHR).

Table II
Comparison of the harmonic ratio [HR] and improved HR (iHR) among participants stratified by index knee K&L grade ($n = 131$)

Variable	Mean ± SD	Difference in mean (95% CI)*	*P* for pairwise comparison†	*P* for trend†
HR				
Medio-lateral				
K&L = 1 ($n = 43$)	1.68 ± 0.47	–		0.338
K&L = 2 ($n = 71$)	1.67 ± 0.40	0.032 (−0.133, 0.198)	0.720 (vs. K&L 1)	
K&L = 3 or 4 (n = 17)	**1.50 ± 0.33**	**0.140 (0.012, 0.268)**	**0.033 (vs. K&L 1)**; 0.147 (vs. K&L 2)	
Vertical				
K&L = 1 ($n = 43$)	2.63 ± 0.85	–		0.278
K&L = 2 ($n = 71$)	2.61 ± 0.72	0.020 (−0.287, 0.326)	0.981 (vs. K&L 1)	
K&L = 3 or 4 ($n = 17$)	2.42 ± 1.14	0.164 (−0.127, 0.455)	0.263 (vs. K&L 1); 0.520 (vs. K&L 2)	
Antero-posterior				
K&L = 1 ($n = 43$)	2.77 ± 0.91	–		0.171
K&L = 2 ($n = 71$)	2.55 ± 0.68	0.234 (−0.073, 0.541)	0.206 (vs. K&L 1)	
K&L = 3 or 4 ($n = 17$)	2.46 ± 1.10	0.233 (−0.072, 0.539)	0.132 (vs. K&L 1); 0.455 (vs. K&L 2)	
iHR				
Medio-lateral				
K&L = 1 ($n = 43$)	79.5 ± 10.8	–		0.500
K&L = 2 ($n = 71$)	81.2 ± 9.07	−1.280 (−5.017, 2.458)	0.534 (vs. K&L 1)	
K&L = 3 or 4 ($n = 17$)	77.2 ± 9.25	2.347 (−0.768, 5.462)	0.137 (vs. K&L 1); 0.259 (vs. K&L 2)	
Vertical				
K&L = 1 ($n = 43$)	92.5 ± 7.48	–		0.143
K&L = 2 ($n = 71$)	93.1 ± 5.87	−0.873 (−3.437, 1.690)	0.439 (vs. K&L 1)	
K&L = 3 or 4 ($n = 17$)	90.2 ± 6.29	0.643 (−1.584, 2.870)	0.565 (vs. K&L 1); 0.168 (vs. K&L 2)	
Antero-posterior				
K&L = 1 ($n = 43$)	92.2 ± 8.56			0.107
K&L = 2 ($n = 71$)	92.2 ± 6.01	−0.241 (−3.024, 2.541)	0.718 (vs. K&L 1)	
K&L = 3 or 4 ($n = 17$)	88.5 ± 11.0	1.696 (−1.284, 4.676)	0.259 (vs. K&L 1); 0.074 (vs. K&L 2)	

CI: Confidence interval; HR: Harmonic ratio; iHR: Improved harmonic ratio; K&L: Kellgren and Lawrence.
Bold type represents a statistically significant result.
* Difference in mean (95% CI) was calculated after adjustment for age, sex, BMI, and gait velocity (vs. K&L grade 1).
† Jonckheere–Terpstra trend test.

Table III
Predictive ability of the HR and iHR on pain and disability level in individuals with knee OA ($n = 131$)

Variable	JKOM pain and stiffness		JKOM activities of daily living	
	Difference in mean (95% CI)*	*P*-value	Difference in mean (95% CI)*	*P*-value
HR				
Medio-lateral	−1.244 (−2.807, 0.319)	0.118	−1.239 (−2.539, 0.061)	0.062
Vertical	−0.660 (−1.541, 0.222)	0.141	0.100 (−0.636, 0.837)	0.788
Antero-posterior	−0.684 (−1.497, 0.130)	0.099	−0.035 (−0.719, 0.650)	0.921
iHR				
Medio-lateral	**−0.077 (-0.147, -0.007)**	**0.031**	**−0.070 (-0.129, -0.012)**	**0.018**
Vertical	−0.103 (−0.210, 0.003)	0.057	−0.047 (−0.136, 0.041)	0.292
Antero-posterior	−0.072 (−0.159, 0.015)	0.102	−0.022 (−0.099, 0.054)	0.561

CI: Confidence interval; HR: Harmonic ratio; iHR: Improved harmonic ratio; JKOM: Japanese Knee Osteoarthritis Measure.
Bold type represents a statistically significant result.
* Difference in mean (95% CI) per increasing 1 unit of HR/iHR was calculated after adjustment for age, sex, BMI, K&L grade, gait velocity, bilateral knee pain, and bilateral OA.

Table IV
Predictive ability of the HR and iHR on quadriceps and hip abductor muscle strength inter-limb difference in individuals with knee OA ($n = 131$)

Variable	Quadriceps muscle inter-limb difference		Hip abductor muscle inter-limb difference	
	Difference in mean (95% CI)*	*P*-value	Difference in mean (95% CI)*	*P*-value
HR				
Medio-lateral	**−0.069 (-0.127, -0.011)**	**0.020**	0.012 (−0.033, 0.027)	0.606
Vertical	−0.017 (−0.046, 0.013)	0.265	0.019 (−0.037, 0.041)	0.101
Antero-posterior	0.006 (−0.017, 0.029)	0.593	0.006 (−0.017, 0.029)	0.593
iHR				
Medio-lateral	**−0.003 (-0.006, -0.001)**	**0.008**	0.000 (−0.002, −0.002)	0.885
Vertical	−0.003 (−0.006, 0.001)	0.179	0.029 (−0.060, 0.118)	0.046
Antero-posterior	−0.001 (−0.004, 0.002)	0.423	0.002 (−0.001, 0.004)	0.180

CI: Confidence interval; HR: Harmonic ratio; iHR: Improved harmonic ratio.
Bold type represents a statistically significant result.
* Difference in mean (95% CI) of per increasing 1 unit of HR/iHR was calculated after adjustment for age, sex, K&L grade, gait velocity, bilateral knee pain, and bilateral OA.

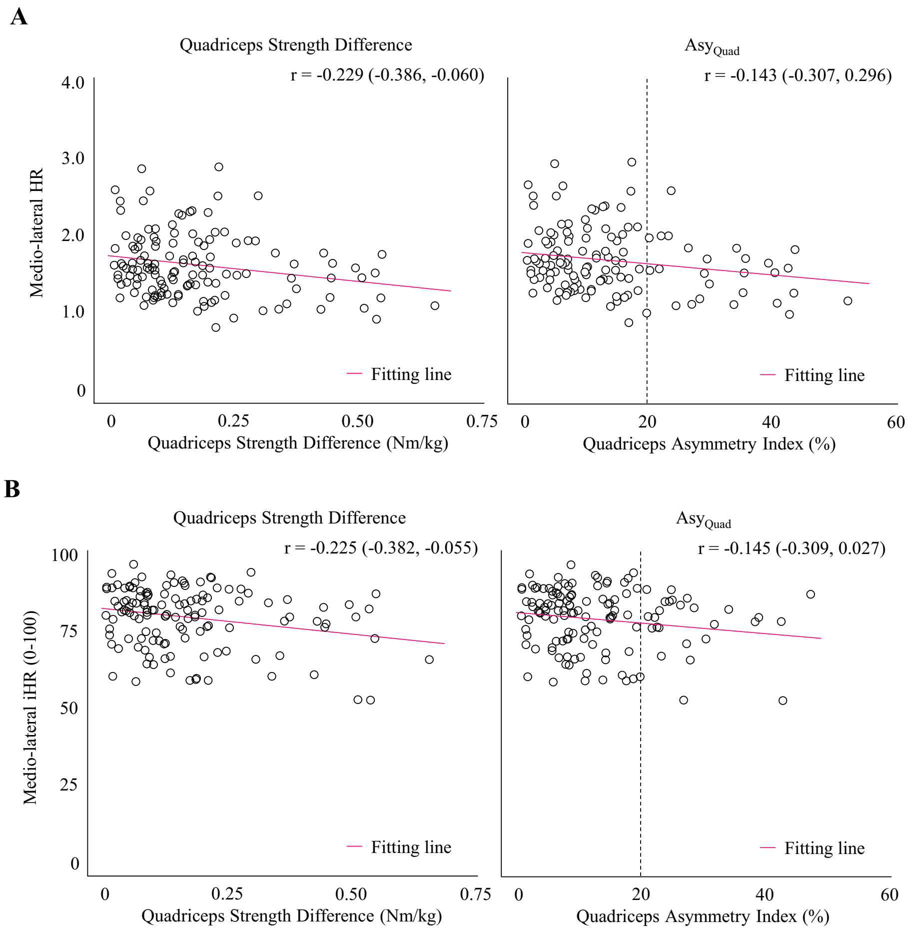

Fig. 2. A graphic illustration of the relationship between quadriceps strength difference or Asy_{Quad} and medio-lateral trunk asymmetry. **A,** Relationship between medio-lateral HR and quadriceps strength difference and Asy_{Quad}. **B,** Relationship between medio-lateral iHR and quadriceps strength difference and Asy_{Quad}. Pearson correlation coefficients (95% confidence intervals (CIs)) are provided in the figure. The vertical dotted line corresponds to the average value (Asy_{Quad} = 20%) in older adults[46,47] and indicates a potential cut-off point for quadriceps strength asymmetry over the natural aging process[16,49].

Discussion

This study found that 1) individuals with severe knee OA (K&L grade ≥3) had greater trunk movement asymmetry in the medio-lateral axis than those with a K&L grade of 1, and increased trunk movement asymmetry was associated with a greater knee pain and disability. This increased trunk movement asymmetry was also significantly associated with increased quadriceps strength asymmetry (see the graphic abstract in Fig. 3).

Trunk movement asymmetry in individuals with knee OA and its clinical relevance

Proximal biomechanical deviation was more prevalent in individuals with severe knee OA and may contribute to disease

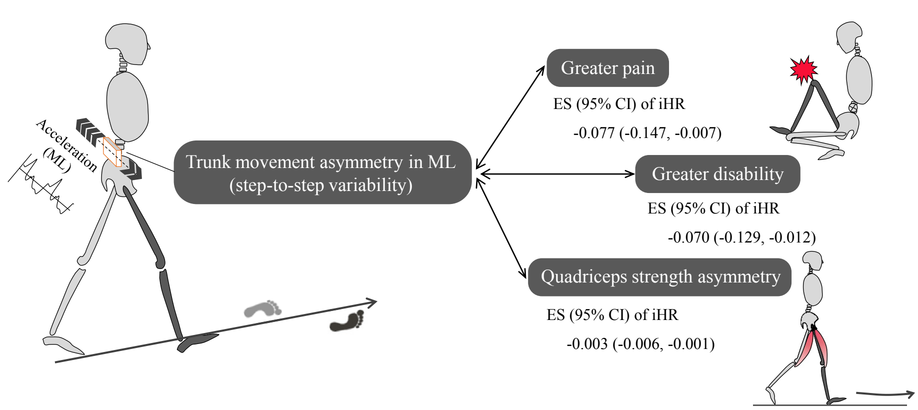

Fig. 3. Graphical abstract. Trunk movement asymmetry (step-to-step variability) in the medio-lateral (ML) direction was associated with 1) greater knee pain, 2) greater disability, and 2) inter-limb quadriceps strength asymmetry. Effect sizes (ESs) with their 95% CIs of iHR are provided.

progression[36–38]. Supporting these reports, this study revealed that patients with severe knee OA had greater trunk movement asymmetry in the medio-lateral axis than those with a K&L grade of 1. Although it is unclear why OA-related trunk asymmetry was observed in the medio-lateral axis, our study supports previous findings that medio-lateral trunk movement variability may play a role in locomotor control distinct from trunk movement variability along the antero-posterior and vertical directions[12,39–41]. We found that the correlations between HR/iHR in the medio-lateral direction and those in antero-posterior and vertical directions were lower than those found between the vertical and antero-posterior directions themselves (see Supplemental Appendix S1, Table III), data which supports these interpretations.

A practical relevance of this study was that trunk-mounted IMU-detected trunk movement asymmetry in the medio-lateral direction was significantly associated with OA-related pain and disability. This result indicates an important role for medio-lateral trunk movement asymmetry as a clinical hallmark in individuals with knee OA who experience knee pain and difficulty in daily living. Our findings of a significant relationship between decreased medio-lateral iHR (i.e., increased trunk movement variability) and greater knee pain and disability would generally support the results from a previous cross-sectional study, suggesting that a decreased medio-lateral HR was associated with greater disability in stroke patients[10]. However, the magnitude of the clinical impact of medio-lateral HR/iHR on pain and disability level is unclear because of the lack of a minimal clinically important difference (MCID)[42]. Although the mechanism why trunk movement asymmetry was associated with greater disability was unclear, it is worth noting that severe knee pain was a mediator between lower medio-lateral iHR and greater disability. Determining whether treatment that reduces variability in trunk movement can improve disability by reducing pain should be determined in a future study.

It should be acknowledged that vertical and antero-posterior iHR, but not medio-lateral iHR, was associated with poor TUG performance. Given that trunk movement asymmetry in the medio-lateral direction was associated with self-perceived knee pain and disability, these findings indicate a discrepancy between self-reported and performance-based physical function and support the results from previous studies demonstrating that these measures capture different aspects of physical function and offer complementary information[43,44]. IMU-based measurement of trunk movement asymmetry using an orthogonal coordinate system may capture both self-reported and performance-based physical function by monitoring trunk acceleration in a distinct axis. This hypothesis should be validated in future studies.

Association between trunk movement and lower limb muscle strength asymmetries

Another practical relevance was that increased medio-lateral trunk movement asymmetry was significantly associated with quadriceps strength asymmetry, even after adjustment for covariates, including bilateral knee pain and bilateral radiographic knee OA, which have been suggested to be significant factors associated with trunk movement asymmetry[4,5]. Our observations generally support the previous finding that strength asymmetry in older women is associated with increased gait asymmetry and variability[16], although this does not support previous studies demonstrating that physically fatigued lower limb muscles in older adults resulted in decreased interstride medio-lateral trunk acceleration variability[39] and balance control[45]. Our findings imply that medio-lateral trunk movement asymmetry increases quadriceps strength asymmetry, or vice versa, although the study's cross-sectional nature limits our interpretations about causality. As medio-lateral trunk movement variability is associated with a greater degree of disability as mentioned above, paying close attention to medio-lateral trunk movement asymmetry may be key to understanding OA-related impaired muscle function and disability. A longitudinal cohort study is required to address the causal relationship between medio-lateral trunk movement asymmetry and OA-related impairment.

This study cannot clarify the mechanism of the significant relationship between trunk movement and quadriceps muscle strength asymmetries. No significant relationship between a difference in hip abductor muscle strength and medio-lateral trunk movement asymmetry was detected. Quadriceps muscle contraction in the early stance phase contributes to lateral backwards, and upwards acceleration of the center of mass during normal walking[15]. However, hip abductor muscle strength contributes more to regulation of the center of mass in the medio-lateral direction than quadriceps strength does[15]. A significant relationship between quadriceps muscle strength asymmetry and trunk movement asymmetry in only the medio-lateral direction cannot be completely explained by this biomechanical theory.

In this study, Asy_{Quad} was 12.3%, which is comparable to that observed in older adults[46,47], indicating that included participants with knee OA exhibited mild clinical profiles that would not cause extreme inter-limb muscle imbalance. Indeed, 87% participants were K&L grade 1–2. These points should be considered when interpreting our findings and translating them into a clinical setting.

Comparison of two different measures of trunk movement asymmetry

The use of specific measurement parameters for trunk movement asymmetry is crucial for capturing different levels of knee pain and disability. This study used both the HR and iHR as measurements of trunk movement asymmetry. The results revealed that the medio-lateral iHR had a higher predictive ability than HR for knee pain and disability level although the HR displayed a greater discriminatory ability than the iHR for different K&L grades. The non-linear relationship between these two measures likely causes the difference in their discriminatory and predictive abilities (see Supplemental Appendix S1, Fig. 3). These two measures may capture different aspects with regards to pathological condition, pain, and disability; the clinical utility of these two metrics may be a function of their evaluation objectives. Given that iHR allows a more intuitive interpretation than HR and improves comparability to other relevant studies[9], iHR should be applied if the clinician and physical therapists wish to target patients' increased pain and disability.

Limitations

The present study has some limitations. First, the cross-sectional nature of this study limits our ability to discern causality between variables. Trunk movement asymmetry may be a consequence of increased disability, and our findings do not necessarily emphasize intervention for increased trunk movement asymmetry to improve knee pain and disability. Second, the HR and iHR are global measures that do not account for phase during gait; thus, they cannot explain where the deviations from symmetry occur. Third, the calculated HR and iHR did not consider postural effects; participants' IMU inclination angle would affect the static gravity component, thereby changing the acceleration amplitude during walking. Nevertheless, only a small effect from the inclination angle was observed in the significant relationship between the medio-lateral HR and disability, and between the quadriceps strength difference and the medio-lateral HR (see Supplemental Appendix S1, Fig. 4). Finally, the HR and iHR were calculated from five consecutive strides during walking, which can be easily evaluated in a clinical setting. As stride number may affect results[9,48], further studies with a greater number of strides are warranted to verify our findings.

Conclusion

Individuals with severe knee OA had increased medio-lateral trunk movement asymmetry, which was associated with a greater knee pain and disability. Increased trunk movement asymmetry was significantly associated with increased quadriceps strength asymmetry. Paying close attention to medio-lateral trunk movement asymmetry may be key to understanding OA-related impairment and disability.

Author contributions

All authors have made substantial contributions to (1) the conception and design of the study, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be submitted.

The specific contributions of the authors are as follows:

(1) Conception and design of the study: HI and MT.
(2) Analysis and interpretation of the data: HI, RE, TA, and MT.
(3) Drafting of the article: HI.
(4) Critical revision of the article for important intellectual content: HI and TA.
(5) Final approval of the article: HI, RE, TA, and MT.
(6) Statistical expertise: HI.
(7) Obtaining funding: HI.
(8) Data collection and assembly: HI, RE, TA, and MT.

Competing interest statement

The authors did not receive financial support or other benefits from commercial sources for the work reported in this manuscript, or any other financial support that could create a potential conflict of interest or the appearance of a conflict of interest with regard to the work.

Role of the funding source

This study was supported in part by a Grant-in-Aid from the Japan Society for the Promotion of Science (https://www.jsps.go.jp/) Research Fellows to HI.

Acknowledgments

The authors thank the members of the Aoyama laboratory (Kyoto University, Kyoto) for assistance with data collection. The authors would like to thank Editage (www.editage.jp) for English language editing.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2018.10.012.

References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, *et al*. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163–96.
2. Briem K, Snyder-Mackler L. Proximal gait adaptations in medial knee OA. J Orthop Res 2009;27:78–83.
3. Shakoor N, Block JA, Shott S, Case JP. Nonrandom evolution of end-stage osteoarthritis of the lower limbs. Arthritis Rheum 2002;46:3185–9.
4. Mills K, Hettinga BA, Pohl MB, Ferber R. Between-limb kinematic asymmetry during gait in unilateral and bilateral mild to moderate knee osteoarthritis. Arch Phys Med Rehabil 2013;94:2241–7.
5. Creaby MW, Bennell KL, Hunt MA. Gait differs between unilateral and bilateral knee osteoarthritis. Arch Phys Med Rehabil 2012;93:822–7.
6. Staab W, Hottowitz R, Sohns C, Sohns JM, Gilbert F, Menke J, *et al*. Accelerometer and gyroscope based gait analysis using spectral analysis of patients with osteoarthritis of the knee. J Phys Ther Sci 2014;26:997–1002.
7. Bellanca JL, Lowry KA, Vanswearingen JM, Brach JS, Redfern MS. Harmonic ratios: a quantification of step to step symmetry. J Biomech 2013;46:828–31.
8. Smidt GL, Arora JS, Johnston RC. Accelerographic analysis of several types of walking. Am J Phys Med 1971;50:285–300.
9. Pasciuto I, Bergamini E, Iosa M, Vannozzi G, Cappozzo A. Overcoming the limitations of the Harmonic Ratio for the reliable assessment of gait symmetry. J Biomech 2017;53:84–9.
10. Iosa M, Fusco A, Morone G, Pratesi L, Coiro P, Venturiero V, *et al*. Assessment of upper-body dynamic stability during walking in patients with subacute stroke. J Rehabil Res Dev 2012;49:439–50.
11. Lowry KA, Smiley-Oyen AL, Carrel AJ, Kerr JP. Walking stability using harmonic ratios in Parkinson's disease. Mov Disord 2009;24:261–7.
12. Moe-Nilssen R, Aaslund MK, Hodt-Billington C, Helbostad JL. Gait variability measures may represent different constructs. Gait Posture 2010;32:98–101.
13. Deasy M, Leahy E, Semciw AI. Hip strength deficits in people with symptomatic knee osteoarthritis: a systematic review with meta-analysis. J Orthop Sports Phys Ther 2016;46:629–39.
14. Omori G, Koga Y, Tanaka M, Nawata A, Watanabe H, Narumi K, *et al*. Quadriceps muscle strength and its relationship to radiographic knee osteoarthritis in Japanese elderly. J Orthop Sci 2013;18:536–42.
15. Pandy MG, Lin YC, Kim HJ. Muscle coordination of mediolateral balance in normal walking. J Biomech 2010;43:2055–64.
16. Laroche DP, Cook SB, Mackala K. Strength asymmetry increases gait asymmetry and variability in older women. Med Sci Sports Exerc 2012;44:2172–81.
17. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. Ann Rheum Dis 1957;16:494–502.
18. Hart DJ, Spector TD. Kellgren & Lawrence grade 1 osteophytes in the knee–doubtful or definite? Osteoarthritis Cartilage 2003;11:149–50.
19. Cibere J, Sayre EC, Guermazi A, Nicolaou S, Kopec JA, Esdaile JM, *et al*. Natural history of cartilage damage and osteoarthritis progression on magnetic resonance imaging in a population-based cohort with knee pain. Osteoarthritis Cartilage 2011;19:683–8.
20. Robbins S, Waked E. Balance and vertical impact in sports: role of shoe sole materials. Arch Phys Med Rehabil 1997;78:463–7.
21. Arnadottir SA, Mercer VS. Effects of footwear on measurements of balance and gait in women between the ages of 65 and 93 years. Phys Ther 2000;80:17–27.

22. Light LH, McLellan GE, Klenerman L. Skeletal transients on heel strike in normal walking with different footwear. J Biomech 1980;13:477–80.
23. Bautmans I, Jansen B, Van Keymolen B, Mets T. Reliability and clinical correlates of 3D-accelerometry based gait analysis outcomes according to age and fall-risk. Gait Posture 2011;33: 366–72.
24. Menz HB, Lord SR, Fitzpatrick RC. Acceleration patterns of the head and pelvis when walking on level and irregular surfaces. Gait Posture 2003;18:35–46.
25. Zijlstra W, Hof AL. Assessment of spatio-temporal gait parameters from trunk accelerations during human walking. Gait Posture 2003;18:1–10.
26. Wang CY, Olson SL, Protas EJ. Test-retest strength reliability: hand-held dynamometry in community-dwelling elderly fallers. Arch Phys Med Rehabil 2002;83:811–5.
27. Akai M, Doi T, Fujino K, Iwaya T, Kurosawa H, Nasu T. An outcome measure for Japanese people with knee osteoarthritis. J Rheumatol 2005;32:1524–32.
28. Kraus VB, Vail TP, Worrell T, McDaniel G. A comparative assessment of alignment angle of the knee by radiographic and physical examination methods. Arthritis Rheum 2005;52:1730–5.
29. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142–8.
30. Dobson F, Hinman RS, Roos EM, Abbott JH, Stratford P, Davis AM, *et al*. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. Osteoarthritis Cartilage 2013;21:1042–52.
31. Jonckheere AR. A distribution-free k-sample test against ordered alternatives. Biometrika 1954;41:133–45.
32. Markman HJ, Rhoades GK, Stanley SM, Peterson KM. A randomized clinical trial of the effectiveness of premarital intervention: moderators of divorce outcomes. J Fam Psychol 2013;27:165–72.
33. Brach JS, McGurl D, Wert D, Vanswearingen JM, Perera S, Cham R, *et al*. Validation of a measure of smoothness of walking. J Gerontol A Biol Sci Med Sci 2011;66:136–41.
34. Mazza C, Iosa M, Picerno P, Cappozzo A. Gender differences in the control of the upper body accelerations during level walking. Gait Posture 2009;29:300–3.
35. Muraki S, Oka H, Akune T, Mabuchi A, En-yo Y, Yoshida M, *et al*. Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: the ROAD study. Osteoarthritis Cartilage 2009;17:1137–43.
36. Astephen JL, Deluzio KJ, Caldwell GE, Dunbar MJ. Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. J Orthop Res 2008;26:332–41.
37. Huang SC, Wei IP, Chien HL, Wang TM, Liu YH, Chen HL, *et al*. Effects of severity of degeneration on gait patterns in patients with medial knee osteoarthritis. Med Eng Phys 2008;30: 997–1003.
38. Hunt MA, Wrigley TV, Hinman RS, Bennell KL. Individuals with severe knee osteoarthritis (OA) exhibit altered proximal walking mechanics compared with individuals with less severe OA and those without knee pain. Arthritis Care Res 2010;62:1426–32.
39. Helbostad JL, Leirfall S, Moe-Nilssen R, Sletvold O. Physical fatigue affects gait characteristics in older persons. J Gerontol A Biol Sci Med Sci 2007;62:1010–5.
40. Aaslund MK, Moe-Nilssen R. Treadmill walking with body weight support effect of treadmill, harness and body weight support systems. Gait Posture 2008;28:303–8.
41. Moe-Nilssen R, Helbostad JL. Interstride trunk acceleration variability but not step width variability can differentiate between fit and frail older adults. Gait Posture 2005;21:164–70.
42. Pham T, van der Heijde D, Altman RD, Anderson JJ, Bellamy N, Hochberg M, *et al*. OMERACT-OARSI initiative: osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. Osteoarthritis Cartilage 2004;12:389–99.
43. Wright AA, Cook CE, Baxter GD, Garcia J, Abbott JH. Relationship between the western Ontario and McMaster Universities osteoarthritis index physical function subscale and physical performance measures in patients with hip osteoarthritis. Arch Phys Med Rehabil 2010;91:1558–64.
44. Kivinen P, Sulkava R, Halonen P, Nissinen A. Self-reported and performance-based functional status and associated factors among elderly men: the Finnish cohorts of the Seven Countries Study. J Clin Epidemiol 1998;51:1243–52.
45. Toebes MJ, Hoozemans MJ, Dekker J, van Dieen JH. Effects of unilateral leg muscle fatigue on balance control in perturbed and unperturbed gait in healthy elderly. Gait Posture 2014;40: 215–9.
46. Perry MC, Carville SF, Smith IC, Rutherford OM, Newham DJ. Strength, power output and symmetry of leg muscles: effect of age and history of falling. Eur J Appl Physiol 2007;100: 553–61.
47. Skelton DA, Kennedy J, Rutherford OM. Explosive power and asymmetry in leg muscle function in frequent fallers and non-fallers aged over 65. Age Ageing 2002;31:119–25.
48. Riva F, Bisi MC, Stagni R. Gait variability and stability measures: minimum number of strides and within-session reliability. Comput Biol Med 2014;50:9–13.
49. Chon J, Kim HS, Lee JH, Yoo SD, Yun DH, Kim DH, *et al*. Association between asymmetry in knee extension strength and balance in a community-dwelling elderly population: a cross-sectional analysis. Ann Rehabil Med 2018;42:113–9.