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Original article

A most painful knee does not induce interlimb differences in knee and hip moments during gait in patients with knee osteoarthritis

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ABSTRACT

Background: Patients with knee osteoarthritis can adapt their gait to unload the most painful knee joint in order to try to reduce pain and improve physical function. However, these gait adaptations can cause higher loads on the contralateral joints. The aim of the study was to investigate the interlimb differences in knee and hip frontal plane moments during gait in patients with knee osteoarthritis and in healthy controls.

Methods: Forty patients with knee osteoarthritis and 19 healthy matched controls were measured during comfortable treadmill walking. Frontal plane joint moments were obtained of both hip and knee joints. Differences in interlimb moments within each group were assessed using statistical parametric mapping and discrete gait parameters.

Findings: No interlimb differences were observed in patients with knee osteoarthritis and control subjects at group level. Furthermore, the patients presented similar interlimb variability as the controls. In a small subgroup ($n = 12$) of patients, the moments in the most painful knee were lower than in the contralateral knee, while the other patients ($n = 28$) showed higher moments in the most painful knee compared to the contralateral knee. However, no interlimb differences in the hip moments were observed within the subgroups.

Interpretation: Patients with knee osteoarthritis do not have interlimb differences in knee and hip joint moments. Patients and healthy subjects demonstrate a similar interlimb variability in the moments of the lower extremities. In this context, differences in knee pain in patients with knee osteoarthritis did not induce any interlimb differences in the frontal plane knee and hip moments.

1. Introduction

Knee osteoarthritis (OA) is a highly prevalent disease leading to pain and decline in physical function (Woolf and Pfleger, 2003). Patients with knee OA can adapt their gait to unload the most painful knee joint, relative to the contralateral knee, in order to try to reduce pain and improve physical function (Lewek et al., 2004; Winter and Eng, 1995). However, these gait adaptations might result in overloading of other joints, especially the contralateral knee and hip joint (Briem and Snyder-

Mackler, 2009). It is known from literature that 87% of the patients with knee OA have multiple joints simultaneously affected (Günther et al., 1998), and that 72% of patients develop OA in the contralateral hip joint instead of the ipsilateral hip joint (Shakoor et al., 2002). This onset of OA could be due to interlimb differences in joint load (Briem and Snyder-Mackler, 2009; Shakoor et al., 2002). Joint moments, estimated with gait analysis, are often used to infer magnitude of joint load (Chang et al., 2005; Mündermann et al., 2005). Several studies have examined joint moments during gait in the most painful limb of knee OA patients

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compared to controls (Astefan et al., 2008; Linley et al., 2010), but research is limited on interlimb differences of patients with knee OA (Briem and Snyder-Mackler, 2009; Messier et al., 2016).

To our knowledge, only a few studies investigated interlimb differences in knee and hip moments in patients with knee OA during gait (Briem and Snyder-Mackler, 2009; Messier et al., 2016) and they reported contradicting results. One study found no interlimb differences (Messier et al., 2016) and another study observed higher frontal plane moments in the contralateral hip joint (Briem and Snyder-Mackler, 2009). Both studies lacked a healthy control group. Therefore, it is not clear whether the differences between the studies are just a consequence of natural interlimb variability. In addition to lacking a control group, these studies have analyzed differences in discrete scalar parameters (i. e. peaks) rather than continuous curves, potentially missing differences over the stance phase. Therefore, the aim of this study was to investigate the interlimb differences in knee and hip frontal plane moments during gait in patients with knee OA and in healthy control subjects. It was hypothesized that patients unload the most painful knee and that as a consequence the hip and knee joints on the contralateral side have increased loading.

2. Methods

2.1. Study population

Forty patients with knee OA were recruited from the Amsterdam Osteoarthritis cohort of Reade, Center of Rehabilitation and Rheumatology, Amsterdam, the Netherlands or from the database of the Department of Rehabilitation Medicine, Amsterdam UMC, location VUmc, Amsterdam, the Netherlands (VUmc). Inclusion criteria were (1) diagnosis of knee OA according to the clinical American College of Rheumatology (ACR) criteria (Altman et al., 1986), (2) able to walk 5 min without stopping, (3) body mass index (BMI) between 20 and 35 kg/m² and (4) maximal score of 7 on the Numeric Pain Rating Scale (NPRS). Exclusion criteria were (1) diagnosis of hip OA, rheumatoid arthritis or any other form of inflammatory arthritis, (2) lower extremity joint replacement, (3) a knee related injury last year and (4) not willing to walk without a walking aid. Nineteen healthy control subjects were included and sex, age and BMI-matched with the patient group. Exclusion criteria were (1) diagnosed with a musculoskeletal disease, (2) a knee related injury in the last 5 years or (3) knee-related problems. The study was approved by the medical ethics committee of the VUmc. All subjects signed informed consent.

2.2. Data collection

The measurements were performed in a virtual reality environment on an instrumented treadmill with two incorporated force plates (GRAIL system, Motekforce Link BV, Amsterdam) surrounded by ten motion capture cameras (Vicon, Oxford, United Kingdom). The session started with completing the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Collins et al., 2011) questionnaire and Numeric Pain Rating Scale (NPRS) (Ferreira-Valente et al., 2011) about knee pain at the moment. After obtaining the anthropometrics, the subject was prepared for treadmill walking by placing 40 reflective markers on the body according to the calibrated anatomical systems technique (CAST) model (Cappozzo et al., 1995). A familiarization trial of 4 min walking was performed in which also the comfortable walking speed was determined. Next, a trial of 4 min treadmill walking was captured. After this trial, the NPRS for knee pain during gait was completed. Finally, radiographs of the knee joints were obtained

according to the Buckland-Wright protocol (Buckland-Wright, 1995) and scored by an experienced clinician using the Kellgren & Lawrence (K&L) classification system (Kellgren and Lawrence, 1957).

2.3. Data analysis

The marker and ground reaction force data were input in a custom-made Matlab program, BodyMech (Harlaar and Doorenbosh, 2006), to obtain the frontal plane knee and hip joint moments. Raw marker data were filtered by the cross-validated quintic spline (Woltring, 1978). The raw force data were filtered using a two-way 10Hz 4th order low-pass Butterworth filter. Next, inverse dynamics was used to calculate the knee and hip joint moments. The moments were time-normalized to percentage stancetime using a cubic interpolation function and marker-based initial contacts and toe-offs (Zeni Jr et al., 2008). The moments were amplitude-normalized to bodyweight. The ensemble-average frontal plane knee and hip moments over approximately 60 steps were calculated for each subject. After averaging, discrete gait parameters were obtained from these time series (max, min and range values). Interlimb variability was calculated for the OA and control group by computing the difference in interlimb knee and hip peak moments over the approximately 60 steps per participant and determining the 95% confidence interval. The ipsilateral knee and hip was at the start of the study determined by the patient as the most painful knee and for the control group a random generator was used.

2.4. Subgroup analysis

Subgroup analysis was performed to explore the hypothesis that patients who unload the ipsilateral knee joint, increase the load on the contralateral hip joint. Therefore, patients showing lower ipsilateral than contralateral external knee adduction moments (KAM) (averaged over the stance phase) were defined as the low KAM group (OA LK). Patients that exhibited no interlimb knee moment difference or higher ipsilateral than contralateral KAM were assigned to the high KAM group (OA HK).

2.5. Statistical analysis

Descriptive statistics of each group were calculated of the anthropometrics, gait speed and scores on the questionnaires. These variables were screened for normality by a Shapiro-Wilk test. Normal distributed variables were compared between groups with independent samples t-tests. Otherwise, the variables were compared with Mann Whitney-U tests.

The interlimb differences within each group were assessed at each point of the stance phase using Statistical Parametric Mapping (SPM) (Pataky et al., 2013) implemented in Matlab (MATLAB R2018a, The MathWorks, Inc, Natick, United States of America) and with discrete gait parameters using Statistical Package for the Social Sciences (SPSS) software (ver.24 SPSSInc., Chicago, United States of America). With both methods paired samples t-test were used to analyze interlimb differences in normal distributed variables. Otherwise, Wilcoxon signed-rank tests were applied. Interlimb variability was compared between the OA and control group with independent samples t-tests or non-parametric Mann-Whitney U tests. The significance level was $\alpha < 0.05$.

3. Results

No differences were observed in anthropometrics between the patients and healthy controls (Table 1). All knee OA patients had bilateral

Table 1

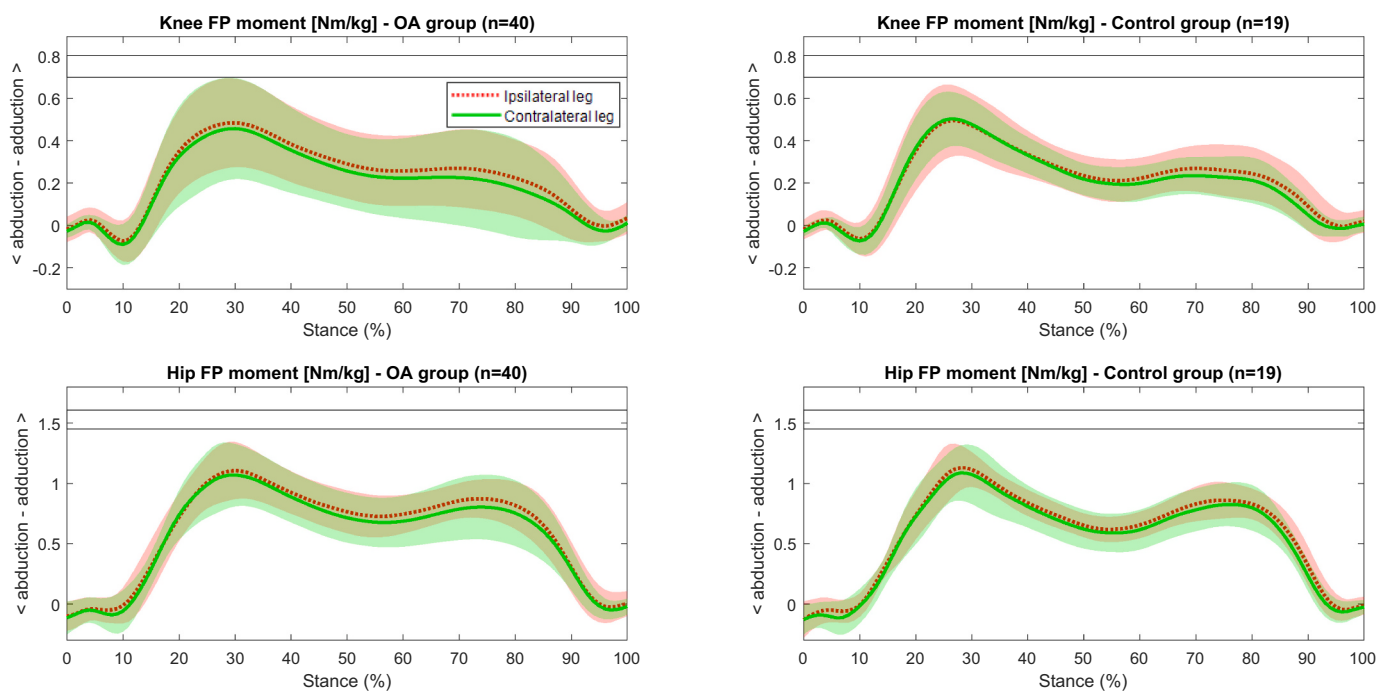
Characteristics of patients with knee OA (n = 40), healthy control subjects (n = 19) and differences between groups.

	OA group (n = 40)	Control group (n = 19)	p-value
	Mean (SD)	Mean (SD)	
Female (n (%))	24 (60)	10 (53)	0.59
Age (yr)	66 (8)	65 (6)	0.39
Height (m)	1.77 (0.10)	1.75 (0.08)	0.43
Weight (kg)	80.8 (13.8)	73.5 (12.2)	0.06
BMI (kg/m ²)	25.7 (3.1)	24.0 (3.3)	0.06
K&L grade (≤ 2) – ipsilateral (n (%))	23 (58%)		-
K&L grade (≥ 3) – ipsilateral (n (%))	17 (42%)		-
K&L grade (≤ 2) – contralateral (n (%))	30 (75%)		-
K&L grade (≥ 3) – contralateral (n (%))	10 (25%)		-
NPRS knee – ipsilateral (0-10)	3 (3) ⁿⁿ		-
NPRS knee – contralateral (0-10)	0 (2) ⁿⁿ		-
NPRS knee during gait – ipsilateral (0-10)	2 (4) ⁿⁿ		-
NPRS knee during gait – contralateral (0-10)	0 (1) ⁿⁿ		-
WOMAC – Pain (0-20)	9 (9) ⁿⁿ		-
WOMAC – Stiffness (0-8)	3 (3) ⁿⁿ		-
WOMAC – Functional (0-68)	28 (33) ⁿⁿ		-
Gait speed (m/s)	1.30 (0.29) ⁿⁿ	1.40 (0.20) ⁿⁿ	0.03

BMI = Body Mass Index, K&L = Kellgren & Lawrence classification, NPRS = Numeric Pain Rating Scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Bold p-value = Statistically significant difference ($p < 0.05$)

ⁿⁿ = non-normal distribution i.e. median and interquartile range are provided.

**Fig. 1.** Interlimb differences in the frontal plane (FP) knee and hip moments in the OA group (n = 40) and control group (n = 19).

Dotted line (red) = ipsilateral leg, solid line (green) = contralateral leg.

The solid and dotted lines of the graph represent the mean pattern of the group and the shaded area shows the standard deviation of the patterns of the group. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

knee OA. The ipsilateral knee joint was more painful than the contralateral knee joint, as reflected by the NPRS (mean difference (MD) = 3 points). Twenty-three patients had radiographically moderate OA of the ipsilateral knee joint (K&L score ≤ 2) and 17 patients showed severe radiographic knee OA (K&L score ≥ 3). Thirty-six patients showed a

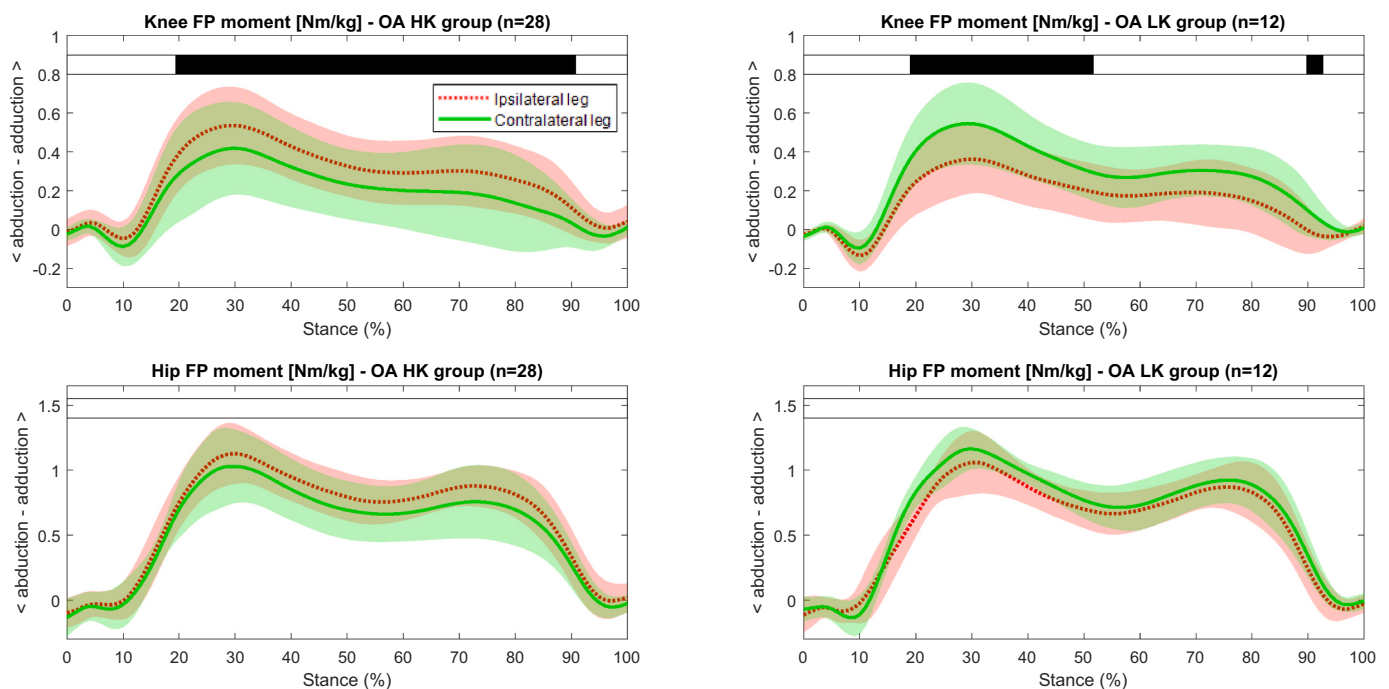
higher or equal K&L score for the ipsilateral knee joint than for the contralateral knee joint. The OA group walked 8% slower than the control group (MD = 0.10 m/s, $p = 0.03$).

No interlimb differences were observed in the SPM results (Fig. 1) nor for the discrete gait parameters (Table 2) of the frontal plane knee

Table 2

Discrete gait parameters and interlimb variability in the frontal plane (FP) knee and hip moments in the OA group (n = 40) and control group (n = 19).

	OA group (n = 40)	p-value	Control group (n = 19)	p-value
	Mean (SD)		Mean (SD)	
	(ipsi/contra)		(ipsi/contra)	
Discrete parameters- moments (Nm/kg)				
Knee – First peak adduction moment	0.39 (0.22)/0.50 (0.40)	0.45 ⁿⁿ	0.52 (0.16)/0.52 (0.13)	0.96
Knee – Second peak adduction moment	0.23 (0.21)/0.28 (0.24)	0.15	0.29 (0.11)/0.25 (0.10)	0.22
Knee – Peak abduction moment	0.14 (0.08)/0.11 (0.07)	0.10	0.10 (0.06)/0.08 (0.04)	0.89
Knee – Range frontal plane moment	0.51 (0.22)/0.61 (0.26)	0.87 ⁿⁿ	0.62 (0.13)/0.62 (0.14)	0.96
Hip – First peak adduction moment	1.11 (0.46)/1.14 (0.33)	0.87 ⁿⁿ	1.14 (0.17)/1.04 (0.23)	0.20 ⁿⁿ
Hip – Second peak adduction moment	0.86 (0.23)/0.90 (0.25)	0.23 ⁿⁿ	0.89 (0.14)/0.85 (0.18)	0.39
Hip – Peak abduction moment	0.20 (0.10)/0.20 (0.09)	0.98	0.20 (0.09)/0.24 (0.11)	0.18
Hip – Range frontal plane moment	1.22 (0.28)/1.34 (0.31)	0.29 ⁿⁿ	1.33 (0.26)/1.34 (0.49)	0.72 ⁿⁿ
	Mean (2*SD)		Mean (2*SD)	p-value
Interlimb variability - moments (Nm/kg)				
Knee – First peak adduction moment	0.03 (0.40)		0.00 (0.37)	0.54
Hip – First peak adduction moment	0.03 (0.59)		0.05 (0.32)	0.78

ⁿⁿ = non-normal distribution i.e. median and interquartile range are provided.**Fig. 2.** Interlimb differences in the frontal plane (FP) knee and hip moments in patients with a high (n = 28, OA HK group) versus a low (n = 12, OA LK group) ipsilateral knee adduction moment.

Dotted line (red) = ipsilateral leg, solid line (green) = contralateral leg. Black bars represent significantly differences in interlimb moments.

The solid and dotted lines of the graph represent the mean pattern of the group and the shaded area shows the standard deviation of the patterns of the group. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

and hip joint moments for the patients with knee OA or control group. The patients showed also no differences in interlimb variability of the first peak KAM (MD = 0.03 Nm/kg, $p = 0.54$) and first peak hip adduction moment (MD = 0.02 Nm/kg, $p = 0.78$) compared to the control group (Table 2).

The subgroup analysis showed that the OA HK group (n = 28) had a lower contralateral than ipsilateral KAM during 19–91% (MD = 0.11

Nm/kg, $p < 0.01$) of stance (Fig. 2). No interlimb differences were observed in the hip joint moments of the OA HK group (Fig. 2 and Table 3). The OA LK group (n = 12) had a higher contralateral than ipsilateral KAM during 18–51% (MD = 0.16 Nm/kg, $p < 0.01$) and 90–93% (MD = 0.10 Nm/kg, $p = 0.03$) of stance. Furthermore, the OA LK group presented no interlimb moment differences in the hip joints (Fig. 2 and Table 3).

Table 3

Discrete gait parameters in the frontal plane (FP) knee and hip moments in moments in patients with a high (n = 28, OA HK group) versus a low (n = 12, OA LK group) ipsilateral knee adduction moment.

	OA HK group (n = 28)	p-value	OA LK group (n = 12)	p-value
	Mean (SD)		Mean (SD)	
	(ipsi/contra)		(ipsi/contra)	
Discrete parameters- moments (Nm/kg)				
Knee – First peak adduction moment	0.53 (0.22)/0.45 (0.32)	0.00	0.39 (0.20)/0.53 (0.28)	0.00ⁿⁿ
Knee – Second peak adduction moment	0.32 (0.22)/0.26 (0.27)	0.00	0.21 (0.17)/0.33 (0.15)	0.01
Knee – Peak abduction moment	0.08 (0.09)/0.13 (0.12)	0.02ⁿⁿ	0.14 (0.08)/0.11 (0.08)	0.18
Knee – Range frontal plane moment	0.64 (0.16)/0.67 (0.23)	0.05	0.52 (0.18)/0.67 (0.19)	0.00
Hip – First peak adduction moment	1.12 (0.35)/1.07 (0.16)	0.26 ⁿⁿ	1.09 (0.23)/1.18 (0.17)	0.37
Hip – Second peak adduction moment	0.87 (0.18)/0.88 (0.16)	0.06 ⁿⁿ	0.90 (0.16)/0.96 (0.16)	0.68
Hip – Peak abduction moment	1.30 (0.29)/1.28 (0.19)	0.98	0.20 (0.10)/0.20 (0.09)	0.88
Hip - Range frontal plane moment	1.30 (0.26)/1.28 (0.27)	0.00	1.22 (0.26)/1.37 (0.32)	0.18 ⁿⁿ

Bold p-value = Statistically significant difference (p<0.05)

ⁿⁿ = non-normal distribution i.e. median and interquartile range are provided.

4. Discussion

The aim of the study was to investigate interlimb differences in frontal plane knee and hip moments during comfortable gait in patients with knee OA and in healthy controls. We found that interlimb pain differences of on average 3 points on the NPRS scale were present in the knee OA patients. Nevertheless, no interlimb differences in frontal plane knee and hip moments were observed in this group. Also our subgroup analysis did not reveal a compensatory mechanism. Furthermore, the knee OA patients presented similar interlimb variability in peak knee and hip adduction moments as we found in the controls. Therefore, in this context, differences in knee pain in patients with knee OA did not induce any interlimb differences in the frontal plane knee and hip moments.

The absence of interlimb differences in the OA group is in line with the results of Messier et al (2016) (Messier et al., 2016), who measured the kinematics and kinetics of patients with unilateral and bilateral knee OA. However, another study by Briem and Snyder-Mackler (2009), reported higher contralateral frontal plane hip moments compared to ipsilateral frontal plane hip moments in patients with unilateral knee OA (Briem and Snyder-Mackler, 2009). Interestingly, despite having radiographic bilateral knee OA, our patients showed similar interlimb variability as the controls. It is plausible that patients with unilateral knee OA isolated to the medial compartment relates to a gait adaptation that relieves the load on the affected knee and increases the load on the contralateral hip joint. This gait adaptation could be a trunk lean strategy, but we did not evaluate this. Future studies should consider the effect of the location of knee OA on interlimb joint moment differences.

A limitation of this study is the inclusion of only bilateral knee OA patients. However, bilateral knee OA is more prevalent than unilateral OA (Günther et al., 1998; Shakoor et al., 2002). A second limitation is the small sample size of the study. Measuring more knee OA patients might give significant results in interlimb hip moments. A third limitation was the absence of hip radiographs. Therefore, some subjects might have had radiographic hip OA which could have influenced their gait pattern. However, subjects with clinical symptoms of hip OA were excluded from the study. A fourth limitation is that the subjects walked on a treadmill during the measurements. Walking on a treadmill can result in small differences in gait kinetics compared to over ground walking (Riley et al., 2007). However, collection of treadmill-based data has the advantage of collecting a large amount of kinetic data while allowing a consistent gait speed. Finally, although our analysis was limited to the frontal plane moments these moments are most frequently used in literature and are associated with OA progression (Astéphen et al., 2008; Chang et al., 2005).

5. Conclusion

During comfortable gait speed, patients with knee OA and healthy subjects demonstrate a similar interlimb variability in the moments of the lower extremities. In this context, differences in knee pain in patients with knee OA did not induce any interlimb differences in the frontal plane knee and hip moments.

Declaration of competing interest

The authors confirm that there are no conflict of interest regarding the work described in the current manuscript.

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References

- Altman, R., Asch, E., Bloch, D., Bole, G., Borenstein, D., Brandt, K., Christy, W., Cooke, T. D., Greenwald, R., Hochberg, M., Howell, D., Kaplan, D., Koopman, W., Longley, S., Mankin, H., McShane, D.J., Medsger, T., Meenan, R., Mikkelsen, W., Moskowitz, R., Murphy, W., Rothschild, B., Segal, M., Sokoloff, L., Wolfe, F., 1986. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis Rheum.* 29, 1039–1049. <https://doi.org/10.1002/art.1780290816>.
- Astephen, J.L., Deluzio, K.J., Caldwell, G.E., Dunbar, M.J., 2008. Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. *J. Orthop. Res.* 26, 332–341. <https://doi.org/10.1002/jor.20496>.
- Briem, K., Snyder-Mackler, L., 2009. Proximal gait adaptations in medial knee OA. *J. Orthop. Res.* 27, 78–83. <https://doi.org/10.1002/jor.20718>.
- Buckland-Wright, C., 1995. Protocols for precise radio-anatomical positioning of the tibiofemoral and patellofemoral compartments of the knee. *Osteoarthr. Cart* 3, 71–80, 10071.
- Cappozzo, A., Catani, F., Della Croce, U., Leardini, A., 1995. Position and orientation in space of bones during movement: anatomical frame definition and determination. *Clin. Biomech.* 10, 171–178. [https://doi.org/10.1016/0268-0033\(95\)91394-T](https://doi.org/10.1016/0268-0033(95)91394-T).
- Chang, A., Hayes, K., Dunlop, D., Song, J., Hurwitz, D., Cahue, S., Sharma, L., 2005. Hip abduction moment and protection against medial tibiofemoral osteoarthritis progression. *Arthritis Rheum.* 52, 3515–3519. <https://doi.org/10.1002/art.21406>.
- Collins, N.J., Misra, D., Felson, D.T., Crossley, K.M., Roos, E.M., 2011. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS). *Knee Ou. Arthritis Care Res. (Hoboken)*. 63, S208–S228. <https://doi.org/10.1002/acr.20632>.
- Ferreira-Valente, M.A., Pais-Ribeiro, J.L., Jensen, M.P., 2011. Validity of four pain intensity rating scales. *Pain* 152, 2399–2404. <https://doi.org/10.1016/j.pain.2011.07.005>.

- Günther, K.P., Stürmer, T., Sauerland, S., Zeissig, I., Sun, Y., Kessler, S., Scharf, H.P., Brenner, H., Puhl, W., 1998. Prevalence of generalised osteoarthritis in patients with advanced hip and knee osteoarthritis: the Ulm Osteoarthritis Study. *Ann. Rheum. Dis.* 57, 717–723. <https://doi.org/10.1136/ard.57.12.717>.
- Harlaar, J., Doorenbosh, C., 2006. 3D kinematic analysis by BodyMech, A Matlab based open source software package for research and education. Dept. Rehabil. Med. VU Univ. Med. Center, Res. Inst. MOVE 1–4.
- Kellgren, J.H., Lawrence, J.S., 1957. Radiological assesment of osteo-arthritis. *Ann. Rheum. Dis.* 16, 494–502.
- Lewek, M.D., Rudolph, K.S., Snyder-Mackler, L., 2004. Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. *Osteoarthr. Cartil.* 12, 745–751. <https://doi.org/10.1016/j.joca.2004.05.005>.
- Linley, H.S., Sled, E.A., Culham, E.G., Deluzio, K.J., 2010. A biomechanical analysis of trunk and pelvis motion during gait in subjects with knee osteoarthritis compared to control subjects. *Clin. Biomech.* 25, 1003–1010. <https://doi.org/10.1016/j.clinbiomech.2010.07.012>.
- Messier, S.P., Beavers, D.P., Herman, C., Hunter, D.J., DeVita, P., 2016. Are unilateral and bilateral knee osteoarthritis patients unique subsets of knee osteoarthritis? A biomechanical perspective. *Osteoarthr. Cartil.* 24, 807–813. <https://doi.org/10.1016/j.joca.2015.12.005>.
- Mündermann, A., Dyrby, C.O., Andriacchi, T.P., 2005. Secondary gait changes in patients with medial compartment knee osteoarthritis: Increased load at the ankle, knee, and hip during walking. *Arthritis Rheum.* 52, 2835–2844. <https://doi.org/10.1002/art.21262>.
- Pataky, T.C., Robinson, M.A., Vanrenterghem, J., 2013. Vector field statistical analysis of kinematic and force trajectories. *J. Biomech.* 46, 2394–2401. <https://doi.org/10.1016/j.jbiomech.2013.07.031>.
- Riley, P.O., Paolini, G., Della Croce, U., Paylo, K.W., Kerrigan, D.C., 2007. A kinematic and kinetic comparison of overground and treadmill walking in healthy subjects. *Gait Posture* 26, 17–24. <https://doi.org/10.1016/j.gaitpost.2006.07.003>.
- Shakoor, N., Block, J.A., Shott, S., Case, J.P., 2002. Nonrandom evolution of end-stage osteoarthritis of the lower limbs. *Arthritis Rheum.* 46, 3185–3189. <https://doi.org/10.1002/art.10649>.
- Winter, D.A., Eng, P., 1995. Kinetics: our window into the goals and strategies of the central nervous system. *Behav. Brain Res.* 67, 111–120. [https://doi.org/10.1016/0166-4328\(94\)00154-8](https://doi.org/10.1016/0166-4328(94)00154-8).
- Woltring, H., 1978. A Fortran Package for generalized, cross-validatory spline smoothing and differentiation. *Adv. Eng. Softw.* 8 (2), 104–113.
- Woolf, A.D., Pfleger, B., 2003. Burden of major musculoskeletal conditions. *Bull. World Health Organ.* 81, 646–656. *ERD Work. Pap. Ser.* 81, 1–27.
- Zeni Jr., J.A., Richards, J.G., Higginson, J.S., 2008. Two simple methods for determining gait events during treadmill and overground walking using kinematic data. *Gait Posture* 27, 1–7. <https://doi.org/10.1038/jid.2014.371>.