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Changes in gait characteristics of women with early and established medial knee osteoarthritis: results from a 2-years longitudinal study

Running head: Evolution of gait characteristics associated with knee OA

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Abstract

Background: Despite the large number of cross-sectional studies on gait in subjects with knee osteoarthritis, there are scarcely any longitudinal studies on gait changes in knee osteoarthritis.

Methods: Gait analysis was performed on 25 women with early and 18 with established medial knee osteoarthritis, as well as a group of 23 healthy controls. Subjects were asked to walk at their comfortable speed. Kinematic and kinetic data were measured at baseline and after 2 years follow-up.

Findings: Results indicated that the early osteoarthritis group, similar to established osteoarthritis group, showed significantly higher maximum knee adduction angles compared to the controls during the early stance phase of gait. None of the kinematic or kinetic measures, changed over two years in the early osteoarthritis group. In the established osteoarthritis group, at the time of entry, an increased first and second peak knee adduction moment, as well as higher mid-stance knee adduction moment and knee adduction moment impulse, were present compared to the control and the early osteoarthritis groups. Mid-stance knee adduction moment and knee adduction moment impulse, further increased over two years only in the established osteoarthritis group. For all three groups, the peak knee flexion angle during the stance phase decreased significantly over time.

Interpretation: Increased maximum knee adduction angle during stance phase was the only alteration in the gait pattern of subjects with early knee osteoarthritis compared to...
the controls. This suggests that, unlike in the later stages of the disease, gait is rather stable over two years in early osteoarthritis.

**Keywords:** Gait analysis, OA severity, knee adduction moment, knee
**Introduction**

Knee osteoarthritis (OA) has been reported as one of the major causes of disability, mainly in women [1]. Knee joint loading in walking and other activities of daily living provokes pain and discomfort in this joint, which has a substantial negative influence on locomotion, and quality of life [2, 3].

The role of biomechanical factors in the initiation and progression of knee OA has been supported by a vast number of studies [4, 5]. Altered gait patterns, compared to controls, have been reported frequently in people suffering from knee OA [6-9]. They walk with lower speed [8, 10], increased knee flexion at heel-strike [11, 12], and reduced knee flexion excursion during the stance phase of gait [6, 10]. Several studies have shown that the external knee adduction moment (KAM), is greater in people with knee OA compared to healthy controls [8, 13].

The observed gait deviations in subjects suffering from knee OA may be compensatory strategies aimed at reducing stresses on, and the range of motion of the affected joint [6-9]. However, with progression of the disease and associated morphological changes, the effectiveness of the aforementioned strategies may decrease. Moreover, previous reports suggest that neuromuscular and proprioceptive deficits in subjects with knee OA may actually lead to altered gait strategies that increase joint loading [14-17].

Gait alterations associated with knee OA are found to vary with OA severity [18-20]. Thorp et al. reported an increase in both the peak knee adduction moment (KAM) and the KAM impulse, with an increase in radiographic severity of knee OA [21]. A study on gait alteration in patients with early knee OA, reported no gait alterations in this group.
compared to the healthy controls [13]. Hurwitz et al. found decreased stance phase knee flexion angles, as well as decreased early stance phase knee flexion moments in patients with severe knee OA compared to controls, but not in subjects with moderate knee OA [9].

Despite the large number of cross-sectional studies on gait of subjects with knee OA [8, 21-24] there are scarcely any longitudinal studies on gait changes in knee OA. However, to obtain more insight in the role of disease severity and time in gait alterations, longitudinal studies are necessary. Therefore, we performed a longitudinal study on the kinematic and kinetic characteristics of gait in women with early knee OA, women with established knee OA and in healthy controls over a two-year follow-up period. We hypothesized that both early and established OA groups will show gait variable differences compared to controls, with fewer differences between the early OA group and the control group. We also hypothesized that the early OA group will demonstrate progressive changes over time, moving towards a pattern similar to the established OA group.

Methods

Study population

Sixty-six women participated in this study. All subjects were informed of the procedures of the study and signed informed consent forms approved by the local ethical committee of Biomedical Science, KU Leuven, Belgium prior to testing. The study was conducted in agreement with the principles of the Declaration of Helsinki.
Forty-three individuals with knee OA were clinically diagnosed by a rheumatologist or orthopedic surgeon of the University Hospitals Leuven. Recruitment of the control subjects (n=23) was done through social organizations. The inclusion criteria for the control group were, K&L grade 0 or 1 on the radiography of both knees, asymptomatic, no history of knee OA and other pathology involving any lower extremity joints. Standard anterior-posterior weight-bearing radiographs in fixed flexed position were obtained from each subject bilaterally (Siemens, Siregraph CF, Agfa CR HD5.0 detector 24*30). A single experienced observer (FPL) graded each radiograph, using the Kellgren and Lawrence (K&L) grading scale, to establish and categorize the presence of structural knee OA [25]. An MRI was taken only from the (most) affected side of the OA patients and a random side in the control group. A 3.0 Tesla scanner (Philips Achieva TX, The Netherlands) using an eight-channel phased array knee coil in a non-weight bearing supine position [26] was used. The standardized Boston-Leeds Osteoarthritis Knee Score (BLOKS) scoring system was used by two separate readers (NN, GVDS) to score structural features in the tibiofemoral joint [27].

The OA group was sub-classified into groups of “Early OA” and “Established OA” based on the classification by Luyten et al [28]. Subjects were categorized as early OA (n=25) if they had knee pain, KL grade of 0 to 2 (just joint space narrowing) for the medial compartment on radiography, and two out of four MRI criteria: (1) ≥ BLOKS grade 2 for size cartilage loss, (2) ≥ BLOKS grade 2 for percentage full-thickness cartilage loss, (3) signs of meniscal degeneration and (4) ≥ BLOKS grade 2 for size of bone marrow lesions (BMLs) in any one compartment. Subjects in the established OA (n=18) group were classified based on the adjusted American College of Rheumatology (ACR) classification criteria [14].
The exclusion criteria for all groups of subjects were musculoskeletal disorders other than knee OA in both lower limbs in the last six months, previous surgery of lower extremities and/or low back, neurological disorders, chronic intake of corticosteroids or contra-indications for MRI.

**Knee symptoms and function**

The Knee Injury and Osteoarthritis Outcome Score (KOOS) (Dutch version) was filled in by all subjects to assess knee symptoms and function.

**Gait data acquisition and analysis**

A 3D motion analysis system (Krypton, Metris and Vicon Nexus, Oxford Metrics Group) was used to record the spatial position of markers on relevant body segments at 100 samples/s (Figure 1).

Ground reaction forces were recorded through two force plates (Bertec Corporation, Ohio, USA and AMTI, MA, USA) at a sample rate of 1000 samples/s. The recorded data were low-pass filtered with a fourth-order filter with a cut-off frequency of 25 Hz. The force time series were down-sampled to match the kinematic data. All the analyses were done using Custom-made MATLAB 7.14.0 (The MathWorks, Natick, MA) programs. Participants walked (barefoot) along the 12m walkway at a comfortable habitual speed. Three complete force plate strikes for each foot were registered. Based on the pelvis anatomical markers, the position of the hip joint centers was estimated using regression equations reported by Bell et al [29]. Subsequently, the hip joint centers were used together with the medial and lateral femoral epicondyle marker data to calculate the
thigh Anatomical coordinate systems (ACSs) according to the ISB recommendations [30]. For the shank ACS, the longitudinal axis was defined as the vector between the ankle joint center (midpoint between medial and lateral malleolus) and the knee joint center (midpoint between medial and lateral femoral epicondyle). The anterior-posterior axis was defined as the vector perpendicular to the plane containing the ankle joint center and the medial and lateral femoral epicondyle. The sideward axis was defined as vector perpendicular to the frontal and longitudinal axis (sagittal plane).

**Calculation of Spatiotemporal variables**

The analysis was performed on the most affected side of the OA patients and a random side side in the control group. To determine stance time, the vertical ground reaction force was used. The "heel-strike" event was detected as the first sample of the vertical ground reaction force that was above 10N. The "toe-off" event was chosen as the first sample at which the vertical ground reaction force was below 10N [31]. Stance time was defined as the time from one heel-strike to the toe-off on the same side. Walking speed was calculated by taking the time derivative of the pelvis displacement.

**Calculation of knee joint kinematics and kinetics**

3D Cardan angles of the knee were calculated using the decomposition order according to Grood & Suntay [32]:

- First rotation: flexion-extension (sideward axis of the proximal thigh segment)
- Second rotation: abduction-adduction (floating axis)
- Third rotation: internal-external rotation (longitudinal axis of the distal shank segment).
Note that because the frontal plane of the shank was based on the femur epicondyles, the knee internal-external rotation was assumed to be zero in the reference posture.

Knee moments were calculated through a bottom-up dynamic linked segment model, using kinematics of the body segments and the ground reaction forces [33]. These knee moments were projected onto the shank coordinate system. Extracted joint moments were normalized to the product of body weight and height (BW*Ht) [34]. Knee adduction impulse was calculated as the integral of the frontal plane joint moment during the stance phase of gait [21].

**Dependent variables**

The variables of interest were walking speed, stance time, knee flexion angle at initial contact, peak knee flexion angle, knee flexion excursion, knee adduction angle at initial contact, peak knee adduction angle, first and second peak knee flexion moment, first and second peak knee adduction moment, mid-stance knee adduction moment, and knee adduction moment impulse.

**Statistics**

Descriptive statistics were used to report subjects’ demographic characteristics in each group at baseline (Table 1). In order to compare subjects’ characteristics, One-way Analysis of Variance (ANOVA) or The Kruskal Wallis Signed rank test were used. To investigate Group differences and the effect of Time (as well as interaction, Time × Group, effects) on gait related parameters, Generalized Estimating Equations (GEEs) were used. When a main effect or an interaction was significant, a post hoc analysis was
conducted to test the pairwise differences. To account for the possible effect of static (mal)alignment on frontal plane kinematics during stance phase of gait, static alignment was included as covariate when testing group differences for knee adduction angle at the initial contact as well as for the peak knee adduction angle during stance phase of gait. P-values < 0.05 were used to indicate significance in all cases. Effect sizes (ES) (Cohen's d) were calculated and reported wherever applicable: an effect size of 0.2-0.49 is considered small, 0.5-0.79 moderate and > 0.8 large.

Results

Subjects’ demographic characteristics at the time of entry are presented in Table 1. There was no significant difference between groups regarding the age, weight, height, and BMI (table 1). After 2 years, in the early OA group, 3 patients progressed by 1 unit on K&L score. In addition, 5 patients in the established OA group progressed based on K&L score. The early and established OA groups reported significantly more knee pain along with worse symptoms and lower self-reported functional ability compared to the healthy controls at baseline (table 2). Comparing the baseline measures with the follow-up data, no changes were detected for any of the study groups (table 2).

Spatiotemporal variables
No statistically significant differences were found between the three groups in walking speed and stance time (Table 2). The main effect of Time, was significant for walking speed, but no significant differences were found between baseline and follow-up measures of walking speed for any of the three groups (Table 2). Similarly, no significant changes were found for stance time over two years of follow-up in any of the three groups (Table 2).

**Kinematic variables**

There was a trend towards a significant difference between groups regarding knee flexion angle at initial contact, with the established OA group showing the highest value (\( P = 0.099 \)) (Figure 2). Knee flexion angle at initial contact decreased after two years compared to the baseline measures in all three groups (\( P = 0.001, \text{ES}_{\text{Control}} = 0.66, \text{ES}_{\text{Early OA}} = 0.40, \text{and ES}_{\text{Established OA}} = 0.51 \)) (Figure 3). There were no significant differences among the groups regarding peak knee flexion angle (Figure 2), but peak knee flexion decreased significantly over time in all three groups (\( P = 0.009, \text{ES}_{\text{Control}} = 0.32, \text{ES}_{\text{Early OA}} = 0.43, \text{and ES}_{\text{Established OA}} = 0.50 \)) (Figure 3). The three groups were significantly different with respect to flexion excursion (\( P = 0.004 \)), with the established OA group showing significantly less knee flexion excursion compared to the early OA, as well as the controls (\( P = 0.007, \text{ES} = 0.61 \) and \( P = 0.004, \text{ES} = 0.56 \), respectively). There were no significant differences between the baseline and follow-up measures of knee flexion excursion for any of the three groups (\( P = 0.486 \)).

Regarding frontal plane knee kinematics, no significant differences were found between the three groups for knee adduction angle at initial contact (\( P = 0.105 \)). Over the 2 years
follow-up, none of the groups showed changes in knee adduction angle at initial contact ($P = 0.556$). For the peak knee adduction angle, the main effect of the group was significant ($P = 0.031$) and post-hoc analysis revealed that both the early OA group and the established OA group had significantly higher maximum knee adduction angles compared to the healthy controls ($P = 0.036$, ES = 0.86 and $P = 0.02$, ES = 1.02 respectively). After adjustment for static alignment, the differences between the early and the established OA groups compared to the control group stayed significant ($p = 0.023$ and $p = 0.021$, respectively). There were no significant differences between the two OA groups regarding the peak knee adduction angle ($P = 0.919$). No significant effect of time was found regarding the peak knee adduction angle ($P = 0.098$).

Kinetic variables

No significant differences were found between the three groups regarding the first or second peak external knee flexion moment ($P = 0.457$ and $P = 0.754$, respectively) (Figure 2). There was a significant Time × Group interaction for the second peak external knee flexion moment ($P = 0.047$, ES = 0.69) (Figure 4). Post-hoc analysis revealed that the second peak knee flexion moment decreased significantly in the established OA group over the 2 years follow-up, while this was not the case for the other groups. No significant changes were found for any of the other sagittal plane kinetic characteristics of the stance phase of gait, after 2 years follow-up.

For the frontal plane kinetics, there was a significant effect of group for the first peak KAM ($P = 0.007$). Post hoc analysis revealed that the first peak KAM was significantly higher in the established OA group compared to the early OA as well as the healthy
control group ($P = 0.004$, ES = 0.66 and $P = 0.005$, ES = 0.76, respectively) (Figure 2). There was a significant effect of group for the second peak KAM ($P = 0.002$) as well (Figure 2). Post-hoc analysis revealed that the second peak KAM was significantly higher in the established OA group compared to the early OA as well as the healthy control group ($P = 0.001$, ES = 0.87 and $P = 0.004$, ES = 1.04, respectively). No significant differences were found for the first and second peak KAM between the early OA and the control groups ($P = 0.823$ and $P = 0.587$, respectively). There was no significant effect of time regarding first and second peak KAM (Figure 4). Regarding the mid-stance KAM, the established OA group showed significantly lower values compared to the early OA and the healthy controls ($P = 0.001$, ESs = 0.60 and 0.66, both). No significant differences were found between the early OA and the healthy control groups, regarding the mid-stance KAM ($P = 0.879$). After two years, the established OA group showed a significant increase in the mid-stance KAM compared to the baseline ($P = 0.017$, ES = 0.73). No significant changes over time for the mid-stance KAM were found in the early OA group or the healthy control group. The KAM impulse was significantly higher in the established OA group compared to the early OA and the healthy control group ($P < 0.001$, ESs = 0.88 and 0.89, both). No significant differences were found between the KAM in the early OA group and the healthy control group ($P = 0.815$). There was a significant Time × Group interaction for the KAM impulse ($P = 0.028$). Post hoc analyses revealed that only in the established OA group the KAM impulse increased over two years ($P = 0.012$, ES = 0.55).
Discussion

To the best of our knowledge, this was the first study that evaluated the effect of OA severity and time on gait characteristics in a long-term follow-up study. Results from the current study indicated that the early OA group, similar to established OA group, showed significantly higher maximum knee adduction angles compared to healthy controls during the early stance phase of gait. While this was the only alteration in the gait pattern of subjects with early knee OA observed in this study, the established OA group showed other significant differences in gait kinematics and kinetics compared to the healthy controls, which confirmed our first hypothesis. Higher first and second peak KAM, mid-stance KAM, as well as higher KAM impulse were observed at the time of entry in the established OA group compared to healthy controls and the early OA group. Contrary to our second hypothesis, mid-stance KAM and KAM impulse, further increased over two years only in the established OA group.

Gait speed is an important determinant of gait kinematics and kinetics [35, 36]. An increase in center of mass accelerations associated with higher speed, might coincide with higher ground reaction forces and joint moments. In patients with knee OA, increased joint loading has been shown to play an essential role in disease progression [37]. Therefore, decreased walking speed, as observed in patients with knee OA, has been suggested as a potential mechanism to reduce knee joint loading [38]. In the current study, we found no significant differences in gait speed between groups. Also, after 2 years, regardless of an overall effect of time on gait speed, changes within groups were not significant. Therefore, differences in gait characteristics between groups and
Changes in sagittal plane knee kinematics, observed in this study suggest an age-related alteration of gait over two years, as all three groups showed a decreased knee flexion angle at initial contact, along with a decrease in peak knee flexion angle during the stance phase of gait, after two years. Previous findings reported reduced ankle dorsiflexion at initial contact in older adults when compared to young adults [39]. In addition, an association between greater dorsiflexion ROM and greater knee-flexion displacement, during landing, has been reported previously [40]. Unfortunately, we did not include measurements of ankle kinematics in this study, to further explore this association. Possibly, these changes may be caused by a decreased knee joint range of motion and knee muscle strength, observed with aging [41-43].

In line with the current findings, Weidow et al. reported a higher maximum knee adduction angle in a group of subjects with medial knee OA, compared to a group of healthy controls [44]. They also suggested that the maximum knee adduction angle is a strong predictor of KAM magnitude and impulse [45]. Results from the current study are partially in line, as the established OA group in this study showed increased peak adduction angle coinciding with elevated KAM magnitude and impulse. On the other hand, the greater knee adduction angle was already present at the early stages of the disease, without an increased KAM, suggesting that perhaps altered frontal plane knee kinematics precedes changes in the medial joint loading in women with medial knee OA [46].

Early OA subjects in the present study showed no significant increase in KAM magnitude and impulse, which implies no alterations in medial knee joint loading during stance.
phase of gait in the early stages of the disease. Also, the knee joint loading did not change over 2 years follow-up in patients with early medial knee OA. For the established OA group, on the other hand, higher first and second peak, and mid-stance KAM as well as KAM impulse compared to the healthy controls and the early OA were observed at the time of entry, in line with previous findings [6, 8, 13]. It is believed that knee OA progresses more rapidly with higher loading of the affected knee [47]. Previous findings also demonstrated that the effect of the integral of loading on the articular surface is as important as the load magnitude [48]. The increased impulse over time once OA is established, might be due to the reduced ability to unload the joint during mid-stance (over time), as also proposed before by Hatfield et al [49]. This important pattern, referred to as the reduced ability to unload the joint during mid-stance, has previously been shown to be associated with increased odds of progressing to total knee arthroplasty (TKA) [49]. Other factors that might also contribute to the aforementioned findings are severe structural abnormalities, decreased muscular strength, proprioceptive deficiency, or increased varus malalignment at the more severe stages of the disease [13, 50].

Findings of the current study is the first reference to longitudinal changes in gait associated with OA severity in a population of women with medial knee OA. The present results indicate that in the early stages of knee OA, gait is relatively normal and gait characteristics associated with knee OA are quite stable over 2 years. The only longitudinal changes related to knee OA, were found in the established OA group and consisted of a decreased second peak external knee flexion moment, increased mid-stance KAM, and KAM impulse. These are not likely to reflect compensatory strategies, but rather a consequence and potentially also a cause of disease progression.
There are some limitations of this study that should be taken into account. First, although the classification criteria for early OA have been proposed as a result of several rounds of discussion (Delphi approach), they are still in an early phase and further refinement of this classification is needed. Early OA in our definition implies symptomatic, pre-radiographic, but with clear MRI abnormalities, according to the criteria defined by Luyten et al, published together with ESSKA in 2012 [7]. Furthermore, in the current study barefoot walking was chosen in order to a better track markers, however this may limit the generalization of the results. In addition, the current sample size could be considered relatively small, but was based on numbers reported in the literature for the parameters studied and was sufficient to identify statistical differences. The very fact that we found significant differences between early or the established OA groups compared to the controls, as well as significant differences between the two OA groups, suggest that the statistical power was adequate to reveal the differences between the two OA groups. Also, only women were included in this study, as osteoarthritis of the knee is more common in women than men. Therefore, results from this study cannot be generalized to men. Moreover, including only women results in a more homogenous study population which in turn provides a better signal to noise ratio. In the current study, given its exploratory nature, we did not correct the P-value, as we were concerned of a possibility of occurrence of Type II errors due to very low corrected P-values. But, we avoided any P-hacking and reported all significant as well as non-significant results, so that the readers can make their own judgment based on the whole picture and not just some selected results [51].
Conclusion

We studied the effect of OA severity and time on kinetics and kinematics during the stance phase of gait. Our aim was to evaluate gait changes in a prospective longitudinal study, in order to determine whether the early OA group would show gait characteristics close to the established OA group, after 2 years. We found that an increased maximum knee adduction angle during stance phase was the only alteration in the gait pattern of subjects with early knee OA compared to the controls, a finding similar to the established OA group. The longitudinal changes in the gait pattern of patients with early OA were age-related, as they were also present in the two other groups. The established OA group, on the other hand, showed a decreased second peak external knee flexion moment and an increased mid-stance KAM and KAM impulse after 2 years, compared to baseline, a pattern previously shown to be associated with increased odds of progressing to TKA.

Author contributions

AM, IB, FL, and SV contributed to the conception and design of this study. AM, IB and FL contributed to the collection of the data. AM contributed to the analysis of the data with expertise of JvD, SB, and GF. AM, IB, JvD, SB, FL, GF and SV contributed to the interpretation of the data. Article drafts were written by AM and SV and critically revised by all authors. The final version of the article was approved by all authors. AM takes responsibility for the integrity of the work as a whole (armaghan.mahmoudian@gmail.com).
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The authors declare that they have no conflicts of interest.

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4. Radin E, Burr D, Caterson B, Fyhrie D, Brown T, Boyd R. Mechanical determinants of
   increased chronic loading on articular cartilage material properties in the Lapine tibio-
   during walking are present in subjects with knee osteoarthritis. Osteoarthritis and cartilage
7. Debi R, Mor A, Segal O, Segal G, Debbi E, Agar G, et al. Differences in gait patterns, pain,
   function and quality of life between males and females with knee osteoarthritis: a clinical
8. Gök H, Ergin S, Yavuzer G. Kinetic and kinematic characteristics of gait in patients with medial
9. Hurwitz D, Ryals A, Block J, Sharma L. Knee pain and joint loading in subjects with
10. Astephen J, Deluzio K. Changes in frontal plane dynamics and the loading response phase of
    the gait cycle are characteristic of severe knee osteoarthritis application of a
11. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity
    movement and muscle activation patterns in individuals with knee osteoarthritis. Clinical
12. Mündermann A, Dyrby CO, Andriacchi TP. Secondary gait changes in patients with medial
    compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking.
13. Baert IA, Jonkers I, Staes F, Luyten FP, Truijen S, Verschueren SM. Gait characteristics and
    lower limb muscle strength in women with early and established knee osteoarthritis. Clinical
    Biomechanics 2012.
    20: 97-104.
15. Hurley MV. Muscle dysfunction and effective rehabilitation of knee osteoarthritis: what we
    know and what we need to find out. Arthritis Care & Research 2003; 49: 444-452.
16. Johansson H, Pedersen J, Bergenheim M, Djupsjobacka M. Peripheral afferents of the knee:
    their effects on central mechanisms regulating muscle stiffness, joint stability, and
    proprioception and coordination. Proprioception and neuromuscular control in joint stability
    2000: 5-22.
17. Lewek MD, Ramsey DK, Snyder-Mackler L, Rudolph KS. Knee stabilization in patients with
    moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis.
    Arthritis & Rheumatism 1998; 41: 1233-1240.
19. 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. Journal of
    Orthopaedic Research 2008; 26: 332-341.
    pattern changes are associated with differences in knee osteoarthritis severity levels. Journal
    of biomechanics 2008; 41: 868-876.
21. Thorp LE, Sumner DR, Block JA, Moisio KC, Shott S, Wimmer MA. Knee joint loading differs in
    individuals with mild compared with moderate medial knee osteoarthritis. Arthritis &
    Rheumatism 2006; 54: 3842-3849.


