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2		osteoarthritis.
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1 Abstract

2 The relationship between age and gait characteristics in people with and without medial compartment 3 osteoarthritis (OA) remains unclear. We aimed to characterize this relationship and to relate 4 biomechanical and structural parameters in a subset of OA patients. Twenty five participants with 5 diagnosed unilateral medial knee OA and 84 healthy participants, with no known knee pathology were 6 recruited. 3D motion capture was used to analyse sagittal and coronal plane gait parameters while 7 participants walked at a comfortable speed. Participants were categorized according to age (18-30, 31-8 59 and 60+ years), and those with and without OA were compared between and within age groups. In a 9 subset of OA patients, clinically available Computed Tomography images were used to assess joint 10 structure. Differences in coronal plane kinematics at the hip and knee were noted in participants with 11 OA particularly those who were older compared with our healthy controls, as well as increased knee 12 moments. Knee adduction moment correlated with structural parameters in the subset of OA patients. 13 Increased knee moments and altered kinematics were observed in older participants presenting with OA 14 only, which seem to be related to morphological changes in the joint due to OA, as opposed to being related to the initial cause of medial knee OA. 15 Key words: aging; gait; knee; osteoarthritis. 16

1 Introduction

2 Knee joint osteoarthritis (OA) is one of the commonest diseases affecting the aging population, so there 3 is a growing interest in the mechanisms underlying this degenerative disease. The progression of knee 4 OA has been related to gait mechanics (1), specifically relating to tempo-spatial parameters (2). 5 However, this can be complex since gait adaptations that occur in normal aging can be similar to those 6 seen in pathological participants. A better understanding of normal and pathological aging would assist 7 in the management of OA, if disease development or progression is directly related to certain 8 characteristics of gait. 9 10 The development of medial knee OA has been postulated to result from repetitive loading, leading to 11 meniscal fatigue failure or acute injury, with subsequent medial compartment articular cartilage loss. 12 This is supported by reports that OA incidence significantly increases with age (3, 4), as well as evidence 13 indicating that its incidence is associated with obesity, knee trauma and female gender (4). In addition, 14 an increase in external knee adduction moment (KAM), which is associated with increased medial knee-

15 joint forces, has been reported in people with moderate to severe medial knee OA (5-7), and has been

16 correlated with disease progression (8) and severity (9-11). However, there is little evidence supporting

17 the presence of higher KAMs in the early stages of knee OA (2, 11-13), indicating higher medial loads

18 may not be causative of medial knee OA. Recent studies have suggested that KAM can be influenced by

19 trunk motion (14). People with knee OA demonstrate significant hip muscle weakness (15), which has

20 been suggested to be a risk factor in the development of knee OA (16) due to pelvic drop increasing

21 KAM magnitude (17). Others however have proposed that hip abductor strength has little influence on

hip and knee adduction moments during gait (18, 19).

23

1 Changes in gait mechanics with healthy aging include decreased stride length and increased cadence 2 (20, 21), and associated alterations in sagittal plane hip and ankle kinematics and kinetics (20-22). 3 Altered knee flexion range of motion has also been proposed in healthy aging (22-24), but changes in 4 the coronal plane are less well understood. A slight increase in valgus static alignment has reported (25) 5 as well as increased abduction during early stance in gait (24). Reduced medial knee-joint forces with 6 advancing age have also been reported (22). The association between aging, biomechanical loading, 7 structural joint changes and OA development warrants further investigation, in particular coronal plane 8 biomechanics due to their implication in knee OA.

9

The aim of this study was to demonstrate the relationship between age and gait characteristics in people with and without medial compartment OA. Gait and structural parameters at the knee joint were also investigated in a subset of OA patients. We hypothesized that; i) younger OA subjects would have similar KAMs as healthy subjects; ii) older healthy subjects would have altered gait mechanics compared with young healthy subjects and; iii) older OA subjects would show deviations in gait parameters compared with healthy young and older subjects.

16

17 Methodology

This study had ethical approval from the South West London Research Ethics Committee and all participants provided written informed consent. Twenty-five participants with a clinical diagnosis of unilateral knee OA affecting the medial compartment were recruited from Charing Cross Hospital and local district regional hospitals, and 84 participants with no known knee pathology were recruited from staff and students of Imperial College London. Participants were excluded from the study if they demonstrated any neurological or musculoskeletal condition other than knee OA, rheumatoid or other

systemic inflammatory arthritis, morbid obesity (Body Mass Index >35 Kg/m<sup>2</sup>) or had undergone 1 2 previous surgical treatment for knee OA. 3 4 Gait Analysis 5 Two Kistler portable force plates (Kistler Type 9286B, Kistler Instrumente AG, Winterthur, Switzerland) 6 were embedded into a 6m walkway, and a 10 camera Vicon motion capture system (Vicon Motion 7 Systems Ltd, Oxford, UK) were used to capture the position of reflective markers attached to the 8 subject. Force plate data were recorded using an analogue signal data acquisition card provided with the 9 Vicon system and the Vicon Nexus software at a sampling rate of 1000Hz. The motion capture was 10 recorded at a rate of 100Hz and synchronised with the force data. 11 12 Twenty reflective markers were positioned on the subject's pelvis and lower limbs and four marker 13 clusters positioned on the subject's left and right thigh and calf segments (26). Participants were asked 14 to walk at a comfortable speed along the 6m walkway 5 times, or until three clean foot strikes had been 15 recorded from each force plate. 16 17 Kinematic and kinetic parameters were calculated using a custom model written in body builder 18 software (26). Joint moments were normalised to the subject's bodyweight x height. Data was separated 19 into gait cycles for each leg based on vertical ground reaction forces and time-normalised. Hip, knee and 20 ankle joint angles at heel strike (HS), toe-off (TO) and the time point at which 1<sup>st</sup> peak vertical ground 21 reaction force (GRF) occurred were extracted using custom written code in Matlab. Only joint moments 22 at 1<sup>st</sup> peak GRF were extracted. The average of three trials was taken.

1

Sub-group Computed Tomography Analysis

2 A subset of 6 of the OA participants additionally underwent preoperative CT scans of their affected knee 3 using the Imperial knee protocol as part of their routine surgical preparation (27). The scans were 4 reconstructed (Robin's 3D Software) and femoral and tibial frames of reference were established. The 5 radii of the medial and lateral flexion facets (LFF) were measured from spheres best fit to markers 6 placed evenly across their surfaces, on the posterior aspect of the femur. To measure the radius of the 7 medial extension facet (MEF), the femur was initially orientated so that its inferior aspect faced 8 anteriorly and the flexion facets faced superiorly. The anterior and posterior borders of the MEF were 9 then distinguished with markers located using the sagittal CT views. The posterior border defined the 10 transition of the extension facet to the flexion facet, and the anterior border defined the transition from 11 the extension facet to the trochlea. The bony surface between these two borders was subsequently also 12 covered with markers and a sphere best fit to their positions. The radius of the sphere was determined 13 as the MEF radius. The radii of the medial and lateral tibial plateaus (MTP and LTP, respectively) were 14 measured 20mm below the most proximal aspect of the tibial spines. All measures were normalised to 15 the medial flexion facet as this structure is relatively well preserved in OA.

16

## 17 Statistical analysis

Participants were separated into three age groups as follows; 18-30, 31-59 and 60+ years. Data from the
left and right sides were averaged for healthy participants, and data for the affected and unaffected
sides of OA participants were presented separately. All statistical analysis was carried out in SPSS (SPPS
v21, IBM Corp, USA). Initially, multiple analysis of variance (MANOVA) was carried out to assess the
overall effects of age and OA group. Where the MANOVA attained significance multiple comparisons
were carried out using one-way analysis of variance (ANOVA), two sample t-tests (OA versus healthy)
and paired t-tests (OA unaffected versus affected sides). Linear regression was used to assess the

relationship between structural measures and knee joint kinetics in the subset of OA participants that
 underwent CT imaging.

3

4 Results

5 Healthy and OA subject details and spatio-temporal gait parameters for each age category are provided 6 in Table 1. MANOVA revealed significant differences between OA and healthy participants for weight 7 (p<0.01), walking speed (p<0.001) and stride length (p<0.05). There was no effect of age group on these 8 parameters and no interaction (p>0.05). Post hoc analysis revealed that OA participants were 9 significantly heavier, walked slower and with shorter stride lengths in the 60+ age category (Table 1). 10 11 All kinematic and kinetic data have been presented in Tables 2 and 3. MANOVA for gait parameters 12 revealed significant effects of both OA (p<0.001) and age (p<0.001) group, and significant interactions 13 (p<0.005). Post hoc analysis revealed that coronal plane hip (p<0.001) and knee (p<0.05) angles and 14 knee moment (p=0.001), and sagittal plane ankle moment (p<0.001) were affected by OA presence. 15 Parameters effected by age group were coronal plane hip (p<0.05) and knee (p<0.01) angles and knee 16 moment (p=0.002), and sagittal plane knee angle (p<0.05). Further statistical tests were carried out on 17 these parameters only. 18 .

19

20 Coronal Plane Differences

All significant kinematic differences were found in the 60+ age group (Table 2). Hip adduction angle was
significantly lower in OA participants affected side (at peak GRF) and significantly higher in their
unaffected side (at TO), compared with healthy participants of similar age. At the knee, OA participants
had significantly higher knee adduction angles at both HS and peak GRF compared with healthy

1	participants (Fig 1; p=0.04). Knee adduction angle at peak GRF was also significantly higher in the
2	affected compared with unaffected sides of 60+ OA participants (Fig. 1; p=0.007). Knee adduction
3	moment (at peak GRF) was higher in the affected side of 60+ OA compared with healthy participants of
4	a similar age (p=0.006) and younger OA participants (p=0.001; Fig 1).
5	
6	Sagittal Plane differences
7	In the sagittal plane, 60+ OA participants had significantly higher ankle plantar-flexion moments in the
8	affected side (p=0.001; Table 3). Within the healthy group, knee angle in the sagittal plane was
9	significantly higher in the 60+ group compared with the 18-30 group at HS (P=0.01).
10	
11	CT sub-group findings
12	Regarding the correlation between joint shape and kinematics, as the relative size of the lateral femoral
13	condyle increased, the KAM reduced ( $R^2$ =0.67; Fig 2a) while as the size of the medial tibial plateau
14	increased, the KAM increased (R <sup>2</sup> =0.70; Fig 2b). Correlations were lower for all other comparisons
15	investigated (R <sup>2</sup> <0.35).
16	
17	Discussion
18	In this study we used motion capture to characterize gait parameters across a range of ages in healthy
19	participants, and in older and younger participants with medial knee OA. We noted differences in
20	coronal plane kinematics at the hip and knee across different OA age groups compared with healthy
21	participants, as well as increased knee moments in OA participants in the older age groups. There were
22	also differences in sagittal plane kinematics at the ankle in our older OA age group compared with
23	healthy controls.

## 1 Spatio-temporal parameters

2 Older OA participants (60+ years) walked significantly slower and with a shorter stride length compared 3 with healthy participants of a similar age; adaptations that are commonly reported among OA patients 4 (2), which may be a strategy to reduce pain and/or loading in the affected knee. Both kinematic and 5 kinetic parameters are known to be affected by walking speed (28), therefore the effect of altered speed 6 should be acknowledged in interpretation of the results in the present study. There were no significant 7 differences in walking speed in healthy older participants compared with the younger group, which 8 conflicts with previous reports (29). This may have been due to the relatively short walkway used in the 9 present study (6m), possibly causing some healthy participants to walk at a lower velocity than their 10 usual walking speed.

11

## 12 Coronal plane gait parameters

13 The main kinematic and kinetic impact of OA was noted in the coronal plane, with altered hip and knee 14 adduction angles and higher KAM's in older OA participants. The magnitude of the increased KAMs are 15 in agreement with several previous reports (5-7), and have been correlated with both disease 16 progression (8) and severity (9-11). Several mechanisms related to gait mechanics have been proposed 17 to cause greater KAMs in OA participants. For example, a 'medial knee thrust', the abrupt appearance of 18 varus alignment during the mid-stance phase of gait (30), has been described previously in people with 19 medial knee OA (30, 31). However, this seems unlikely since the knee adduction angle appeared to be 20 increased throughout the stance phase, as opposed to appearing abruptly in mid-stance.

21

Alternatively, pelvic drop caused by contralateral hip abductor weakness has been proposed as a risk
 factor in medial OA progression (16). We did note differences in coronal plane hip kinematics in our
 data, indicative of reduced hip ab/adduction range of motion in older OA participants. However, hip

abductor weakness was unlikely to be the cause of higher KAMs in our data because OA participants
 actually showed greater hip abduction than healthy participants, and previous studies have reported no
 clear relationship between hip abductor muscle strength and specific KAM characteristics (18, 19).

4

5 As shown in Fig 1, these changes were only evident in the older OA participants; OA participants aged 6 31-59 years presented gait kinematics and kinetics that were similar compared with healthy participants 7 of similar age and younger. Since the difference in walking speed between younger and older OA 8 participants was not significant, it is unlikely that this result was due to differences in walking speed 9 alone. It was notable that the increased KAM reflected an increase in lever arm rather than GRF in these 10 participants, which is supported by the significant increase in knee adduction angle. The adaptations in 11 coronal plane mechanics noted here, and in previous studies, do not appear to be causal of OA nor do 12 they occur as a result increasing age in healthy participants; thus these adaptations likely occur as a 13 result of increasing medial knee OA severity with increasing age. In support of this view, we previously 14 reported no significant differences in KAMs between participants with early medial knee OA and healthy 15 participants of a similar age during both gait (13) and sit-to-stand tasks (12). Increased KAMs in 16 advanced OA may therefore relate to morphological changes in the joint, which have been reported to 17 occur in knee OA including meniscus or cartilage wear (32) with subsequent bone loss and other 18 changes in the subchondral bone (33). Loss of joint material ought to cause these individuals to generate 19 higher KAMs. Altered cartilage volume and indeed subsequent erosion of bone in the wear scar of the 20 weight-bearing regions of the knee joint, the consequential greater medial (relative to lateral) tibial 21 bone area (34) may result in altered (less balanced) load distribution between medial and lateral 22 compartments.

23

KAMs have also been associated with trunk motion (14), and therefore alterations in the activation of
the trunk musculature may contribute to increased KAMs in advanced OA. For example, weak hip
musculature may cause pelvic drop (17), increasing the KAM lever arm. Furthermore, an imbalance in
medial-lateral activation of lower limb muscles (for example hamstrings or gastrocnemius) due to
selective atrophy may impact medial knee displacement (35, 36), affecting KAMs.

6

## 7 Sagittal plane gait parameters

8 The main sagittal plane changes related to increased age in our healthy participants. Older participants 9 (60+) had significantly less knee extension compared with younger participants at HS, which is in 10 agreement with previous work (22, 23). Favre et al. (23) proposed this was due to reduced tilt at the 11 shank, attributed to reduced quadriceps strength with aging and a distal to proximal shift in power 12 production (23). Our data provide support for this proposal. Sagittal plane kinetic parameters were not 13 affected by increased age in our healthy participants, which is in agreement with some previous work 14 (23). However others noted increased hip extensor moments and associated reductions in knee 15 extensor (22, 37) and ankle plantarflexor (22) moments in elderly compared with young participants. 16 These differences appear to become more pronounced with higher walking speeds (37), and the study 17 by DeVita & Hortobagyi (22), which proposed a redistribution of joint torques during gait in elderly 18 participants, asked participants to walk at a relatively fast speed (1.48m/s); a speed substantially greater 19 than that adopted by older participants in the present study. Therefore, kinetic changes in healthy 20 participants in the older age groups may be evident only at faster walker speeds. 21

22 Biomechanical vs structural parameters in OA participants

In a subset of our knee OA patients, we noted significant correlations between KAM during gait and both
 the medial tibial plateau and lateral flexion facet radii. Higher KAM at 1<sup>st</sup> peak GRF was associated with a

larger MTP radius. In agreement, a positive correlation between KAM impulse and medial tibial plateau
bone area, and medial-lateral rotation of tibial bone size was previously noted in a larger group of OA
participants (34). These data support the theory that bone adapts structurally to cope with load and
mechanical stress, and these changes may cause altered gait biomechanics. We also found a significant
inverse correlation between KAM and LFF radius. It is possible that offloading of the lateral
compartment also results in morphological adaptations on the lateral side of the joint; however, a larger
study is necessary to corroborate this finding.

8

9 There are two main limitations to this study, which should be acknowledged. Most importantly, we did 10 not measure severity of OA. OA severity increases with age, however the age at which an individual 11 develops OA may vary widely. In addition, healthy participants were recruited based on the criteria that 12 they had no diagnosis of trauma or OA to the knee joints; therefore, we cannot rule out the possibility 13 that some of these participants had early signs of knee OA, since they did not undergo imaging of the 14 knee joint. However, we have previously shown that individuals with early OA have similar gait 15 kinematics and kinetics compared with healthy participants (13), therefore this possibility should not 16 affect our interpretation of the data. It should also be acknowledged that the accuracy of kinematic and 17 kinetic parameters in the lower extremities can be affected by soft tissue artefacts, resulting in high 18 inter-subject variability particularly in the coronal plane (26). This should be taken into consideration in 19 the present data where only small kinematic or kinetic changes were found. However, a cluster-based 20 model was utilised in this study, which has been shown to reduce the inter-subject variability of 21 kinematics when compared with a more commonly used model (Duffell 2014 (26).

22

In conclusion, older participants with medial knee joint OA had significantly higher KAMs as well as
 altered coronal plane hip and knee kinematics. Increased KAMs were correlated with joint morphology.

- 1 Altered gait parameters appear in older participants with OA only, which seem to be related to
- 2 morphological changes in the joint due to OA.

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